KPMG

Improving Quality of Care in Acute Myeloid Leukaemia

Terms of reference

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- Other contributing specialists: All interviewees from the centres that were visited were given an opportunity to review the corresponding centre-specific sections of this report. Guidance and feedback from all interviewees were incorporated into this report.

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Contents

Foreword

Message from the Chair of the SteerCo

Haematological malignancies such as Acute Myeloid Leukaemia (AML) can significantly impact the quality of life of patients, their families, and their carers. The nature of the disease coupled with the intensity of treatment can place a substantial social, psychological, and financial burden on these individuals.

AML is a complex condition with prevailing unmet needs. Awareness and education amongst the general population and medical community can contribute to early diagnosis and prompt treatment. Care teams and patient advocates continue to raise awareness of AML, and a suite of new therapies are revolutionising our field of practice. To maximise the benefits of this innovation, the pathways of diagnosis, treatment and management will need to continue to adapt.

The challenges that we face as providers of AML care require us to collaborate with our peers, other specialists, nurses, pharmacists, community-based clinicians, and patient advocacy groups, to share knowledge and continue to learn from one another.

We welcome the release of this report, in which KPMG has documented robust examples of good practice in AML care from seven centres across the world. The findings in this report demonstrate how dedicated care teams are tackling AML-associated challenges in varied and innovative ways. We hope these examples can inspire readers to improve their own services and ultimately improve quality of life and treatment outcomes for patients living with AML.

Professor Paresh Vyas

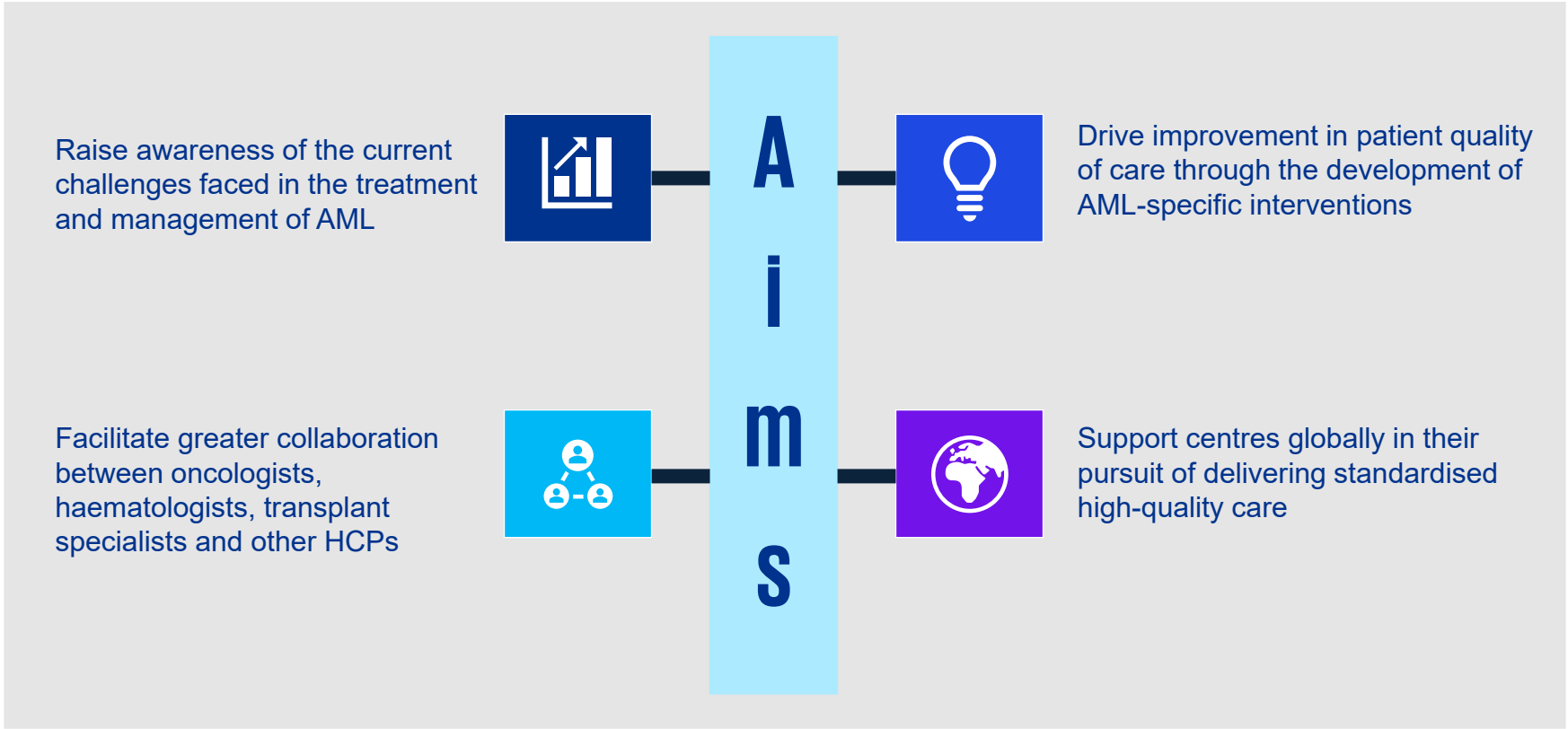
University of Oxford, UK

01

Executive summary

The Quality of Care initiative aims to improve Acute Myeloid Leukaemia (AML) patient care across the globe

By exploring, documenting and sharing features of good practice in caring for AML and associated comorbidities, the initiative aims to ensure all patients globally can benefit from the best care possible



KPMG combined primary and secondary research with guidance from experts in AML care delivery to produce this final report

Conduct literature review

Reviewed key published evidence on recommended good practice care and management e.g. local and international guidelines, academic/clinical publications

Carry out site visits

Observed the AML patient pathway to understand how practitioners deliver good practice and overcome key challenges in care by conducting HCP interviews

Document good practices in AML care

Recorded and affirmed interventions specific to each centre through collaboration with the centres visited.

Collated and arranged all interventions by common themes

Review findings with AML experts

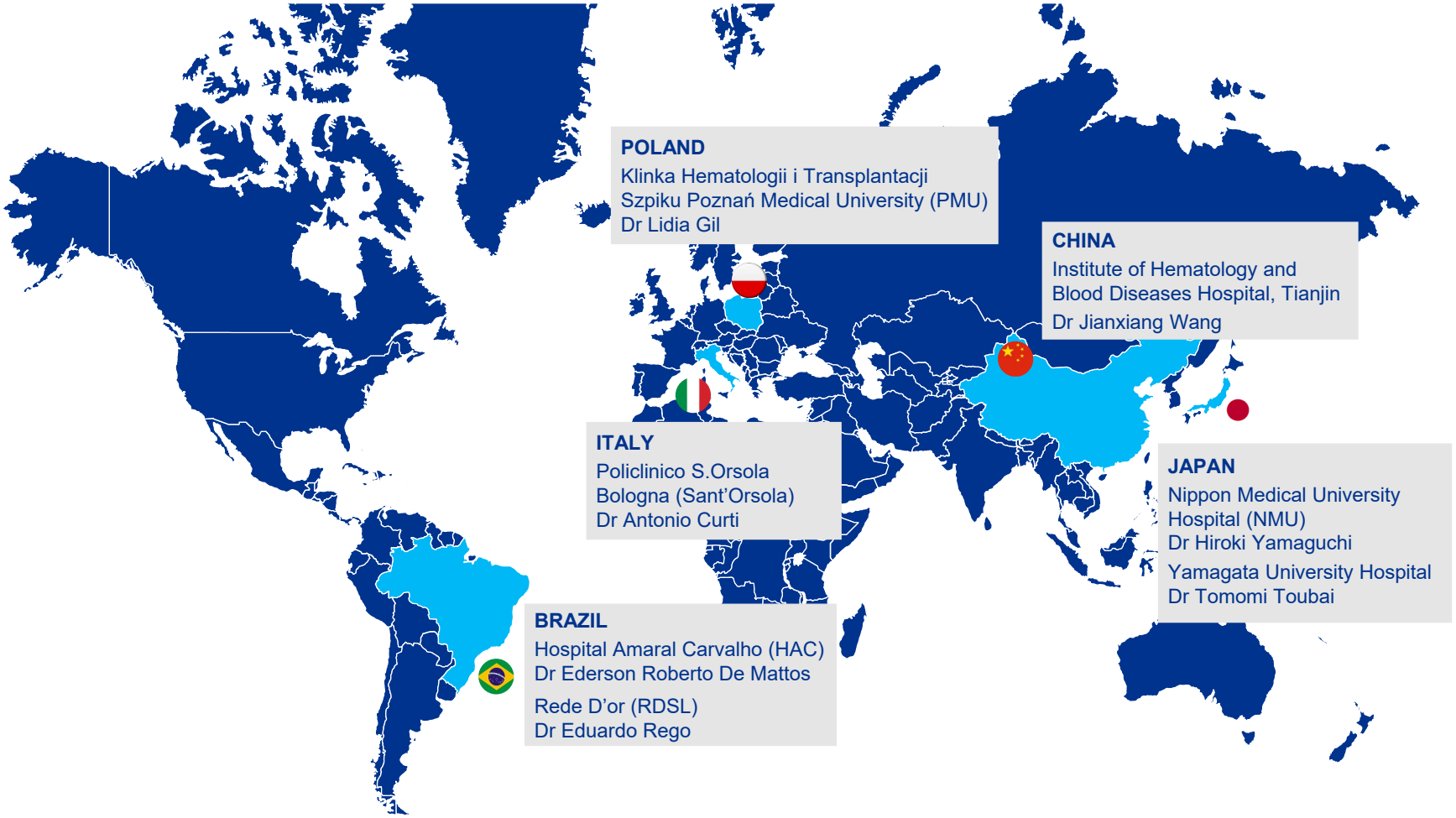
Tested findings from both the literature review and the site visits with a panel of experts in AML care.

AML experts provided sufficient challenge, established the global applicability, and effectiveness of the findings

Finalise report

Documented the reviewed findings and AML expert recommendations for good practice in patient care and management in this final report

In order to document examples of AML care, KPMG visited 7 centres from across the globe



Observed challenges and unmet needs for healthcare providers (HCPs) delivering AML care

Awareness and symptom recognition

Non-specific symptoms can delay referrals

Initial symptoms of AML are not specific in nature and may not immediately raise suspicion of malignancy amongst primary care physicians, and delay referral to specialist care[a]

Limited awareness of AML amongst primary care

GPs may have received limited education and training on AML and its symptoms, which may lead to a delay in referral[b]

Diagnosis, classification, and prognosis

Inconsistent referral process to specialist care

Variation in the diagnostics available in primary care, initial work-up investigations, and referral timelines can affect the time taken to receive a diagnosis[b]

Keeping pace with frequent developments in diagnostic technology and equipment

Mutational profiling can be helpful in identifying AML drivers and targetable genetic aberrations, and the technology used to do this is constantly evolving[c]. Faster genetic testing is required for diagnosis and monitoring as this affects prognosis and treatment decisions (speed varies, from a few days to a few weeks[c]

Inconsistent access to comprehensive testing

Comprehensive molecular and genetic testing informs AML classification, and as a result, the prognosis and treatment decisions for each patient[c]. Testing practices can vary due to inconsistent reimbursement options and inconsistent integration of genetics in clinical practice[d]

Treatment (intensive + non-intensive) and relapse care

MDT composition and care is not standardized

There is variation in the composition, functions, and protocols followed in the haematology MDTs treating patients with AML(b). Services, such as infectious disease specialists, are not generally included in the MDT[b]

Healthcare providers are working at capacity

Globally there is shortage of HCPs in oncology, with rigorous training required in the field. Staff often work long hours under pressure[e],[f]

Limited resources

Fixed yearly funding for the departments is a challenge across regions. It impacts access to innovative equipment, new beds and the ability to create separate area for immuno-compromised as well as infected patients[e]

Gaps in knowledge to keep up with developments in AML care

AML research is ongoing at a large scale, and centres are challenged to consistently keep pace with developments[g],[h]

Active surveillance for relapse is inconsistent

Lack of standard training to support HCPs in effectively counselling and advising patients on active surveillance for relapse[b]

Remission

Inconsistent referral process to specialist care

Support for patients following treatment of AML in the local community through isolated primary health care teams and oncology clinics is limited, as they may have received limited education regarding AML maintenance[b]

Need to improve collaboration with community centres

There are gaps in communication between specialist centres, primary care teams and rural oncology clinics[b]

Palliative care

Delayed transfer to palliative care

AML patients have unique needs given the nature of the disease and would benefit from dedicated palliative care. Typically, the transition from haematologist-led care to palliative care is only considered at late stages and is not integrated from early on in the patient pathway[i]

Sources: (a) StatPearls. leukaemia. 2021; (b) ACI Blood and Marrow Transplant Network. NSW Model of Care for Acute Myeloid Leukaemia.(c) Haferlach T. and Schmidts I. The power and potential of integrated diagnostics in acute myeloid leukaemia. Br J Haematol. 2020 Jan; 188(1): 36; (d) Barnell e. et.al. Impact of a 40-Gene Targeted Panel Test on Physician Decision Making for Patients With Acute Myeloid leukaemia, CO Precision Oncology no. 5 (2021) 191-203; (e) State of Health in the EU, Poland, 2021; (f) Global Survey of Clinical Oncology Workforce, J Glob Oncol. 2018; 4: JGO.17.00188; (g) Psychooncology. Patient experiences of acute myeloid leukaemia: A qualitative study about diagnosis, illness understanding, and treatment decision-making. 2017; (h) J Natl Compr Canc Netw. Addressing Knowledge Gaps in Acute Myeloid leukaemia to Improve Referral for Hematopoietic Cell Transplantation Consultation. 2019; (i) Chan K.Y. et.al. Impact of enhanced haematology palliative care services in patients with myelodysplastic syndrome and acute myeloid leukaemia: study protocol for a randomized controlled trial. Ann Palliat Med. 2021 Sep;10(9):10013-10021

Observed challenges and unmet needs for patients with AML

Awareness and symptom recognition

Limited awareness of AML

AML is a rare disease with low levels of awareness amongst the general population[a]

Non-specific symptoms can delay presentation

Symptoms of AML are usually non-specific at presentation and can lead to delay in patients presenting to primary care[a]

Diagnosis, classification, and prognosis

Psychological stress

Patients often suffer from anxiety, depression, and psychological distress starting from the initial shock of diagnosis[b]. Sudden changes in health, the volume of new information to process, and the pressure to make quick treatment decisions can be difficult for patients[c]

Late onset age of disease leads to unfavourable prognosis

Incidence of AML rises with age, increasing the likelihood of comorbidities which can result in poor responses to treatment[d]

Treatment (intensive + non-intensive) and relapse care

Impacted quality of life

AML treatment can impact patients' quality of life – both the disease and therapy-related toxicity and side effects[e]

Need for continuous psychological support

Psychosocial support throughout treatment is critical, and many patients with AML and their caregivers require more support than is provided[e],[i]. Patients often report feeling depressed or anxious throughout their treatment[a],[h]

High risk of infection

Patients with haematologic malignancies are at increased risk of infection. AML patients have lower number of lymphocytes and experience reduced cell-mediated immunity, thus predisposing them to various bacterial, viral, and fungal infections[f]

Associated physical weakness

AML-associated fatigue can be debilitating for patients and is linked to poor appetite, muscle loss, and psychological stress[g]. Physical fitness also influences the goals of care and choice of therapy for patients (as fitness affects their ability to tolerate treatment)[i]

High clinical unmet need

Despite advancement in treatment of AML with the advent of novel therapies, there remains a substantial unmet need for treatment options in certain patient cohorts (including the elderly, those who have a poor response to chemotherapy, and patients who relapse)[j]

Remission

Social isolation

Patients spend ~50% of their time in the hospital or clinic (post diagnosis). This often results in social isolation and psychological distress in remission[b]

Most patient support organisations have limited resources, and primarily focus on providing support to patients during active treatment, and do not extend the support post treatment[e]

Palliative care

Limited access to palliative care

Haematological malignancy patients, including patients with AML are less than likely to receive palliative or hospice care compared to patients with other cancers[b][f]

Sources: (a) Leukaemia Care Living with Leukaemia 2018 report; (b) Clinical Challenges: Specialist Palliative Care in Acute Myeloid leukaemia, Medpage Today, Dec 2021; (c) AJMC. Unmet Clinical Needs and Economic Burden of Disease in the Treatment Landscape of Acute Myeloid leukaemia. 2018; (d) Acute myeloid leukaemia (AML) incidence statistics, Cancer Research UK; (e) J Natl Compr Canc Netw. Addressing Knowledge Gaps in Acute Myeloid leukaemia to Improve Referral for Hematopoietic Cell Transplantation Consultation. 2019; (f) Logan C. et.al. Updates in infection risk and management in acute leukaemia, Hematology Am Soc Hematol Educ Program (2020) 2020 (1): 135–139; (g) Evaluation of PeRsOnalised PrEhabilitation in acute myeloid Leukaemia (PROPEL), NIHR, 2022; (h) Anxiety and depression predict unfavorable survival in acute myeloid leukaemia patients; (i) Larson R., Acute myeloid leukemia: Management of medically-unfit adults, UptoDate, Sep 2022; (j) Unmet clinical needs and economic burden of disease in the treatment landscape of acute myeloid leukaemia

Eight common themes of good practice interventions were identified

- Continuity of multidisciplinary care
- Standards, protocols, and ways of working
- Importance of specialised nurses
- HCP education and support
- Integration of pharmacy
- Access to social care
- Focus on clinical research
- Technology and data management

02
Context

AML is a complex disease which can significantly impact patient Quality of Life (QoL)

AML is a rare haematologic malignancy, with a median age of diagnosis of 68 years old[a]

Definition

AML is characterised by malignant transformation and uncontrolled proliferation of myeloid progenitor cells in the blood and bone marrow. It is the most common leukaemia in the adult population, and accounts for approximately 30% of all cases[a]

Symptoms

AML symptoms usually develop in a few weeks and worsen over time. These include:

- Looking pale and feeling tired or weak
- Frequent infections, shivering, and fever
- Unusual bruising or bleeding, such as bleeding gums or nosebleeds
- Abrupt weight loss, bone and joint pain
- Swollen glands in the neck, armpits, and groin[b][c]

Prevalence and incidence

AML global incidence has increased from 1.3 to 1.54 per 100,000 people from 1990 to 2017(d)

The risk for AML rises with age and the disease is more prevalent in males. Individuals who have either a personal or family history of blood disorders, and those exposed to tobacco or nuclear radiation are at a higher risk of developing the disease[f]

Diagnosis

The diagnosis of AML involves a physical examination, medical history taking, and analysis of diagnostic tests[b],[c],[e],[f]

Key diagnostic tests

Blood tests and bone marrow biopsy

A complete blood count is done to confirm the quantity and the characteristics of the different types of cells in the blood

Blood smear and bone marrow samples are looked at under a microscope to observe the features of the cells. The presence of at least 20% myeloid blasts in the bone marrow or blood is generally required for a diagnosis of AML

Flow cytometry, cytogenetics, and immunophenotyping
There are many subtypes of AML, and these tests can help to classify each patient's diagnosis and inform treatment decisions and prognosis

Flow cytometry is done to analyse characteristics of cells including size, shape, and the presence of markers on the cell surface. Cytogenetic analysis is done to identify chromosomal anomalies related to AML, and a molecular evaluation may also be done to assess the type of mutation. Immunophenotyping uses antibodies to identify cells based on the types of antigens or markers on the surface of the cells

Other associated tests

Imaging

Echocardiogram is often performed to establish baseline cardiac function prior to starting any cardiotoxic treatment

CT, X-ray, and ultrasound scans may also be carried out if there are signs of infection, or suspicion of organ or lymph node involvement

Sources: (a) Forsythe A and Sandman KE. What Does the Economic Burden of Acute Myeloid leukaemia Treatment Look Like for the Next Decade? An Analysis of Key Findings, Challenges and Recommendations. Dovepress. May 2021;Vol 2021:12 P245—255; (b) Acute myeloid leukaemia, NHS; (c) Tests for Acute Myeloid leukaemia (AML), American Cancer Society; (d) Dong Y. et.al. leukaemia incidence trends at the global, regional, and national level between 1990 and 2017, Experimental Hematology & Oncology, 2020 volume 9, Article number: 14; (e) Acute Myeloid leukaemia Treatment (PDQ®)–Patient Version, National Cancer Institute; (f) Acute Myeloid leukaemia Treatment (PDQ®)–Patient Version, NCI

AML can have a significant psychological, financial, and social impact on patients and caregivers

Psychological impact

- AML prognosis has improved in recent years; however, diagnosis and prognosis still take a significant psychological toll on patients. The five-year survival rate for AML is ~50% in younger patients, and lower in the elderly[(a)]. Many AML patients experience anxiety and depression following diagnosis related to prognosis and treatment[(a)]
- Psychological stress can also negatively impact treatment outcomes. A study conducted in China indicated that anxiety and depression may influence treatment efficacy and medication compliance[(1),(a)]

Financial impact

- AML treatment can be a complex process, and may involve multiple chemotherapy treatment cycles, stem cell transplantation, and management of infections. Patients often face financial costs for treatment and/or management of symptoms (dependent on region)[(b)]
- Patients and caregivers may also be impacted by a loss or reduction in income throughout treatment and recovery

Social impact

- AML treatment is intensive and often long-term, with side effects that can result in frailty, weakness, fatigue, poor mobility, and a high risk of infections. These factors can all contribute to social isolation[(c)]
- The overall burden of AML care on families and caregivers is high, often causing disruption in family activities and routine. In many cases, they receive little social support. Psychological distress, PTSD[(2),] disrupted sleep, and a decline in quality of life is commonly reported for caregivers[(d),(e)]

Notes: (1) Anxiety and depression were measured through HADs (Hospital anxiety and depression scale) score, (2) PTST: Post-stress traumatic disorder

Sources: (a) Ting Ding et. al. Anxiety and depression predict unfavorable survival in acute myeloid leukaemia patients, Medicine, Oct 2019; Vol 98; Issue 43; (b) Forsythe A and Sandman KE. What Does the Economic Burden of Acute Myeloid leukaemia Treatment Look Like for the Next Decade? An Analysis of Key Findings, Challenges and Recommendations. Dovepress. May 2021;Vol 2021:12 P245—255; (c) Clinical Challenges: Specialist Palliative Care in Acute Myeloid leukaemia, Medpage Today, Dec 2021; (d) Yucel E. et.al. Health-Related and Economic Burden Among Family Caregivers of Patients with Acute Myeloid leukaemia or Hematological Malignancies, Adv Ther. 2021; 38(10): 5002–5024; (e) Grover S. et.al. Caregiver Burden in the Patients of AML, Indian J Hematol Blood Transfus. 2019 Jul; 35(3): 437–445.

The economic burden of AML on the global economy is multifactorial, driven mainly by the associated healthcare costs

AML healthcare costs globally include:

Hospitalisation

Patients experience multiple hospitalisations during the course of treatment, accounting for ~60% of the overall healthcare expenditure for AML

Drug therapy

AML treatment involves multiple targeted drug therapies, some of which are high cost drugs

Haematopoietic stem cell transplantation (HSCT):

Stem cell or bone marrow transplantation is a complex procedure, and it requires long term follow-up care

Regional economic impacts

United States

- The US has reported some of the most expensive episodes of AML care, including relapsed care ($439,104), HSCT ($329,621) and induction intensive chemotherapy ($198,657)

Europe

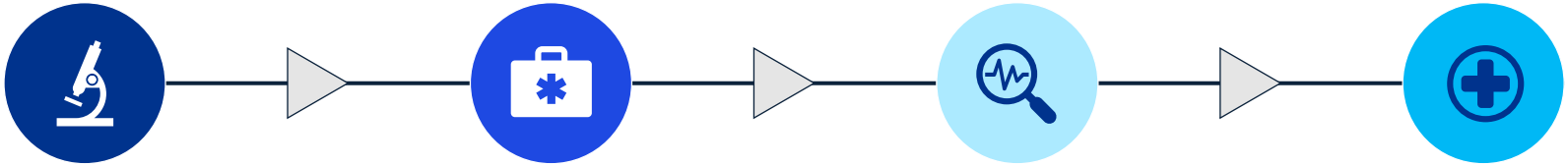
- Spain's annual direct cost per patient has increased by 3.7-fold from 1999 to 2011
- Sweden's total cost of patient management from HSCT to death is the largest, amounting to over US$160,000, with inpatient costs accounting for ~60% of the total

The economic burden of AML is not expected to decline in the coming years

- Recent developments in research have resulted in a significant increase in the number of treatment options, and research is ongoing to further expand the therapeutic options in AML
- Enhanced use of oral and outpatient therapies could potentially reduce costs; however, the overall economic impact of AML is expected to increase as more patients become eligible for novel therapies across different stages of the disease

Sources: (a) Forsythe A and Sandman KE. What Does the Economic Burden of Acute Myeloid leukaemia Treatment Look Like for the Next Decade? An Analysis of Key Findings, Challenges and Recommendations. Dovepress. May 2021;Vol 2021:12 P245—255

Medical and non-medical management of AML



Chemotherapy

Chemotherapy is the primary treatment for most AML patients[a]. It is divided into two phases:

- Induction therapy is short and intensive. The goal is to eliminate all leukaemic cells (blasts) in the blood[c]
- Consolidation therapy is the chemotherapy given after the patient has recovered from induction. It aims to kill the small number of leukaemic cells remaining in the blood[c]

Targeted therapy

Therapy used to target specific cancer cells based on the type of mutation they exhibit

- These drugs can be used in combination with chemotherapy based on the patient's condition[b],[c]
- These drugs target specific cells or proteins to prevent the growth of cancer cells[b]

Bone marrow transplantation

Bone marrow or stem cell transplantation is considered if the patient is not responding well to chemotherapy[b],[c],[d]

- Pre-transplantation, the patient is given intensive chemotherapy to destroy the leukaemic cells in their bone marrow
- Bone marrow is then transplanted – in AML patients this is usually allogenic (where the bone marrow is taken from a donor), but autologous transplant is also possible (where a patient's own bone marrow is used) [b],[c],[d]

Radiotherapy

Radiation therapy uses high-energy radiation to kill cancer cells[b],[c]. It is not commonly used in AML, but may be indicated in specific circumstances including:

- To treat leukaemia that has spread to the central nervous system (e.g. the brain and spinal fluid), or to the testicles
- To treat patients undergoing stem cell transplantation

Additional AML patient care

- Psychological and social support: Counselling and social support are for the management of psycho-social aspects of AML[e]
- Physiotherapy: Physiotherapy to help maintain cardiorespiratory fitness, muscle strength, and functional mobility
- Palliative care: Involvement of palliative care can improve patient management and facilitate the transition to end-of-life care, if needed[e]

Sources: (a) Acute myeloid leukaemia, NHS; (b) Tests for Acute Myeloid leukaemia (AML), American Cancer Society; (c) Acute Myeloid leukaemia Treatment (PDQ®)–Patient Version, National Cancer Institute; (d) Döhner H. et.al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN Blood (2022) 140 (12): 1345–1377.; (e) Ting Ding et. al. Anxiety and depression predict unfavorable survival in acute myeloid leukaemia patients, Medicine, Oct 2019; Vol 98; Issue 43; (f) Zhou Y. et al. Efficacy of Exercise Interventions in Patients with Acute Leukemia: A Meta-Analysis, PLOS One (2016)

There are a number of metrics used to measure patient status and treatment impact globally

Generic instruments		Leukaemia-specific instruments	
EORTC	Quality of Life Questionnaire (from European Organisation For Research And Treatment Of Cancer): Framed to assess quality of life in a wide range of cancer patients. It covers physical, psychological and social functions associated with the disease	FACT-Leukaemia	Functional Assessment of Cancer Therapy - Leukaemia: Measures the health-related quality of life of patients with acute and chronic leukaemia
HADS	Hospital Anxiety and Depression Scale: Utilises 14 questions designed to assess anxiety and depression symptoms	HM-PRO	Haematological Malignancy-Patient-Reported Outcome: Measures the quality of life of people with haematological malignancy
FACT-BMT	Functional Assessment of Cancer Therapy - Bone Marrow Transplantation: Measures the Quality of life in patients undergoing bone marrow transplantation	FACIT-Fatigue	Functional Assessment of Chronic Illness Therapy: Measures an individual's level of fatigue during their usual daily activities over the past week (impact of anaemia) using a 13-metric based tool
EQ-5D-3L/ VAS	EuroQol five dimensions-three levels/visual analog scale: Measures patients' condition across five parameters: mobility, self-care, usual activities, pain/discomfort and anxiety/depression	HCT- CI	Haematopoietic Cell Transplantation - Co-morbidity Index: A specific index that predicts treatment related mortality in patients treated with induction chemotherapy as well as transplant outcome
SF-36	SF-36 Health Survey: Measures general health (such as pain, mental health, vitality, physical strength) through 36 questions	AML- PRT	Acute Myeloid Leukaemia Post Remission Treatment Score: Indicates overall survival after complete remission
		AML-QOL	Acute Myeloid Leukaemia-Quality of Life: Measures the health-related quality of life (HRQOL) in patients with AML and myelodysplastic syndrome (MDS)
		MDASI	MD Anderson Symptom Inventory: Measures burden of symptoms for patients with AML and MDS

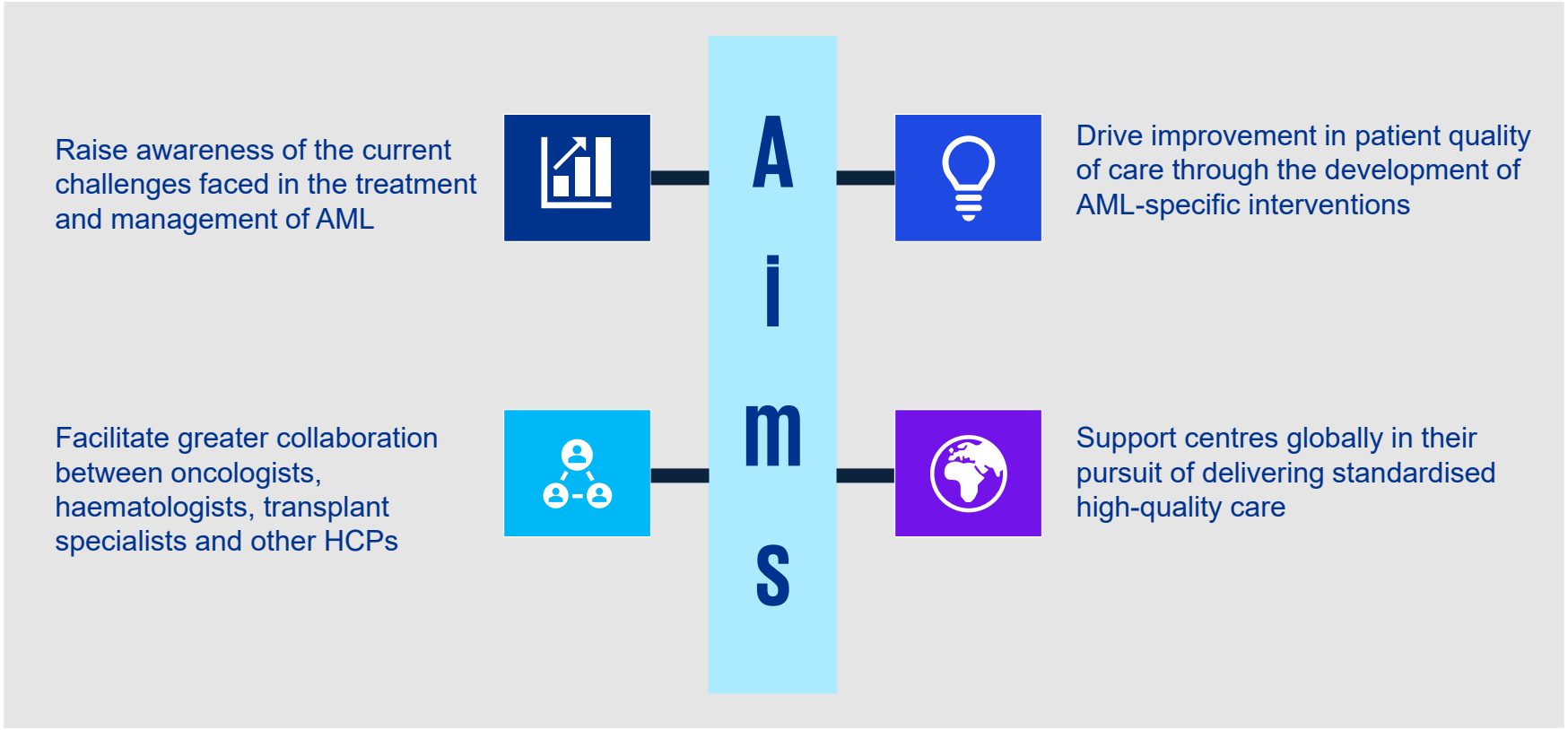
Sources: (a) Stauder R. et. al. Patient-reported outcome measures in studies of myelodysplastic syndromes and acute myeloid leukaemia: Literature review and landscape analysis, Eur J Haematol. 2020 May; 104(5): 476–487.; (b) Kathleen F. Tennant, The FACIT Fatigue Scale, Hign; (c) Acute myeloid leukaemia in adult patients: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, 2020 March

03
Objectives

Objectives

The Quality of Care initiative aims to improve Acute Myeloid Leukaemia (AML) patient care across the globe

By exploring, documenting and sharing features of good practice in caring for AML and associated comorbidities, the initiative aims to ensure all patients globally can benefit from the best care possible



03
Methodology

Methodology

This research followed a five-step approach

Conduct literature review	Carry out site visits	Document good practices in AML care	Review findings with AML experts	Finalise report
Why?				
To understand what challenges and good practices in the care and management of AML have already been established through published evidence	To observe the AML patient pathway and understand how practitioners deliver good practice and overcome key challenges in AML care	To document how leading care practitioners manage AML and develop a variety of good practice interventions	To test findings from both the literature review and the site visits with a panel of experts in AML care (the Steering Committee) to establish the global applicability and efficacy of the findings	To present all findings in one comprehensive report that can be used by any AML centre
How?				
We reviewed key published evidence on recommended good practice care and management for AML e.g. local and international guidelines, academic/clinical publications	Seven sites that deliver AML care around the world were visited by KPMG. At each visit we conducted semi-structured interviews, a site tour, and open question interviews with core and extended AML team members to ensure that we developed a complete understanding of their activities	Each site visit was documented in a centre-specific report (available in the appendix) which summarised the centre's approach to AML care and identified common themes of good practice interventions. The reports were shared with and verified by each centre	Good practice case studies were presented at a steering committee meeting, in order to define and prioritise good practice interventions, discuss the global applicability of the interventions, and how they might be made relevant to all AML centres	We summarised the reviewed findings in a global AML report which identifies common themes and challenges in the management of AML and outlines the case studies of good practice

Our literature review focused on identifying the existing global challenges and good practices in AML care

1 **Conduct literature review:** We reviewed the key guidelines and leading publications across AML diagnosis, treatment, and patient outcomes

KPMG reviewed academic, peer-reviewed publications in addition to high-quality grey literature from a number of reputable sources

Major international recommendations and guidelines related to AML were also reviewed, including the American Society of Hematology recommendations, European Society for Medical Oncology (ESMO) Clinical Practice Guidelines, European leukaemia Net (ELN) recommendations, and National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines

KPMG consulted numerous publications by national governments and private institutions detailing AML good practices and future plans

Our literature review formed the basis of our site visit investigation. It helped us form a comprehensive view of the AML care and management landscape, with initial findings providing an insight into where there are potential improvements to be made

Site visits were conducted to observe the patient pathway and identify current and practical good practice initiatives

2 **Carry out site visits:** Following a rigorous process, we selected 7 leading centres

Initial set of centres were identified via AML publications (including guidelines), congress activity, board/council membership and clinical trial participation. Additional analysis of centre type, size, funding model, location and key AML initiatives in place was used to prioritise from a long list of identified leading centres.

We conducted interviews with a wide range of stakeholders involved in AML patient care at the selected centres. KPMG conducted 35+ interviews, with each interview lasting ~30 mins to 1 hour

Who did we speak to?

Core stakeholders in AML care delivery
- Haematologist
- BMT specialist
- Haematology nurse
- Oncology nurse
- Infection control specialist
- Psychologist
- Pharmacist

Other healthcare professionals involved
- BMT assistant
- Social worker
- Physiotherapist
- Occupational therapist

What did we ask them?

Interview questions explored challenges in care and discussed key practices across the patient pathway:
- Awareness of condition
- Diagnosis
- Referral pathway from primary care to specialist care
- Treatment (intensive + non-intensive) and relapse care
- Access to multidisciplinary care
- Clinical management
- Infection control
- Follow-up care
- Training of medical staff
- Any innovative approaches adopted by the centre

What key insights did we gather?

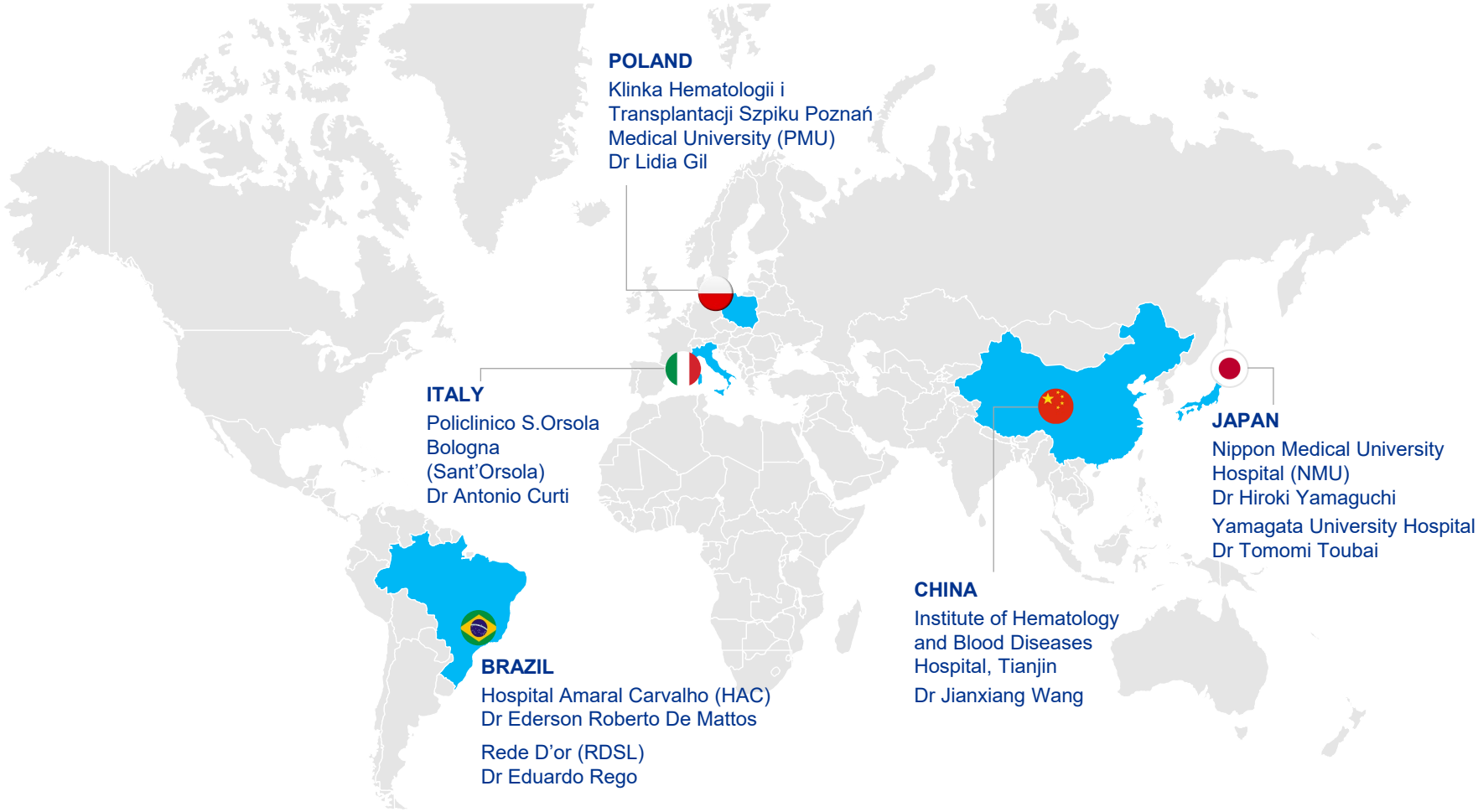
Overview of centre
- Number of patients, services, demographics, funding

Challenges
- What challenges exist in the AML patient pathway

Interventions
- What the intervention involves and what challenge it addresses
- What are the benefits for patients and HCPs

Implementation
- How each intervention is implemented and who is involved
- How and when KPIs and outcomes are captured

In order to document examples of AML care, KPMG visited 7 centres from across the globe



A steering committee of AML experts verified and prioritised our key findings from the site visits

3 Document good practice in AML care

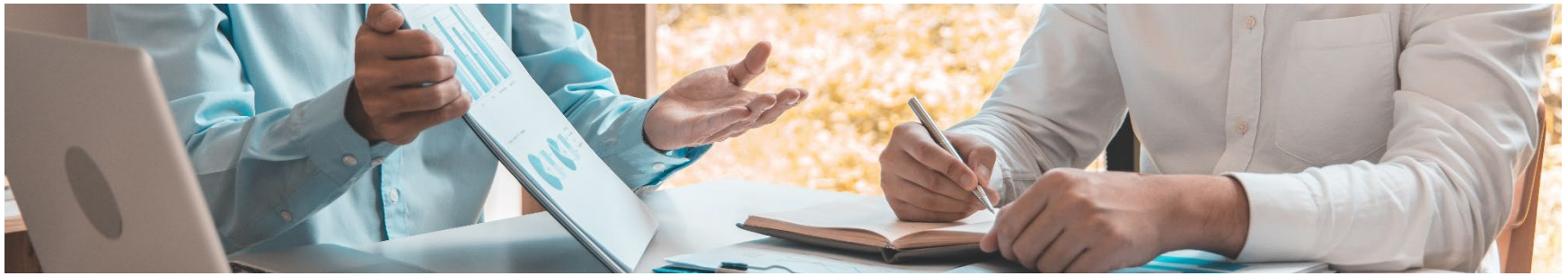
Centre review of findings

- Following each centre visit, KPMG documented the findings in a centre-specific report identifying specifically: Key challenges faced, ‘good practice’ interventions, and measurement of outcomes from interventions
- The report was shared with the centre for review and approval (to validate the findings)

4 Review findings with AML experts

Review of findings (discussion in steering committee)

- Five leading haematologists formed the main steering committee to help shape and define the global good practice interventions
- The case studies identified through centre visits were presented and discussed with a steering committee
- This collaboration enabled the identification of an expert-reviewed set of globally relevant interventions applicable to the management of AML



Following review, we developed a comprehensive report to help sight the AML community on good practices globally

5 **Finalise report:** We have outlined key challenges in AML care and eight overarching themes of good practice initiatives that enable leading centres to deliver high-quality care to AML patients

Themes encompassing good practice initiatives

- Eight common themes of good practices in AML care and management were identified
- These themes hold relevance across the entire patient pathway
- These eight themes are described in detail in the next section of the report, and an example is shared here to highlight the main elements of each individual theme

Challenges addressed

- Cover all the challenges in AML care which can potentially be addressed by a particular theme

Case studies

- Specific case study examples identified from the centres visited, under each theme
- These examples are evidence of the implemented initiatives undertaken across the globe to improve AML care

Theme definition

- This section clearly highlights the meaning of the theme

03
Findings

a) Challenges in AML care

b) Global good practice interventions for AML

Observed challenges and unmet needs for healthcare providers (HCPs) delivering AML care

Awareness and symptom recognition

Non-specific symptoms can delay referrals

Initial symptoms of AML are not specific in nature and may not immediately raise suspicion of malignancy amongst primary care physicians, and delay referral to specialist care[a]

Limited awareness of AML amongst primary care

GPs may have received limited education and training on AML and its symptoms, which may lead to a delay in referral[b]

Diagnosis, classification, and prognosis

Inconsistent referral process to specialist care

Variation in the diagnostics available in primary care, initial work-up investigations, and referral timelines can affect the time taken to receive a diagnosis[b]

Keeping pace with frequent developments in diagnostic technology and equipment

Mutational profiling can be helpful in identifying AML drivers and targetable genetic aberrations, and the technology used to do this is constantly evolving[c]. Faster genetic testing is required for diagnosis and monitoring as this affects prognosis and treatment decisions (speed varies, from a few days to a few weeks[c]

Inconsistent access to comprehensive testing

Comprehensive molecular and genetic testing informs AML classification, and as a result, the prognosis and treatment decisions for each patient[c]. Testing practices can vary due to inconsistent reimbursement options and inconsistent integration of genetics in clinical practice[d]

Treatment (intensive + non-intensive) and relapse care

MDT composition and care is not standardized

There is variation in the composition, functions, and protocols followed in the haematology MDTs treating patients with AML[b]. Services, such as infectious disease specialists, are not generally included in the MDT[b]

Healthcare providers are working at capacity

Globally there is shortage of HCPs in oncology, with rigorous training required in the field. Staff often work long hours under pressure[e],[f]

Limited resources

Fixed yearly funding for the departments is a challenge across regions. It impacts access to innovative equipment, new beds and the ability to create separate area for immuno-compromised as well as infected patients[e]

Gaps in knowledge to keep up with developments in AML care

AML research is ongoing at a large scale, and centres are challenged to consistently keep pace with developments[g],[h]

Active surveillance for relapse is inconsistent

Lack of standard training to support HCPs in effectively counselling and advising patients on active surveillance for relapse[b]

Remission

Inconsistent follow-up care

Support for patients following treatment of AML in the local community through isolated primary health care teams and oncology clinics is limited, as they may have received limited education regarding AML maintenance[b]

Need to improve collaboration with community centres

There are gaps in communication between specialist centres, primary care teams and rural oncology clinics[b]

Palliative care

Delayed transfer to palliative care

AML patients have unique needs given the nature of the disease and would benefit from dedicated palliative care. Typically, the transition from haematologist-led care to palliative care is only considered at late stages and is not integrated from early on in the patient pathway[i]

Sources: (a) StatPearls. leukaemia. 2021; (b) ACI Blood and Marrow Transplant Network. NSW Model of Care for Acute Myeloid Leukaemia.(c) Haferlach T. and Schmidts I. The power and potential of integrated diagnostics in acute myeloid leukaemia. Br J Haematol. 2020 Jan; 188(1): 36; (d) Barnell e. et.al. Impact of a 40-Gene Targeted Panel Test on Physician Decision Making for Patients With Acute Myeloid leukaemia, CO Precision Oncology no. 5 (2021) 191-203; (e) State of Health in the EU, Poland, 2021; (f) Global Survey of Clinical Oncology Workforce, J Glob Oncol. 2018; 4: JGO.17.00188; (g) Psychooncology. Patient experiences of acute myeloid leukaemia: A qualitative study about diagnosis, illness understanding, and treatment decision-making. 2017; (h) J Natl Compr Canc Netw. Addressing Knowledge Gaps in Acute Myeloid leukaemia to Improve Referral for Hematopoietic Cell Transplantation Consultation. 2019; (i) Chan K.Y. et.al. Impact of enhanced haematology palliative care services in patients with myelodysplastic syndrome and acute myeloid leukaemia: study protocol for a randomized controlled trial. Ann Palliat Med. 2021 Sep;10(9):10013-10021

Observed challenges and unmet needs for patients with AML

Awareness and symptom recognition

Limited awareness of AML

AML is a rare disease with low levels of awareness amongst the general population[a]

Non-specific symptoms can delay presentation

Symptoms of AML are usually non-specific at presentation and can lead to delay in patients presenting to primary care[a]

Diagnosis, classification, and prognosis

Psychological stress

Patients often suffer from anxiety, depression, and psychological distress starting from the initial shock of diagnosis(b). Sudden changes in health, the volume of new information to process, and the pressure to make quick treatment decisions can be difficult for patients[c]

Late onset age of disease leads to unfavourable prognosis

Incidence of AML rises with age, increasing the likelihood of comorbidities which can result in poor responses to treatment[d]

Treatment (intensive + non-intensive) and relapse care

Impacted quality of life

AML treatment can impact patients' quality of life – both the disease and therapy-related toxicity and side effects[e]

Need for continuous psychological support

Psychosocial support throughout treatment is critical, and many patients with AML and their caregivers require more support than is provided[e],[i]. Patients often report feeling depressed or anxious throughout their treatment[a],[h]

High risk of infection

Patients with haematologic malignancies are at increased risk of infection. AML patients have lower number of lymphocytes and experience reduced cell-mediated immunity, thus predisposing them to various bacterial, viral, and fungal infections[f]

Associated physical weakness

AML-associated fatigue can be debilitating for patients and is linked to poor appetite, muscle loss, and psychological stress[g]. Physical fitness also influences the goals of care and choice of therapy for patients (as fitness affects their ability to tolerate treatment)[i]

High clinical unmet need

Despite advancement in treatment of AML with the advent of novel therapies, there remains a substantial unmet need for treatment options in certain patient cohorts (including the elderly, those who have a poor response to chemotherapy, and patients who relapse)[j]

Remission

Social isolation

Patients spend ~50% of their time in the hospital or clinic (post diagnosis). This often results in social isolation and psychological distress in remission[b]

Most patient support organisations have limited resources, and primarily focus on providing support to patients during active treatment, and do not extend the support post treatment[e]

Palliative care

Limited access to palliative care

Haematological malignancy patients, including patients with AML are less than likely to receive palliative or hospice care compared to patients with other cancers[b][f]

Psychological impact of palliative care referral

Referral to palliative care is stressful for many patients as most of them associate it with preparation for death[b][f]

Sources: (a) Leukaemia Care Living with Leukaemia 2018 report; (b) Clinical Challenges: Specialist Palliative Care in Acute Myeloid leukaemia, Medpage Today, Dec 2021; (c) AJMC. Unmet Clinical Needs and Economic Burden of Disease in the Treatment Landscape of Acute Myeloid leukaemia. 2018; (d) Acute myeloid leukaemia (AML) incidence statistics, Cancer Research UK; (e) J Natl Compr Canc Netw. Addressing Knowledge Gaps in Acute Myeloid leukaemia to Improve Referral for Hematopoietic Cell Transplantation Consultation. 2019; (f) Logan C. et.al. Updates in infection risk and management in acute leukaemia, Hematology Am Soc Hematol Educ Program (2020) 2020 (1): 135–139; (g) Evaluation of PeRsOnalised PrEhabilitation in acute myeloid Leukaemia (PROPEL), NIHR, 2022; (h) Anxiety and depression predict unfavorable survival in acute myeloid leukaemia patients; (i) Larson R., Acute myeloid leukemia: Management of medically-unfit adults, UptoDate, Sep 2022; (j) Unmet clinical needs and economic burden of disease in the treatment landscape of acute myeloid leukaemia

Eight common themes of good practice interventions were identified

- Continuity of multidisciplinary care
- Standards, protocols, and ways of working
- Importance of specialised nurses
- HCP education and support
- Integration of pharmacy
- Access to social care
- Focus on clinical research
- Technology and data management

Through these intervention themes we aim to impact and improve AML care delivery across the patient pathway

Continuity of multidisciplinary care (1/3)

What do we mean by continuity of multidisciplinary care?

- Establishing a multidisciplinary team or network to manage AML patients that follows a structured and coordinated approach to provide holistic patient care

What challenges does this have the potential to address?

- AML is a rare disease with multiple genetic variations, and patients are at increased risk of infection[(a)]
- Patients often suffer from anxiety, depression, and psychological distress starting from diagnosis[(b)]
- AML associated fatigue can be debilitating for patients and is linked to poor appetite, muscle loss, and psychological stress[(c)]

> “Specialist nurses, lab specialists, and physiotherapists are crucial in care delivery”
> –
> Dr Paresh Vyas,
> University of Oxford, UK

What is the goal?

- Facilitate efficient and complete patient-centered management
- Improve cross-specialty collaboration to further advance AML understanding and management
- Provide easy access to specialty care that may indicated for AML patients (e.g. dental care and palliative care)

Who is often involved?

- Haematologist
- Specialised nurse (Oncology nurse; Haematology nurse)
- Laboratory specialist (cytogenetics specialist; microbiologist etc.)
- Physiotherapist
- Bone marrow transplant specialist
- Psychologist
- Clinical pharmacist
- Social worker

What are the potential outcomes?

Patients

- Enhanced access to specialist multidisciplinary advice/education
- Access to diagnostic tests (including genetic testing) to assess potential differential diagnoses
- Potential to reduce fatigue and improve physical and mental wellbeing through prehabilitation and rehabilitation
- Holistic approach to care offering support for medical and psychosocial needs

HCPs

- Streamlined referral process between HCPs allowing for more efficient patient management
- Increased communication between teams facilitates knowledge sharing

Healthcare system

- Increased efficiency in managing complex AML patients
- Minimal duplication of efforts across specialties/departments (e.g. lab test results)

Sources: (a) Logan C. et.al. Updates in infection risk and management in acute leukaemia, Hematology Am Soc Hematol Educ Program (2020) 2020 (1): 135–139; https://doi.org/10.1182/hematology.2020000098; (b) Clinical Challenges: Specialist Palliative Care in Acute Myeloid leukaemia, Medpage Today, Dec 2021; (c) Evaluation of PeRsOnalised PrEhabilitation in acute myeloid Leukaemia (PROPEL), NIHR, 2022

Continuity of multidisciplinary care (2/3)

What is offered as part of this?

Interventions with global applicability

Interdisciplinary evaluation and care

- Holistic care delivery by a team of specialists to ensure timely management of infection and comorbidities
- Observed in **Policlinico S.Orsola Bologna**, Italy and **Poznań Medical University**, Poland

Dedicated laboratory support

- Integrated laboratory team following a protocol-driven approach to support timely AML diagnosis and treatment
- Observed in **Poznań Medical University**, Poland

Specialised outpatient clinic

- Established outpatient clinic offering weekly consultations for chemotherapy and BMT patients, enabling early identification of any post-transplant complications
- Observed in **Yamagata University Hospital,** Japan

Open patient communication

- Physicians, nurses, and clinical staff communicate openly with patients throughout treatment to build trusting relationships, and improve treatment adherence and the patient experience
- Observed in **Policlinico S.Orsola Bologna**, Italy

Management of side-effects

- Nurses and pharmacists collaborate with treating physicians to manage treatment-associated side effects
- Observed in **Institute of Hematology and Blood Diseases Hospital**, China

Advanced transplant services

- BMT unit that works collaboratively with the wider AML MDT
- Observed in **Poznań Medical University**, Poland and **Yamagata University Hospital,** Japan

Comorbidity management

- Nurses regularly evaluate patients for any signs of comorbidities and raise concerns with physicians
- Observed in **Institute of Hematology and Blood Diseases Hospital**, China

Continuity of multidisciplinary care (3/3)

What is offered as part of this?

Interventions with regional variability

Regular MDT meetings

- Established MDT meetings (weekly or bi-weekly) to discuss patient cases and plan next steps. These can act as a forum to discuss operational improvements, and training as well
- The frequency of these meetings should be adaptable to suit the centre's requirements
- Observed in **Hospital Amaral Carvalho**, Brazil; **Rede D'Or São Luiz**, Brazil; **Yamagata University Hospital,** Japan; **Policlinico S.Orsola Bologna**, Italy and **Institute of Hematology and Blood Diseases Hospital**, China

Personalised physiotherapy and psychology care

- Physiotherapists and psychologists provide care depending on each patient's needs, as many AML patients often experience frailty, reduced strength, anxiety, and isolation
- Observed in **Hospital Amaral Carvalho**, Brazil and **Poznań Medical University**, Poland

Dedicated dental care

- Integrated dentists provide preventative care, and address AML-associated dental problems and side effects
- Observed in **Rede D'Or São Luiz**, Brazil

Early access to palliative care

- The palliative care team is involved early on in the patient pathway to plan and provide support to patients
- Observed in **Yamagata University Hospital,** Japan

Haematologist trained as intensivist

- Haematologists are trained in intensive care, and act as primary caretakers in the ICU
- Implementation can vary in different regions and healthcare systems, as cross-specialty training is not always plausible
- Observed in **Hospital Amaral Carvalho**, Brazil

Standards, protocols, and ways of working (1/2)

What do we mean by standards, protocols, and ways of working?

- Using guidelines or establishing procedures to implement evidence based interventions in clinical practice
- Monitoring and tracking performance is a key aspect of this process and provides quality assurance

What challenges does this have the potential to address?

- Inconsistent timelines (in diagnosis, or treatment) can lead to delay in treatment initiation and impact quality of life for AML patients[(a),(b)]
- Patients with haematologic malignancies are at increased risk of infection[(d)]
- Limited access to genetic tests due to lack of integration and inconsistent reimbursement[(e)]

What is the goal?

- Facilitate implementation of guidelines for diagnosis, treatment, and management of AML patients (including infection monitoring), based on regional guidance
- Ensure tasks are completed according to timelines defined by protocols to achieve diagnosis and treatment initiation targets
- Enhance collaboration among all stakeholders involved in care (including patients' families/carers as well as primary care providers)
- Improve management of comorbidities

Who is often involved?

- Haematologist
- Specialised Nurse (Oncology nurse; Haematology nurse)
- Laboratory specialist (cytogenetics specialist; microbiologist etc.)
- Infection control specialist
- Bone marrow transplant specialist
- Clinical pharmacist

What are the potential outcomes?

Patients

- Increased access to timely testing, which may lead to faster diagnosis, treatment initiation, and infection management
- Regular check-ups and monitoring can help to identify treatment complications and signs of infection early, and improve comorbidity management

HCPs

- Implemented guidelines or protocols establish clear responsibilities, targets, and timelines for the team
- Updates to protocols in line with latest guidelines and literature ensure that HCPs are kept up to date with developments in AML best practice
- Increased collaboration amongst specialists as well as with primary care providers

Healthcare system

- Improved operational efficiency within centres where set standards, protocols, and ways of working are in place
- Consistency in care for AML patients

Sources: (a) ACI Blood and Marrow Transplant Network. NSW Model of Care for Acute Myeloid Leukaemia; (b) J Natl Compr Canc Netw. Addressing Knowledge Gaps in Acute Myeloid leukaemia to Improve Referral for Hematopoietic Cell Transplantation Consultation. 2019; (d) Logan C. et.al. Updates in infection risk and management in acute leukaemia, Hematology Am Soc Hematol Educ Program (2020) 2020 (1): 135–139; (e) Barnell e. et.al. Impact of a 40-Gene Targeted Panel Test on Physician Decision Making for Patients With Acute Myeloid leukaemia, CO Precision Oncology no. 5 (2021) 191-203

Standards, protocols, and ways of working (2/2)

What is offered as part of this?

Interventions with global applicability

Integrated AML protocol
- Consistent protocols for AML treatment and management across all centres within a network
- Observed in **Rede D'Or São Luiz**, Brazil

Focus on infection control
- Established infection control guidelines (covering identification, monitoring as well as management of infection) to reduce the risk of infection for AML patients
- Observed in **Poznań Medical University**, Poland

Protocol-based care delivery
- Established strict protocols for timely diagnostic testing, treatment, and infection control (including monitoring)
- Observed in **Poznań Medical University**, Poland

Collaboration with local hospitals
- Established relationships with local hospitals to facilitate referrals and collaborative care
- Observed in **Yamagata University Hospital,** Japan

Interventions with regional variability

Genetic screening of patients at high risk for a genetic mutation
- Genetic analysis for patients and their families to identify mutations related to leukaemia and understand the presence of a familial predisposition
- Observed in **Policlinico S.Orsola Bologna**, Italy

Centre specific protocols
- Implemented protocols and guidelines (with regular updates) to diagnose, treat, and provide follow-up care for AML patients
- Observed in **Institute of Hematology and Blood Diseases Hospital**, China

ICU appropriate for haemato-oncology patients
- ICU care managed by an MDT to provide specialised monitoring, evaluation, and intensive care
- Observed in **Rede D'Or São Luiz**, Brazil

> "Our centre is a trauma centre and the ICU is very busy, a dedicated oncology ICU with trained staff and equipment would be beneficial"
>
> — Dr Agnieszka Wierzbowska, Medical University of Lodz, Poland

Importance of specialised nurses (1/2)

What do we mean by importance of specialised nurses?

- Defining clear role and responsibilities of specialised nurses in onco haematology care delivery
- Monitoring regular patient care, and raising concerns in case of any signs of distress or challenges

What challenges does this have the potential to address?

- AML is a rare disease with limited awareness among the people. Patient education can be helpful in improving awareness[(a),(b)]
- Patients often suffer from anxiety, depression, and psychological distress starting from diagnosis[(c)]
- Patients with haematologic malignancies are at increased risk of infection[(d)]

What is the goal?

- Improve knowledge and capabilities of specialised nurses in the department
- Enhance patient management through regular check-ups with trained nurses, who can provide patient education as well as detect any signs of concern (e.g. symptoms of comorbidity or infection)

Who is often involved?

- Haematologist
- Specialised Nurse (Oncology nurse; Haematology nurse)

What are the potential outcomes?

Patients

- Increased access to education on the disease, treatment and self-management guidelines, through open and ongoing discussions with the nursing team
- Implemented timely care delivery, reduced risk of infections, improved patient experience, and improved post-surgical outcomes (through integration of specialised nurses from the early stages of treatment)

HCPs

- Enhanced role of nurses is likely to reduce work-load for other specialised HCPs
- Improved dissemination of training and education through specialised AML nurses
- Consistent patient monitoring at the bedside can help to identify clinical concerns early on

Healthcare system

- Increased efficiency of care delivery and improved management of complex patient cases

Sources: (a) Leukaemia Care Living with Leukaemia 2018 report; (b) The Oncology Nurse's Role in AML Management: Focusing on the Patient in an Era of Novel Therapy, Medical Learning Institute; (c) Clinical Challenges: Specialist Palliative Care in Acute Myeloid leukaemia, Medpage Today, Dec 2021; (d) Logan C. et.al. Updates in infection risk and management in acute leukaemia, Hematology Am Soc Hematol Educ Program (2020) 2020 (1): 135–139

Importance of specialised nurses (1/2)

What is offered as part of this?

Interventions with global applicability

Specialised Haemato-oncology nurses

- Dedicated nurses have experience in haemato-oncology (including blood transfusions, chemotherapy and long-term follow-up care), and conduct physical exams, familiarise patients with treatment, administer radioactive drugs and chemotherapy, and assess treatment side effects
- Observed in **multiple centres** such as **Hospital Amaral Carvalho**, Brazil; **Poznań Medical University**, Poland and **Yamagata University Hospital**, Japan

Specialised BMT nurses

- Skilled BMT nurses support patients throughout transplantation, from pre-BMT consultations to follows-ups for monitoring immunosuppressive treatment
- Observed in **Hospital Amaral Carvalho**, Brazil

> Specialised onco-haematology nurses can have high impact with training in haematology as well as oncology procedures"
>
> —
>
> Dr Paresh Vyas, University of Oxford, UK

HCP education and support (1/2)

What do we mean by HCP education and support?

- Supporting the ongoing learning, professional development, and overall wellbeing of HCPs involved in AML care

What challenges does this have the potential to address?

- There are gaps in knowledge of HCPs, as AML is an evolving space, and centres are challenged to consistently keep pace with developments[(a)(b)]
- Healthcare providers are working at capacity, and the demands of the profession are high[(d),(e)]

> "We all agree that education is very important and there should be some training or forums dedicated for all HCPs"
>
> —
>
> Dr Paresh Vyas, University of Oxford, UK

What is the goal?

- Increase HCP AML knowledge through participation in seminars or training (including case-based discussions) delivered by trusted experts in the field
- Improve collaboration amongst HCPs involved in AML care through regular interactions
- Support HCP wellbeing through counselling and mental health support programmes

Who is often involved?

- Haematologist
- Specialised Nurse (Oncology nurse; Haematology nurse)
- Laboratory specialist (cytogenetics specialist; microbiologist etc.)
- Bone marrow transplant specialist
- Clinical pharmacist
- Psychologist

What are the potential outcomes?

Patients

- Access to care that incorporates the latest developments in AML, with healthcare teams who are kept up-to-date with advancements across the patient pathway
- Access to standardised, quality care across both specialist AML centres and local community hospitals

HCPs

- Improved knowledge of AML through attending seminars or meetings focused on sharing latest developments in AML care and clinical experience with management of complex cases
- Exposure to clinical practice guidelines and protocols from multiple specialist centres and teams
- Access to wellbeing support in the workplace

Healthcare system

- Increased potential for collaboration among HCPs from different regions, centres, and specialties
- Continued resilience in the healthcare workforce where support is offered to employees

Sources: (a) Psycho-oncology. Patient experiences of acute myeloid leukaemia: A qualitative study about diagnosis, illness understanding, and treatment decision-making. 2017; (b) J Natl Compr Canc Netw. Addressing Knowledge Gaps in Acute Myeloid leukaemia to Improve Referral for Hematopoietic Cell Transplantation Consultation. 2019

HCP education and support (2/2)

What is offered as part of this?

Interventions with global applicability

National and regional oncology meetings

- Haemato-oncologists from across the country participate in regular meetings to discuss interesting patient cases and share knowledge
- The frequency of these meetings should be practical, perhaps annually or quarterly
- Observed in **Rede D'Or São Luiz**, Brazil

Knowledge sharing forums

- Regular training forums with physicians, nurses, pharmacists, nutritionists, and admin staff to discuss case studies and foster knowledge sharing across the wider MDT
- Observed in **Yamagata University Hospital,** Japan

Trainings for physicians and nurses

- Monthly or fortnightly seminars for physicians and nurses, along with regular collaboration to share case-based learnings
- Observed in **Institute of Hematology and Blood Diseases Hospital**, China

Caring to care programme

- Psychological support and counselling sessions offered to each member of the care team to help manage the psychological impact of delivering cancer care
- This can be a helpful initiative for all HCPs, and support should be implemented in some form. Face-to-face sessions are likely to more beneficial
- Observed in **Rede D'Or São Luiz**, Brazil

Interventions with regional variability

AML consortium

- Consortium focused on studying AML treatment in different countries to reduce the gap in treatment outcomes across nations
- Observed in **Rede D'Or São Luiz**, Brazil

> "Consortiums can be attractive for doctors, but they are not usually directed towards nurses or other HCPs"
>
> —
>
> Dr Hiroki Yamaguchi,
> Nippon Medical School, Japan

Integration of pharmacy (1/2)

What do we mean by integration of pharmacy?

- Involving clinical pharmacist in treatment delivery as well as follow up care offers patients another direct and accessible point of contact
- Including pharmacists in management of drugs in the centre (such as drug procurement, conducting cost analysis)

What challenges does this have the potential to address?

- Inconsistent follow up care can lead to poor treatment adherence among AML patients[(a)]
- AML treatment can impact patients' quality of life, both the disease and therapy related toxicity and side effects[(b)]

What is the goal?

- Utilise pharmacists' regular touchpoints with patients to guide patients regarding usage, dose, frequency, and importance of treatment
- Improve patient adherence by sending prescription refill reminders through accessible channels
- Raise reported therapy side-effects or adverse events with the prescribing physician

Who is often involved?

- Clinical pharmacist (specialised in haematology and oncology)

What are the potential outcomes?

Patients

- Access to information and guidance on the importance of treatment and regular reminders can improve adherence to treatment
- Ability to seek clarification on any concerns regarding treatment instructions, dosage, and side effects

HCPs

- Reported side effects and adverse events can be managed efficiently
- Increased communication between the medical team and the pharmacy can help inform treatment decisions and modifications where needed
- Clear distribution of responsibilities among HCPs in the care delivery team

Healthcare system

- Increased inclusion of pharmacist in drug supply management and prescription management can help to manage centre finances

> "As we deal with dangerous drugs and manage critical patients, pharmacological support is essential – to double check every prescription, conduct drug management and raise data enquiry in case if any errors"
>
> —
>
> Dr Vyas, University of Oxford, UK

Sources: (a) Psycho-oncology. Patient experiences of acute myeloid leukaemia: A qualitative study about diagnosis, illness understanding, and treatment decision-making. 2017; (b) J Natl Compr Canc Netw. Addressing Knowledge Gaps in Acute Myeloid leukaemia to Improve Referral for Hematopoietic Cell Transplantation Consultation. 2019

Access to social care (1/2)

What is offered as part of this?

Interventions with global applicability

Integrated Pharmacy services

- Pharmacists collaborate with prescribing doctors and provide instructions to patients including usage, dose, frequency, and importance of prescription drugs
- A challenge in implementation of this initiative may be a shortage of trained clinical pharmacists in the healthcare system
- Observed in **multiple centres** such as **Hospital Amaral Carvalho**, Brazil; **Institute of Hematology and Blood Diseases Hospital**, China and **Poznań Medical University, Poland**

> "We have a dedicated leukaemia pharmacist, and they are included in inpatient as well outpatient clinic"
>
> —
>
> Dr Eytan Stein, Memorial Sloan Kettering Cancer Center, US

Adherence monitoring

- Pharmacists act as a key point of contact and conduct regular monitoring of patients to ensure treatment adherence
- Observed in **Policlinico S.Orsola Bologna**, Italy and **Institute of Hematology and Blood Diseases Hospital**, China

Prescription management

- Pharmacists evaluate each prescription in line with summary of product guidelines to assess if a drug is both appropriate and cost-effective
- Observed in **Policlinico S.Orsola Bologna**, Italy

Compliance and validation of prescription

- Pharmacists utilise a validation system to track patient prognosis and exams, record queries, and guide dose reduction
- Observed in **Hospital Amaral Carvalho**, Brazil

Drug supply management

- Pharmacists coordinate with pharmaceutical companies closely to track and maintain the inventory levels for relevant drugs
- Observed in **Institute of Hematology and Blood Diseases Hospital**, China

Management of complications

- Pharmacists coordinate with the prescribing physicians to manage treatment-associated complications or side effects
- Pharmacists can modulate the treatment dosage or route of administration to minimise the impact of side effects
- Observed in **Yamagata University Hospital**, Japan

Dedicated haemato-oncology pharmacist

- Inclusion of a pharmacist with haemato-oncology experience in both inpatient and outpatient care to guide patients on new therapies, manage chemotherapy regimens, monitor drug side effects, and help to manage patient comorbidities
- Observed in **Yamagata University Hospital**, Japan

Access to social care (1/2)

What do we mean by access to social care?

- Establishing social support for patients. This might include access to a social worker who can direct patients to financial guidance resources, patient advocacy groups (PAGs) to connect with other AML patients or access at home therapies, and more

What challenges does this have the potential to address?

- Patients suffer from psychological stress. Sudden changes in health, the volume of new information, and the pressure to make quick treatment decisions can be difficult for patients[(a)]
- Patients spend ~50% of their time in the hospital or clinic (post diagnosis). This often results in social isolation[(b)]

What is the goal?

- Increase convenience for patients (through guidance from social worker, access to accommodation), thereby reducing stress for patients and their families
- Improve collaboration with patient advocacy groups through provision of support services to patients

Who is often involved?

- Social worker
- Specialised Nurse (Oncology nurse; Haematology nurse)
- Administrator

What are the potential outcomes?

Patients

- Access to social care can provide education and support to help manage the significant impact that AML has on patients' and caregivers' daily lives
- Social housing, transportation, and meals can help patients access care even if they live far from a specialised centre
- Potential to enhance patients' support networks by providing resources for families and carers

HCPs

- Reduced burden on the HCPs through effective management of patients in the community as appropriate

Healthcare system

- Reduced hospitalisation rates and overall patient load on the centres, as some of the patients could be managed at home by calling upon home care associations

"AML is a complex and taxing disease, and social support is particularly important for these patients"
–
Dr Paresh Vyas, University of Oxford, UK

"Implementation depends on the social care system in a country, as these changes require funding and government authorities' approval"
–
Dr Agnieszka Wierzbowska, Medical University of Lodz, Poland

Sources: (a) AJMC. Unmet Clinical Needs and Economic Burden of Disease in the Treatment Landscape of Acute Myeloid leukaemia. 2018; (b) Clinical Challenges: Specialist Palliative Care in Acute Myeloid leukaemia, Medpage Today, Dec 2021

Access to social care (1/2)

What is offered as part of this?

Interventions with global applicability

Social services

A social worker supports all patients' needs in the ICU and the haematology ward e.g. availability of family attendants, clothing, and transportation to minimise anxiety

Observed in Hospital Amaral Carvalho, Brazil

Patient support

Patient advocacy groups conduct seminars to bring AML patients together through an open forum to share their experiences

Observed in Policlinico S.Orsola Bologna, Italy

Volunteering programme

Supports elderly patients and patients with limited mobility by volunteering for shopping, errands, and companionship

Observed in Poznań Medical University, Poland

Integration with primary care

Haematologists collaborate with primary care physicians to provide integrated follow-up care at home

Observed in Policlinico S.Orsola Bologna, Italy

Education and support for terminally ill patients

Provides educational material as well as support (both inpatient and in home care) for terminally ill patients

Observed in Yamagata University Hospital, Japan

Interventions with regional variability

Complimentary support houses

- Accommodation, meals, transport services, and support from an MDT including social workers, physical therapists, psychologists, and nutritionists within dedicated housing
- Observed in Hospital Amaral Carvalho, Brazil

Patient accommodation

- Housing network with 15-16 rooms for patients, in collaboration with a patient association
- Observed in Policlinico S.Orsola Bologna, Italy

Financial support services

- Provides information on available subsidised schemes for high-cost drugs, and coordinates with local hospitals to ensure support following discharge
- Observed in Yamagata University Hospital, Japan

Home care in collaboration with a patient groups

- Home therapy for AML patients in collaboration with a patient association
- Observed in Policlinico S.Orsola Bologna, Italy

Focus on clinical research (1/2)

What do we mean by focus on clinical research?

- Supporting development of clinical designs, participating in clinical studies, and allowing patients to access novel therapies through clinical trials

What challenges does this have the potential to address?

- AML research is ongoing at a large scale, and centres are challenged to consistently keep pace with developments[(a),(b)]
- AML testing and drug development is an evolving field[(c)]
- There remains a high unmet need for treatment options in certain patient cohorts (including elderly, those who have poor response to chemotherapy, and patients who relapse)[(d)]

What is the goal?

- Facilitate ethical clinical research, with high standards for data collection and management
- Increase patient participation in clinical trials to allow them access to new treatment options and provide alternatives when approved therapies have not been effective
- Improve overall AML care through development of new diagnosis and treatment options
- Facilitate clinical research across all types of centres (small and large) to ensure diverse patient and centre representation

Who is often involved?

- Haematologist
- Specialised Nurse (Oncology nurse; Haematology nurse)
- Laboratory specialist (cytogenetics specialist; microbiologist etc.)
- Bone marrow transplant specialist
- Clinical pharmacist
- Administrator
- Study sponsors

What are the potential outcomes?

Patients

- Increased potential to access novel therapies, which might not otherwise be accessible or reimbursed
- Improved knowledge and understanding of the individual benefits clinical trial participation

HCPs

- Increased knowledge and research capabilities within the AML care team (including ethical research practices, thorough data documentation and management, and a better understanding of drug side effects)
- Improved ability to learn, and stay current with the latest developments or treatment options for AML care through involvement in clinical research

Healthcare system

- Increased potential for development of new treatment options to cater to the unmet needs in AML care
- Enhanced data collection procedures to capture data from all types of centres

Sources: (a) Psychooncology. Patient experiences of acute myeloid leukaemia: A qualitative study about diagnosis, illness understanding, and treatment decision-making. 2017; (g) J Natl Compr Canc Netw. Addressing Knowledge Gaps in Acute Myeloid leukaemia to Improve Referral for Hematopoietic Cell Transplantation Consultation. 2019; (c) Haferlach T. and Schmidts I. The power and potential of integrated diagnostics in acute myeloid leukaemia. Br J Haematol. 2020 Jan; 188(1): 36; (d) Unmet clinical needs and economic burden of disease in the treatment landscape of acute myeloid leukaemia

Focus on clinical research (2/2)

What is offered as part of this?

Interventions with regional variability

Access to innovative therapies

- Involvement in multiple clinical studies, providing increased access to innovative therapies
- Observed in **Policlinico S.Orsola Bologna**, Italy; **Poznań Medical University**, Poland and **Institute of Hematology and Blood Diseases Hospital**, China

Management of trials database

- Established database is used by data managers to capture and track data on patient enrollment, clinical history, demographics, and trial results
- Observed **in Policlinico S.Orsola Bologna**, Italy

Management of clinical studies

- Dedicated data managers and coordinators work with HCPs to ensure enrollment of eligible patients in studies, collection of samples and administration of drugs
- Observed in **Policlinico S.Orsola Bologna**, Italy

Specialised centre for research

- Research institutes conduct a number of clinical studies in transplantation and medical and surgical management of oncological diseases
- Observed in **Rede D'Or São Luiz**, Brazil and **Policlinico S.Orsola Bologna**, Italy

Drug tolerance research

- Research to evaluate efficacy and safety outcomes of various drug combinations and risk levels for patients with different genetic mutation profiles
- Observed **in Institute of Hematology and Blood Diseases Hospital**, China

Clinical research partnerships

- Partnered with the national registry for AML to conduct advanced clinical research
- Observed in **Rede D'Or São Luiz**, Brazil

Investigational drug services

- Pharmacist-led investigational drug service, focused on managing interactions with pharmaceutical companies, conducting pre-monitoring visits and assisting physicians in raising requests
- Observed in **Policlinico S.Orsola Bologna**, Italy

Translational research

- Research in the area of cell biology, haemopoietic stem cells, and investigational drugs is to drive growth of molecular research
- Observed in **Policlinico S.Orsola Bologna**, Italy

Technology and data management (1/2)

What do we mean by technology and data management ?

- Using electronic, mobile, tele technology, and data analysis capabilities to improve communication amongst HCPs and with patients, and enhance the quality and efficiency of AML care delivery

What challenges does this have the potential to address?

- AML is a rare disease with multiple Healthcare providers are working at capacity, limiting their time for frequent interactions with the team as well as patients[(a)]
- AML is a rare disease with limited awareness amongst the general population. Patient education can be helpful in improving awareness[(b)]

> "In some healthcare systems the financial support for digital visits are lower than for in-person visits"
>
> –
>
> Dr Agnieszka Wierzbowska,
> Medical University of Lodz, Poland

What is the goal?

- Increase convenience and communication for patients and HCPs in the delivery of care
- Enhance efficiency of the department through approaches which have the potential to save both time and money
- Improve access and understanding of complex healthcare data (e.g. patient and HCP information)
- Ensure development of user-friendly tools and applications for all cohorts of patents

Who is often involved?

- Haematologist
- Specialised Nurse (Oncology nurse; Haematology nurse)
- Laboratory specialist (cytogenetics specialist; microbiologist etc.)
- Bone marrow transplant specialist
- Clinical pharmacist
- Social worker

What are the potential outcomes?

Patients

- Enhanced ability to better manage their own disease through accessing guidance, consultations and condition updates online and at their convenience
- Access to test results and medical records

HCPs

- Instant and easy access to medical records, often with integration with other departments
- Established technology leads to efficient storage, transfer and analysis of data (e.g. for internal quality reviews, to create patient cohort for research)
- Improved efficiency of meetings and consultations, which can lead to reduction in demand on clinicians' time

Healthcare system

- Reduced number of patients accessing healthcare services in person for services that can be provided remotely
- Improved ability to collect and analyse AML patient data and trends

Sources: (a) Global Survey of Clinical Oncology Workforce, J Glob Oncol. 2018; 4: JGO.17.00188; (b) Leukaemia Care Living with Leukaemia 2018 report; (c) Clinical Challenges: Specialist Palliative Care in Acute Myeloid leukaemia, Medpage Today, Dec 2021

Technology and data management (1/2)

What is offered as part of this?

Interventions with global applicability

Access to electronic medical records (EMR)

- Consistent and detailed patient records are recorded and made accessible to HCPs and patients
- Observed in Hospital Amaral Carvalho, Brazil; **Rede D'Or São Luiz**, Brazil; **Institute of Hematology and Blood Diseases Hospital**, China and **Poznań Medical University**, Poland

Patient database

- A detailed database to record patient details is kept, and used to inform the specific needs of each patient and enable personalised and tailored care
- Observed in **Policlinico S.Orsola Bologna**, Italy

Patient management app for ICU

- A patient management app provides anonymised data on mortality rate, ICU results, and benchmarks from other hospitals to monitor centre progress
- Observed in **Hospital Amaral Carvalho**, Brazil

Patient education

- Educational seminars through social media streaming and broadcasts for patients and their families to raise awareness
- Observed in **Institute of Hematology and Blood Diseases Hospital**, China

Interventions with regional variability

Shared database for BMT

- A shared database capturing all BMT information (including treatment protocols, transplant type, donor details, outcomes, complications) is accessible to BMT professionals
- Observed in **Rede D'Or São Luiz, Brazil**

Remote communication

- Maintain regular connection with patients undergoing chemotherapy, enrolled in clinical studies, and in remission through phone calls and messages
- Observed in **Institute of Hematology and Blood Diseases Hospital**, China

National app for oncology

- An interactive app is used to monitor patients and notify clinical nurses to enable real-time follow-up and teleconsultations with physicians
- Observed in **Rede D'Or São Luiz**, Brazil

Post-BMT data analysis

- Maintain and monitor data on each patient's condition and transplant volume post BMT – data is shared to be used in benchmarking studies
- Observed **in Hospital Amaral Carvalho**, Brazil

Glossary and bibliography

Glossary

AML: Acute Myeloid Leukaemia

HCP: Healthcare Professional

GP: General Practitioners

MDT: Multidisciplinary Team

CT: Computed Tomography scans

PTSD: Post Traumatic Stress Disorder

QoL: Quality of Life

HSCT: Haematopoietic stem cell transplantation

EORTC: Quality of Life Questionnaire from European Organisation For Research And Treatment Of Cancer

HADS: Hospital Anxiety and Depression Scale

FACT-BMT: Functional Assessment of Cancer Therapy - Bone Marrow Transplantation

EQ-5D-3L/VAS: EuroQol five dimensions-three levels/visual analog scale

SF-36: SF-36 Health Survey

FACT- Leukaemia: Functional Assessment of Cancer Therapy – Leukaemia

HM PRO: Haematological Malignancy-Patient-Reported Outcome

FACIT Fatigue: Functional Assessment of Chronic Illness Therapy

HCT-CI: Haematopoietic Cell Transplantation - Co-morbidity Index

AML-PRT: AML Post Remission Treatment Score

AML-QOL: Acute Myeloid Leukaemia-Quality of Life

MDASI: MD Anderson Symptom Inventory

ESMO: European Society for Medical Oncology

ELN: European leukaemia Net

NCCN: National Comprehensive Cancer Network

BMT: Bone Marrow Transplant

KPI: Key Performance Indicator

ICU: Intensive Care Unit

PAGs: Patient Advocacy Groups

EMR: Electronic Medical Record

SUS: Sistema Único de Saúde (Brazil public healthcare funds)

PPs: Private Plans (insurance)

PCPs: Primary Care Physicians

SBTMO: Society of Cell Therapy and Bone Marrow Transplantation

SBOC: Brazilian Society of Clinical Oncology

ABHH: Brazilian Association of Hematology, Hematology and Cell Therapy

AMB: Brazilian Medical Association (Associação Médica Brasileira)

LATAM: Latin American region (countries)

ONA: National Accreditation Organization

CPNE: Clinerion's Patient Network Explorer

INSS: National Institute of Social Security

CIBMTR: Center for International Blood and Marrow Transplant Research

HLA: Human Leukocyte Antigen

TV: Television

PET-CT: Positron Emission Tomography-Computed Tomography scan

HEPA: High Efficiency Particle Arresting

JCI: Joint Commission International

DNA: Deoxyribose Nucleus

FLT3: FMS-like tyrosine kinase 3

IDOR: D'Or institute for research and innovation

PPE: Personal Protective Equipment

PALG: Polish Adult Leukaemia Group

NHF: National Health Fund

PTHiT: Polish Society of Haematologists and Transfusiologists (Polskie Towarzystwo Haematologów i Transfuzjologów)

PKPO: The Polish Cancer Patient Coalition (Polska Koalicja Pacjentów Onkologicznych)

ECOG: Eastern Cooperative Oncology Group index score

Glossary

MRD: Minimal Residual Disease

IT: Information Technology

NGS: Next Generation Sequencing

WHO: World Health Organisation

MPM: Malignant pleural mesothelioma

SmPC: Summary of Product Characteristics

IRCCS: Istituti di Ricovero e Cura a Carattere Scientifico

SSN: Servizio Sanitario Nazionale (National Health Service Italy)

LEAs: Essential levels of care

ASL: Azienda Sanitaria Locale (Local Health Unit Italy)

SIES: Italian Society of Experimental Hematology

GITMO: Italian Group for Bone Marrow Transplantation

EBMT: European Society for Blood and Marrow Transplantation

AIL: Associazone Italiana Contro Leucemie Linfomi e Mielloma

GDP: Gross Domestic Product

SIE: Italian Society of Hematology

GIMEMA: Gruppo Italiano Malattie Ematologiche dell'Adulto

GREFO: Regional Group of Oncological Drugs

AIFA: Agenzia Italiana del Farmaco – the Italian medical agency

HSCs: Haemopoietic stem cells

ADMO: Associazione Donatori di Midollo Osseo

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Appendix: centre-specific reports

Hospital Amaral Carvalho (HAC)
Jaú, São Paulo, Brazil

Site visited by KPMG April 29th, 2022

Centre overview

Centre summary

Centre type: Non-profit, private tertiary hospital

Catchment area: The centre is based in Rua Dona Silvéria, Sãu Paulo, with the majority of patients coming from nearby cities including Ourinhos, São Carlos, Bauru, and Tatuí

Funding: HAC is primarily funded by the public healthcare system – Sistema Único de Saúde (SUS), and 1/5th of its patient have private insurance

Services: Clinical oncology, haematology, advanced clinical laboratory, molecular biology, radiology, bone marrow transplant (BMT), allied healthcare services, and support houses

AML Patient population: 100 AML cases and 300 total bone marrow transplants per year (20%-25% of which are done for AML patients)

Key strengths in delivery of AML care

Multidisciplinary team (MDT) and specialised care: The MDT is made up of dedicated specialists and allied healthcare professionals with extensive experience in providing care for a high volume of AML patients. The team works collaboratively to ensure multidisciplinary care and personalised treatment for AML

Dedicated team of allied HCPs: A dedicated team of allied HCPs including chemotherapy nurses, psychologists, and physiotherapists is trained to work with AML patients to help manage symptoms and challenges as a result of the disease and its treatment

Social support services: Access to accommodation, food, and transportation in support houses is provided to facilitate better stay management for patients travelling from outside the city to undergo BMT

Key challenges faced in delivery of AML care

Slow referral process: The referral pathway is slow for SUS patients. Primary care physicians in smaller cities are not consistently trained to identify AML, causing delays in accessing care through the SUS network

Barriers to treatment: SUS funding for advanced procedures and novel drugs is limited and ungraded, limiting access to advanced treatment options for SUS patients. This is exacerbated by drug shortages for certain therapies

Limited space for allied HCP consultations: The team has had difficulty securing management approval for designated private spaces for consultations with physical therapists and psychologists. This limits the care provided, especially for SUS patients in shared rooms

Acute Myeloid Leukaemia (AML) in Brazil

Healthcare system overview

Structure: The Brazilian healthcare system is a mixed public-private system which transitioned from a purely private system in 1988. All citizens have the right to access free care via the Unified Health System (Sistema Único de Saúde – SUS) at all public and some private healthcare providers.

Insurance and funding: The SUS aims to provide universal access to health services, enable equality of access to health services, and ensure comprehensive continuity of care.(1) AML is a public health issue in Brazil with a poor epidemiological profile. Access to diagnostic tests and availability of advanced procedures and medications differs across regions, and between public (University hospitals) and private centres. Additionally, many diagnostic tests and treatment options are not publicly reimbursed. Individuals can purchase medical Private Plans (PPs) or pay out-of-pocket to access private health care. In 2018, an estimated 23% of the population had PPs with around 70% provided as an employment benefit[1][2]

Primary care physicians (PCPs) primarily work in the public healthcare system, with municipalities encouraged to set up local teams of PCPs, nurses and other HCPs with federal government funding. The outpatient services are mostly operated privately, with patients only able to access them following primary care referral or discharge from hospital. This creates bottlenecks in accessing specialist care, including oncology services.[3]

Guidelines and societies

Guidelines: Brazilian Association of Hematology, Hematology and Cell Therapy (ABHH), European Leukemia Net, Brazilian Society of Cell Therapy and Bone Marrow Transplantation (SBTMO), and Brazilian Society of Clinical Oncology (SBOC)

Professional bodies: Brazilian Medical Association (AMB, Associação Médica Brasileira), Brazilian Society of Oncology Surgery (SBCO, and Sociedade Brasileira de Cirurgia Oncológica)

Patient association groups (PAGs): Abrale (Brazilian Association of Lymphoma and Leukemia)

Statistics

	Brazil	World		Brazil	World
Cancer incidence[6]	215 *	201 *	Cancer incidence[6]	435	556
AML incidence[4],[5]	58*	30*	AML incidence[4],[5]	9.5	9.9
Public healthcare spend (% of all health expenditure)				42	60

Source: (1) The World Bank; (2) BMJ; (3) The Commonwealth Fund; (4) American society of clinical oncology; (5) NCBI; (6) World Health Organisation Global Cancer Observatory, 2020; (7) The World Bank Databank - Brazil, (8) The World Bank Databank - World

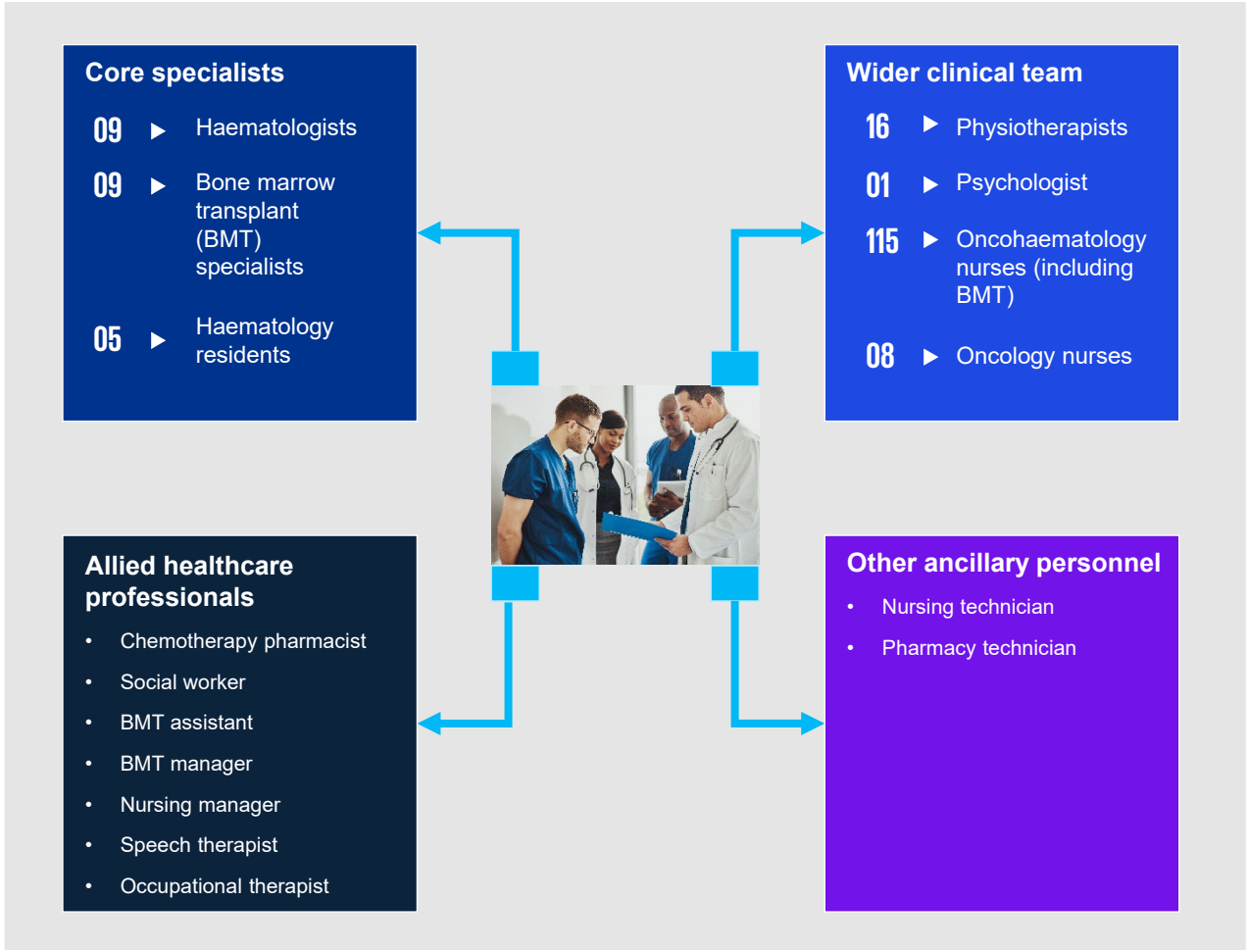
*Per 1,000,000 individuals

The centre and AML unit

The centre	
Centre type	• Non-profit, private tertiary hospital
Size	• 350 oncology beds with 40 dedicated to bone marrow transplant patients
Setting	• Inpatient, outpatient, ambulatory, and support houses
Catchment area	• Primarily provides care to patients coming from nearby cities including Ourinhos, São Carlos, Bauru, and Tatuí in Sãu Paulo. The centre also receives patients from other states across Brazil and LATAM countries
Affiliation & accreditations	• Level I and II accreditation received from the National Accreditation Organization (ONA) • Associated with global community of hospital networks through Clinerion's Patient Network Explorer (CPNE)

The AML unit	
Patient cohort	• 100 AML cases and 300 total bone marrow transplants per year (20%-25% of which are done for AML patients)
Team	• Multidisciplinary team including haematologists, bone marrow transplant specialists, physiotherapists, chemotherapy pharmacists, psychologists, nutritionists, and speech therapists
Services offered	• Comprehensive oncology services including detection, diagnosis, treatment, day hospital, palliative support, and rehabilitation
Guidelines used	• Brazilian Society of Cell Therapy and Bone Marrow Transplantation (SBTMO), European Leukemia Net, National Institute of Social Security (INSS), and Center for International Blood and Marrow Transplant Research (CIBMTR)
Facilities on site	• Pathology, radiology, chemotherapy clinic, bone marrow transplant (BMT) clinic, and advanced clinical laboratory equipped with capabilities to perform flow cytometry, HLA (Human Leukocyte Antigen) typing, virology, cytochemistry, and molecular testing

The team



Governance and processes

Team meetings

A weekly team meeting is conducted on Wednesdays to align on patient treatment plans, transplant referrals, and discharge decisions. There is also a weekly meeting in the outpatient clinic to discuss plans and alignment, with physicians and nurses in attendance.

Patient records

Electronic medical records (EMRs) include case descriptions, exam and test results, treatment details, and prognosis for each patient. EMRs are accessible to the entire multidisciplinary team.

Pharmacy

A dedicated chemotherapy pharmacist dispenses medications, explains prescriptions to patients, and attends MDT rounds for haematology patients

Roles and responsibilities of the team

Intensive haematologist

- Specialist in ICUcare, oncology, and haematology
- Attends to patients on the ward, outpatient clinic, and ICU, and performs cardiological procedures in ICU (e.g. echocardiogram)
- Coordinates the ethics and research committee at HAC

Physiotherapist

- Discusses cases with the multidisciplinary team (MDT) before beginning physical therapy
- Performs motor and respiratory assessments to triage patients according to their fitness levels
- Provides training for exercises to strengthen bronchial and locomotory muscles, and minimise muscle loss

Oncology nurse

- Performs consultations prior to chemotherapy to check vital signs and exam results, conduct physical exams, and familarise patients with treatment and associated side effects
- Administers chemotherapy, provides nursing care, and advises patients on measures to prevent bleeding and mucositis
- Undertakes training for sepsis, comorbidity management, and administration of radioactive drugs

Chemotherapy pharmacist

- Dispenses oral drugs, explaining how and when they should be taken, and raises any adverse effects with the treating physician
- Conducts follow up discussions to explain the importance of treatment and drive patient engagement and adherence
- Uses WhatsApp through the multichannel communication platform ‘Digisac’ to connect with private healthcare patients
- Conducts daily inpatient visits with the MDT to highlight key pharmaceutical indicators e.g. non-compliances, patient concerns etc., and create tailored actions plans

BMT assistant

- Schedules first appointments, contacts patients post treatment to record each patient’s condition, and alerts the treating physician of any clinical concerns
- Evaluates patient’s condition to assess if they are fit to undergo BMT
- Creates admission schedules including date of admission, transplant type, and chemotherapy status
- Accompanies patients during treatment and throughout any follow up

BMT nurse

- Conducts initial discussions to familarise patients with the treatment process and provide specifics related to their chemotherapy regime
- Performs physical exams, outlines infection risk, and gathers patient’s treatment history
- Assists with blood tests, HLA collection and processing, preparation for procedures, and guiding the patient pre-admission through to discharge

Additional team members

- **Social worker:** Documents INSS* data and performs initial social assessment to document details including profession, family members, marital status etc.; provides solutions to minimise treatment associated anxiety, accommodation, and transportation issues
- **Psychologist:** Dedicated haematological psychologists work with patients to help address challenges resulting from their disease or treatment e.g. isolation due to physical limitations and time away from work

Challenges faced in AML care delivery

Delayed referrals and diagnosis in SUS

- The referral process for patients funded by SUS is slow. Primary care physicians in smaller cities are not consistently trained to identify AML, causing delays in accessing care through the SUS network

Treatment barriers for SUS patients

- Funding for medications and invasive procedures (e.g. BMT) is difficult and often inadequate, with reimbursement value remaining ungraded since 2012
- There is an acute shortage of drugs since the drug list includes outdated medications which are not always in supply, and many innovative therapies / novel drugs are not currently funded by SUS

Post-pandemic backlogs and delay

- The average time for referral is longer than before the start of the pandemic
- An increasing number of patients are arriving with advanced and critical stage disease since many patients were not able or willing to attend in-person consultations during the peak of the pandemic
- The critical care unit is more crowded post-pandemic, which is an infection control concern for AML and other oncology patients

Overview of AML patient pathway

Awareness and symptom recognition

Haematologists conduct **monthly lectures at school, TV interviews**, and sessions with 3rd year medical students to share knowledge and raise awareness of AML in the community

Diagnosis, classification, and prognosis

Patients in the public healthcare system are either referred via **the Sistema Único de Saúde (SUS) pathway or through direct referrals** from hospital emergency rooms in urgent cases

The awareness amongst private patients is high and they **usually present to hospital directly**, without previous contact with primary care or a prior diagnosis

Ambulatory nurses schedule appointments based on the urgency

Diagnosis is made primarily based on **immunophenotyping** along with other tests and exams including blood count, karyotype, PET-CT, and myelogram to ensure a comprehensive evaluation

Treatment (intensive + non-intensive) and relapse care

The nursing team performs physical exams and checks vitals to **determine urgency and triage patients**. Treatment of critical patients is initiated within ~six hours of hospitalisation

The nursing team checks the results of the patient's blood tests and investigations, and notifies the treating physician of any areas of concern before initiating chemotherapxy

'Ferrara' criteria is used to determine treatment intensity. ~95-98% of the patients begin treatment with chemotherapy, **with ~30%-40% of patients later undergoing bone marrow transplant** contingent on each patient's preference, age, physical condition, comorbidities, and stage of disease

Members of the **multidisciplinary team (MDT)** including the treating physician, speech therapist, nutritionist, psychologist, infection control, and social workers attend hospitalised patients twice a week to align on the treatment plan

Patients undergoing bone marrow transplant (BMT) are primarily offered **allogenic transplant** and post-surgical monitoring and care for ~100 days

A second transplant is performed if relapse occurs due to grafting failure within six months of the first transplant

Patients are offered **social service support** to assist with transportation and support housing placement after discharge

Remission

The MDT evaluates patients who have achieved remission to monitor blood count, myelogram, and late toxicity

These patients are monitored in person **every two months for a year**, followed by quarterly follow ups in the second year, and **biannual follow ups for next three** years

Post BMT, long-term monthly and bimonthly check-ups are performed in person for international and local patients respectively **until immunosuppre-ssants are tapered**

Palliative care

~60% of AML patients receive palliative care

The medical team, made up of haematologists and physiotherapists, agrees on the most appropriate treatment approach including reinduction, clinical trials, second transplants, and more

Long term supportive care is advised to manage pain when a patient is no longer responding to available treatment options

Interventions and good practices across the care pathway

Bi-weekly multidisciplinary team (MDT) visits

The MDT including treating physician, nutritionist, psychologist, physiotherapist and pharmacist visit inpatient AML patients biweekly to evaluate the patient's physical condition, response to treatment, adverse events, and create a tailored treatment plan.

Personalised physiotherapy and psychology services ★

Allied HCPs specialised in haematology conduct physical and psychological evaluations to assess each patient's condition and any concerns resulting from their disease or treatment to provide personalised support.

Social services ★

A dedicated haematology social worker records each patient's INSS* data and relevant personal details, and works closely with patients in ICU and the haematology ward to address their social needs e.g. availability of family attendants, clothing, and transportation to minimise anxiety and ease the treatment process.

Specialised oncology nurses ★

Oncology nurses are trained to conduct physical exams, familarise patients with treatment, administer radioactive drugs and chemotherapy, and assess treatment side effects and adverse events. Close monitoring of patients in ICU enables timely and responsive care.

Integrated Pharmacy services ★

Chemotherapy pharmacist works jointly with prescribing doctors and provides detailed instructions to patients including usage, dose, frequency, and importance of treatment to increase treatment adherence. They also raise any adverse events to the treating physician.

Haematologist trained as intensivist

Haematologists are trained as intensivists to work as primary caretakers in the ICU, haematology ward, and outpatient clinic. ICU care delivered through haematology specialists results in shorter ICU stays and improved outcomes for patients.

Multi-team access to EMR

The MDT has access to EMR from other hospitals and maintains records throughout the treatment at HAC. Access to treatment records including case details, test results, treatment approach, and prognosis facilitates better treatment planning and outcomes.

Patient management app for ICU

HAC uses 'EpiMed', a patient management app that provides anonymised data on mortality rate, ICU results, and benchmarks from different hospitals. It is used for comparing and monitoring patient's prognosis and performance across different ICUs.

Compliance and validation of prescription

HAC has developed a validation system to track patient's prognosis, record queries, exams, and a dose reduction guide based on toxicity levels. The system is enabled with indicators to identify opportunities for improvement in treatment non-compliance.

Post-BMT data analysis

Admin personnel and nurses monitor data on each patient's condition and transplant volume post BMT to draft reports for weekly BMT team meetings. Data is shared with the Brazilian transplant associations to generate benchmarking studies to improve BMT care and enhance patient safety.

Complimentary support houses

HAC provides accommodation, meals, transport services, and support from an MDT including social workers, physical therapists, psychologists, and nutritionists at support houses to enable long-term treatment, and BMTs for patients coming from distant cities.

Specialised BMT nurses ★

BMT nurses conduct initial interviews to document each patient's medical history, assist with examinations and tests, and support pre-surgical preparation. Pre-BMT consultations and follows-ups to monitor immunosuppressive treatment play an important role in evaluating graft success and planning immunosuppressant weaning.

Keys: Awareness and symptom recognition; Diagnosis, classification and prognosis; Treatment and relapse care; Remission; Palliative care; ★ Spotlight intervention

Notes: *National Institute of Social Security

What are the next steps for the centre?

Dedicated space for consultations with pharmacists

Objective

Establish a dedicated space for pharmacists to conduct patient consultations.

What is the rationale?

Standard AML treatment has evolved from prolonged intravenous chemotherapies to include an increasing number of oral medications which has shifted the onus of daily adherence from provider to patients. Open conversations about treatment and disease-associated symptoms are critical to treatment adherence and the management of side effects. Dedicated spaces for consultations would facilitate these conversations.

How to implement it?

SUS patients have limited access to novel drugs and are usually hospitalised in shared rooms with other patients which may not create the most comfortable environment to share their concerns during visits with the pharmacist and other allied HCPs. Receiving patients and conducting consultations in a dedicated and private space can enable more detailed, open conversations that may increase patient satisfaction and treatment adherence.

Expanding available ICU space and infection control measures

Objective

Expanding physical space and infection control measures to enhance care for patients with compromised immunity in ICU.

What is the rationale?

AML patients in ICU may experience frailty and weakness due to reduced muscle strength and low immunity caused by immunosuppressive medications and require additional measures to prevent infection.

How to implement it?

Expand physical space and incorporate High Efficiency Particle Arresting (HEPA) filters to make ICUs a specialised unit for immunocompromised patients to minimise the risks of infection and improve care delivery.

Spotlight intervention – Pharmacy services

Overview

- HAC has developed a dedicated chemotherapy pharmacy service that works collaboratively with prescribing physicians to validate prescriptions and monitor patient adherence

What is it?

- Pharmacists connect with patients and prescribing physicians through multiple touchpoints to **drive engagement, correspondence, disseminate guidance** on the administration of drugs, perform **clinical validation of prescriptions**, and document adverse events

How does it work?

- Chemotherapy pharmacists maintain a **patient orientation booklet** to provide clear and concise guidance and dispense medication for SUS patients. They **attend biweekly MDT meetings,** highlight pharmaceutical indicators e.g. non-compliances, patient concerns etc., document and report any adverse events to the treating physician, and **create an action plan together**
- They **maintain a compliance and validation sheet for certain chemotherapy drugs** to document non-compliances to the drug, patient's prognosis, exam records, toxicity levels, and dose reduction parameters to compare these metrics with reference values and tailor treatment

What are the potential benefits?

- **Benefit for patients:** Frequent in-person communication and **access to a trained HCP through WhatsApp** increases access to information and drives patient engagement
- **Benefit for the AML team:** Integration of pharmacy services with the MDT and care delivery **enables better communication channels, and comprehensive patient reviews** and treatment plans

> "Convincing the board to establish a dedicated chemotherapy pharmacy staff can be difficult. The key is to start working with available resources until you gradually expand
>
> Chemotherapy pharmacist

Spotlight intervention – Social services

Overview

- HAC provides trained social workers providing support services to address social challenges resulting from long-term treatment for AML patients.

What is it?

- Dedicated social workers connect with patients to document national institute of social security (INSS) data, individual circumstances and preferences for a 24*7 family attendant, accommodation, clothing, and transportation

How does it work?

- Social workers conduct an initial **socioeconomic evaluation** and document personal and professional details, awareness about the disease, concerns, preferences, and the need for an attending companion
- They conduct daily visits to patients in ICU and the haematology ward to address accommodation, food, and transportation issues, and ensure the presence of a family attendant where needed to **minimise anxiety often seen in patients with inadequate support**
- They ensure the **arrangement of support houses for patients from distant cities** scheduled to undergo long-term chemotherapy and BMT
- Approximately 50 AML patients and their families benefit from support houses each year

What are the potential benefits?

- **Benefit for patients:** Frequent check-ins with social workers ensures support with **social challenges, accommodation, and transportation issues** resulting in better management of stress and anxiety faced by AML patients
- **Benefit for the AML team:** Support houses **enable the bone marrow transplant (BMT) team to provide care for a group of patients in need** coming from distant cities who otherwise wouldn't be able undergo long-term treatment and BMT

> "The social workers have a strong commitment to help patients and ease their treatment journey. These efforts go a long way in managing pain and adverse events and is greatly appreciated by patients"
>
> Social worker

> "The situation with patients in need coming from distant places is very difficult, and the provision of support houses is a key differential in their treatment"
>
> Intensive haematologist

Spotlight intervention – Specialised oncology and BMT nurses

Overview

- HAC has a dedicated **team of oncology and BMT** nurses trained to provide care for patients in ICU and those undergoing BMT

What is it?

- The oncology and BMT nurses are integrated in the care pathway from the beginning and over the course of treatment to provide specialised care for hospitalised patients

How does it work?

- There are 8 oncology nurses in ICU **trained in sepsis management, intercurrence care, and administration of radioactive drugs.** They conduct physical exams, familarise patients with treatment, administer drugs and chemotherapy, and monitor side effects and adverse events
- There are 115 oncohaematology nurses, most specialised in BMT, who conduct initial interviews to document each patient's medical history, assist with examinations and tests, and support pre-surgical preparation
- BMT nurses **administer intravenous chemotherapy and bone marrow infusions**
- The BMT nurses also **perform post-surgical follow-ups to evaluate weaning from immunosuppressive treatment and graft success**

What are the potential benefits?

- **Benefit for patients:** Integrating specialised nurses from the early stages of treatment enables timely care, **an improved patient experience, reduced risks of infection, and monitoring of adverse effects and post-surgical outcomes**
- **Benefit for the AML team**: Specialised nursing care **allows the oncology and BMT teams to operate efficiently** and provide a high level of care for AML patients

> "The effort and welcome from the specialised nursing team is appreciated [by patients] within the BMT service
>
> BMT specialist

Spotlight intervention – Personalised physiotherapy and psychology services

Overview

- HAC has a team of physiotherapists and psychologists that provide care to minimise side effects of AML and its treatment

What is it?

- Physiotherapists and psychologists work jointly with patients and treating physicians to provide **care tailored to the specific needs of AML patients** who often experience frailty, reduced strength, anxiety, and isolation as a result of their disease and treatment

How does it work?

- There are 16 physiotherapists and 1 psychologist involved in multidisciplinary visits across the haematology ward, ICU, and outpatient clinics
- The physiotherapist **defines the goal of treatment on the day of hospitalization.** They may offer motor and/or respiratory physiotherapy including lung strengthening exercises, bronchial hygiene routines, and physical activities to reduce muscle loss
- The approach to **physical therapy evolves over the course of treatment based on each patient's response or to accommodate treatment complications,** and the status is documented in medical records
- The psychologist offers support through all stages of the patient pathway from diagnosis to **help manage patients' fears and concerns, help patients process complex information, and communicate with relatives**

What are the potential benefits?

- **Benefit for patients:** Integrating physical therapy and psychology services from the early stages of treatment helps to **improve patients' strength and resilience**
- **Benefit for the AML team:** The team is able to **build trust with the patients**, and provide comprehensive **care for patients' physical and mental health**

> "Humanization, and knowing how to talk to the patient, are important parts of the role
>
> Physiotherapist

Rede D'Or São Luiz (RDSL)
São Paulo, Brazil

Vila Nova Star and OncoStar sites visited by KPMG 5th 18th May 2022

Centre overview

Centre summary

Centre type: Integrated network of 51 private hospitals across Brazil

Catchment area: Patients primarily come from the states of Rio de Janeiro, São Paulo, Pernambuco, Bahia, Maranhão, Sergipe, Ceará, Paraná, and the federal district. Some patients come from across Brazil and other countries in LATAM to access care at the centre

Funding: Primarily provides care for patients with private health insurance and patients who pay out of pocket

Services: Clinical oncology, haematology, bone marrow transplant (BMT), dental surgery and care, clinical pathology, and allied healthcare services

Patient population: 40-50 AML* and ALL* patients per month

Key strengths in delivery of AML care

Multidisciplinary team (MDT) and specialised care: The MDT consists of experienced haematology professionals. A care pathway has been established by the team to provide personalised treatment and enhanced infection control

Specialised dental care: There is a dedicated team of three dental surgeons who are specially trained to evaluate, prevent, and treat oral infections and mucositis in AML patients

Clinical nursing services: Three clinical nurses accompany patients throughout the treatment journey and act as a point of contact regarding care schedules, emergencies, follow-ups

Key challenges faced in delivery of AML care

Inconsistency in health insurance plans and coverage: The coverage for different diagnostic and treatment options for AML patients varies across private insurance providers. Differences in pre-authorisation and reimbursement processes can add a layer of complexity for the team

Infection and risk management: Lack of a dedicated unit for immunosuppressed patients elevates the risk of infection and comorbidity for AML patients

High workload with the medical team running at capacity: There is a need to review the size of the medical team as the demands within onco-haematology are consistently high. Recruiting healthcare professionals in the onco-haematology field is a challenge given the amount of training required and the intensity of the job day to day

Acute Myeloid Leukaemia (AML) in Brazil

Healthcare system overview

Structure: The Brazilian healthcare system is a mixed public-private system which transitioned from a purely private system in 1988. All citizens have the right to access free care via the Unified Health System (Sistema Único de Saúde – SUS) at all public and some private healthcare providers.

Insurance and funding: The SUS aims to provide universal access to health services, enable equality of access to health services, and ensure comprehensive continuity of care.(1) AML is a public health issue in Brazil with a poor epidemiological profile. Access to diagnostic tests and availability of advanced procedures and medications differs across regions, and between public (University hospitals) and private centres. Additionally, many diagnostic tests and treatment options are not publicly reimbursed. Individuals can purchase medical Private Plans (PPs) or pay out-of-pocket to access private health care. In 2018, an estimated 23% of the population had PPs with around 70% provided as an employment benefit.[1][2]

Primary care physicians (PCPs) primarily work in the public healthcare system, with municipalities encouraged to set up local teams of PCPs, nurses and other HCPs with federal government funding. The outpatient services are mostly operated privately, with patients only able to access them following primary care referral or discharge from hospital. This creates bottlenecks in accessing specialist care, including oncology services.[3]

Guidelines and societies

Guidelines: Brazilian Association of Hematology, Hematology and Cell Therapy (ABHH), European Leukemia Net, Brazilian Society of Cell Therapy and Bone Marrow Transplantation (SBTMO), and Brazilian Society of Clinical Oncology (SBOC)

Professional bodies: Brazilian Medical Association (AMB, Associação Médica Brasileira), Brazilian Society of Oncology Surgery (SBCO, and Sociedade Brasileira de Cirurgia Oncológica)

Patient association groups (PAGs): Abrale (Brazilian Association of Lymphoma and Leukemia)

Statistics

	Brazil	World		Brazil	World
Cancer incidence[6]	215 *	201 *	Patient: physician ratio	435	556
AML incidence[4],[5]	58*	30*	% GDP spend on healthcare	9.5	9.9
Public healthcare spend (% of all health expenditure)				42	60

Source: (1) The World Bank; (2) BMJ; (3) The Commonwealth Fund; (4) American society of clinical oncology; (5) NCBI; (6) World Health Organisation Global Cancer Observatory, 2020; (7) The World Bank Databank - Brazil, (8) The World Bank Databank - World

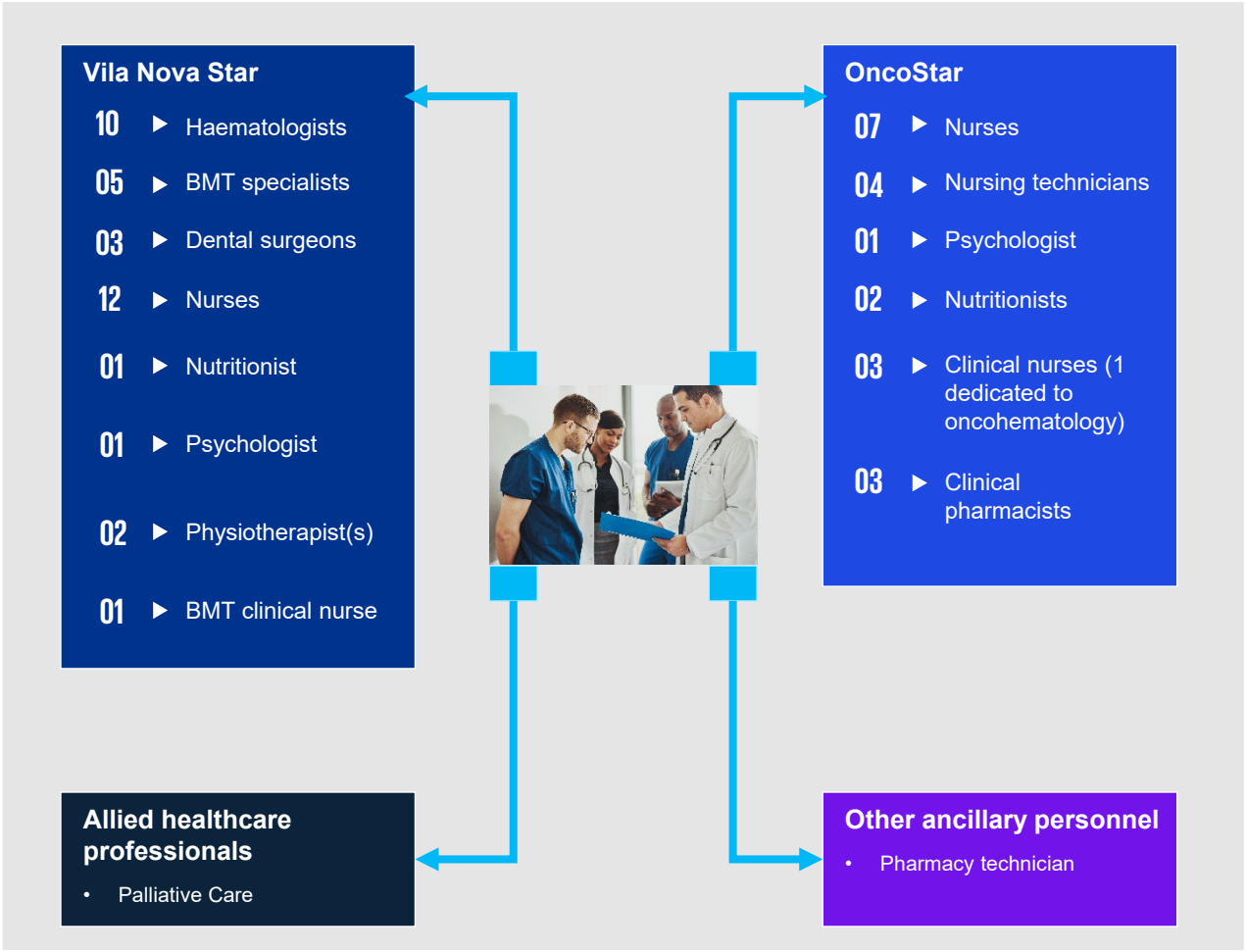
*Per 1,000,000 individuals

The centre and AML unit

The centre	
Centre type	• Integrated network of 51 private hospitals across Brazil
Size	• 11,000 total beds across the 68 hospitals in RDSL (with 8 dedicated beds for AML patients at Vila Nova Star)
Setting	• Inpatient, outpatient, and ambulatory
Catchment area	• RDSL primarily caters to private patients from the states of Rio de Janeiro, São Paulo, Pernambuco, Bahia, Maranhão, Sergipe, Ceará, Paraná, and the federal district. It also provides care to some patients coming from across Brazil and other countries in LATAM
Affiliation & accreditations	• Organização Nacional de Acreditação (ONA) and Joint Commission International (JCI) accreditations

The AML unit	
Patient cohort	• 40-50 AML and ALL patients from Brazil and LATAM per month admitted into the AML units at Vila Nova Star and Oncostar
Team	• MDT made up of experienced haematologists, BMT specialists, dental surgeons, specialized nurses, physiotherapists, psychologists, pharmacists, and nutritionists
Services offered	• Comprehensive oncology service including support in detection, diagnosis, treatment and palliative care
Guidelines used	• Brazilian Association of Hematology, Hematology and Cell Therapy (ABHH), European Leukemia Net, Brazilian Society of Cell Therapy and Bone Marrow Transplantation (SBTMO), and Brazilian Society of Clinical Oncology (SBOC)
Facilities on site	• Facilities include pathology, clinical laboratory equipped to perform cytochemistry, immunohistochemistry, and HLA (Human Leukocyte Antigen) typing, radiology, chemotherapy, and BMT

The team – Vila Nova Star and OncoStar



Governance and processes

Team meetings

At Vila Nova Star, there is a weekly multidisciplinary team meeting including haematologists, nurses, physiotherapists, nutritionists, and dentists to discuss and align on treatment plans for all inpatients. There is also a fortnightly administrative forum to discuss and outline the schedule for allogenic transplants.

Patient records

Physicians access electronic medical records (EMR) via dedicated software. The EMR is integrated with the 'Oncologia D'Or Patient' app that is accessible to physicians, patients and the nursing team. The app includes information on prescriptions, exam results, prognosis, and patient reported symptoms

Pharmacy

Centralised pharmacy performs secondary checks and reconciliation for each prescription received electronically from within the centre

Roles and responsibilities of the team

Haematologist

- National AML expert and coordinator of the international AML consortium
- Haematology practice is spread across the D'Or hospital, Hospital das Clínicas, Hospital São Luiz, and Hospital Vila Nova Star (all part of the RDSL network)
- Outlines the institutional protocol for AML and dedicates ~40% of their time to AML patient
- Conducts daily visits to patients in haematology units and virtual weekly meetings with the team to discuss cases
- Coordinator for haematology at the D'Or Institute for research, manages medical residency programme, and runs educational forum for AML

Dental Surgeon

- Evaluates all hospitalised patients, including those who are scheduled to undergo BMT, and provides guidance on oral hygiene
- Conducts pre-treatment consultations to assess the presence of mucositis, xerostomia, and oral infections
- Performs laser and surgical treatment to treat mucositis and oral infections, and provide medications to prevent xerostomia

Clinical nurse

- Performs initial consultation to evaluate each patient's condition and acts as a point of contact for emergencies and adverse side effects
- Outlines care schedule, familarises patients with treatment protocol, and advises patients on expected side effects
- Responsible for oral chemotherapy administration, blood sample collection, and inpatient care. A separate team of clinical nurses also provide care for outpatients
- Remotely connects with patients via telephone to monitor treatment adherence and any side effects

Clinical pharmacist

- Pharmacists manage the central pharmacy that serves all of RDSL in São Paulo
- Responsible for reconciling and double checking the prescription before dispensing
- Works jointly with other allied HCPs in the assistance team to provide information for patients undergoing treatment and those enrolled in clinical research

BMT clinical nurse

- Involved in the care pathway starting from diagnosis, and provides guidance on treatment and transplantation process
- Assists in DNA collection, looks for suitable matches via the donor bank, and manages the operational aspect of reimbursements
- Works alongside the clinical nursing team and visits all hospitalised patients daily

Psychologist

- Conducts consultations during treatment to build trust, address concerns, validate feelings, and ease disease-associated anxiety
- Provides support to AML patients and bone marrow donors, with online consultations throughout transplantation
- Works with other psychologists who provide support to employees to understand key risks and workload in the medical team

Challenges faced in AML care delivery

Inconsistency in private health insurance plans and coverage

- The eligibility and coverage for AML diagnostics and treatment options varies between different private insurance plans, which impacts what is available to each patient
- Differences in pre-authorisation and reimbursement processes can add a layer of complexity for the team

Lack of dedicated units for immunocompromised patients

- There is no dedicated unit equipped with positive air pressure and the measures required to prevent infection in patients with compromised immunity
- Rooms are adapted on demand, with water and air filters installed each time an immunosuppressed patient is hospitalised

High workload with the medical team running at capacity

- Overall, there is a need to review the size of the medical team as the demands within onco-haematology are consistently high
- Recruiting healthcare professionals in the onco-haematology field is a challenge given the amount of training required and the intensity of the job day to day

> [It would be ideal to] create a centre in São Paulo with greater coverage of health plans and a permanent ward for immunosuppressed patients with positive pressure in the corridor and rooms to remove the current makeshift arrangement
>
> Haematologist

Overview of AML patient pathway

Awareness and symptom recognition

- Overall awareness is low, and the disease remains largely unknown within the community
- The media team within the Rede D'Or network helps to spread cancer awareness during certain months such as pink October (breast cancer) and blue November (prostate cancer)

Diagnosis, classification, and prognosis

- Patients come through **referrals from oncologists or haematologists** at other centres and through **inter-departmental consultations** for patients under the care of other specialties in the same centre
- Patients who display leukaemia-associated symptoms (e.g. anemia and bleeding) may be **diagnosed in the emergency room**
- Patients are admitted and undergo a range of investigations including blood tests, FISH, karyotyping, **immunophenotyping**, myelography, bone marrow biopsy, and NGS-based **genetic testing**
- Patients are **classified in low, intermediate, and high-risk** categories based on molecular testing results, imaging, age, and comorbidities

Treatment (intensive + non-intensive) and relapse care

- Treatment is **decided based on urgency and risks** determined through FISH testing, immunophenotyping, echocardiogram, and the presence of comorbidities
- Risk category is an important factor in determining which patients would benefit from **bone marrow transplant (BMT)** as part of the consolidation strategy
- The decision to refer intermediate and high-risk patients for BMT is made based on each patient's **genetic profile, induction response, and kidney, cardiac, and pulmonary evaluation** results
- Low-risk patients with FLT3 mutations are put on chemotherapy within one week of diagnosis
- **The MDT** including the treating physicians, nurses, dentists, and nutritionists visit all inpatients weekly to align on treatment plans
- Patients undergoing BMT are offered **allogenic transplants** at Vila Nova Star and Hospital Brazil and monitored by the BMT team for up to ~100 days after the transplant
- **Allogenic transplant schedules** are discussed in weekly/fortnightly **administrative forums**

Remission

- Patients who have achieved remission are **followed up quarterly** to have bone marrow samples collected for monitoring
- Patients on maintenance therapy and chemotherapy are followed up once a month to **evaluate treatment progress and renew prescriptions** for the next cycle
- **Post BMT follow-up** occurs monthly for one year, with quarterly check-ups thereafter
- If relapse occurs, patients are **reassessed to evaluate their risk category** before being referred for further treatment or transplant

Palliative care

- **End of life care** is advised to inpatients who become unresponsive to all available treatment options
- A multidisciplinary approach is taken to address **individual patient needs** (this may include pain management, physical therapy, and more)

Interventions and good practices across the care pathway

Rede D'Or Research Institute ★

RDSL has a dedicated research institute conducting clinical research across RDSL, including the Hospital Vila Nova Star and OncoStar centres. Research progress is accessible to all HCPs through a messaging app and enables enrollment and referral of eligible patients in ongoing research.

Clinical research partnerships ★

RDSL is advancing clinical research through their partnership with the Brazilian registry for AML, and continued funding in IDOR*. They have been chosen as a partner to carry out a number of clinical research studies with pharmaceutical companies, with multiple studies and publications currently in progress.

AML consortium

A team of haematologists from RDSL lead an AML consortium sponsored through the American Society of Hematology. The consortium is aimed at studying the AML treatment pathway in different countries to reduce the gap in treatment outcomes observed between Brazil and other nations.

Caring to care programme

Psychology support service offers up to 10 online psychology sessions to each member of the full care team. It aims to identify employee concerns regarding workload and alleviate the psychological impact of delivering cancer care.

National and regional oncology meetings

A group of oncohaematologists, led by one of the lead haematologists at Rede D'Or, conducts weekly meetings to bring together a network of physicians from across Brazil to discuss new cases and share knowledge.

Weekly multidisciplinary meeting

Weekly multidisciplinary team meeting includes prescribing physicians, nurses, psychologists, and admin professionals. It is an open forum to discuss operational improvements, clinical issues, and conduct drug administration and infection control training.

Integrated AML protocol

The haematology practice is split between a number of centres across the RDSL network, including Hospital Vila Nova Star and OncoStar. There are eight dedicated beds available for AML patients at Vila Nova Star. All centres within the network follow a consistent protocol for treating AML patients.

Dedicated dental care ★

The dental surgeons conduct pre-treatment consultations to assess all hospitalised patients for signs of xerostomia and mucositis, and provide guidance on oral hygiene. They perform laser and surgical treatment to treat oral infections.

Electronic Medical Records (EMR)

Physicians use an integrated EMR software to document and access patients' EMRs. It serves as a centralised location to record physicians' prescription and consultation notes and is accessible to the complete care team.

National app for oncology ★

Patients, physicians, and the nursing team use an interactive app that provide access to patients' medical records including exams, prescriptions, and prognosis. The nursing centre monitors patients and notifies clinical nurses to enable real-time follow-up and teleconsultation with physicians.

Oncology ICU

Dedicated oncology ICU is managed by a multidisciplinary team including nurses, nutritionists, and psychologists with an aim to provide specialised monitoring, evaluation, and intensive care. Strict infection control measures are in place to reduce the risk of infection for high-risk patients.

Shared database for BMT ★

A spreadsheet is used to capture clinical information, treatment protocol, transplant type, donor details, outcomes, complications, private health insurance plan, and treating surgeon for each patient. It is a shared repository for BMT professionals and enables access to all the patient data in one place.

Keys: Awareness and symptom recognition; Diagnosis, classification and prognosis; Treatment and relapse care; Remission; Palliative care; ★ Spotlight intervention

Notes: *National Institute of Social Security

What could further drive excellence in care at the centre

EMR Optimisation

Objective

Optimise electronic medical records system.

What is the rationale?

RDSL uses dedicated software to document each patient's electronic medical record (EMR). The data is recorded as open fields wherein the physician inputs details for each patient. The data (e.g. International classification of diseases, incidence, and vital signs) stored in open fields is difficult to extract and analyse.

How to implement it?

The team aims to structure and optimise the EMR to include more closed fields that store predefined data, reflected as a menu of options. The physicians would be able to chose from a list of options when storing information, which will facilitate easier extraction and analysis of data.

Structured outpatient palliative care team

Objective

Enhance outpatient palliative care for AML patients.

What is the rationale?

Patients would benefit from a dedicated palliative care team that provides end-of-life care to both hospitalised and outpatients. While there is a palliative care team that provides integrated psychological, physical, and social support to inpatients, there is a need to structure a team that can provide this service to outpatients as well.

How to implement it?

RDSL has appointed a geriatric and palliative care specialist to establish a dedicated palliative care team for outpatients as well as inpatients. The aim is to set up a structured team that will provide palliative care planning and support for each patient from diagnosis instead of at the point when the patient are already unresponsive to available treatment options.

Spotlight intervention – Dedicated dental care

Overview

- RDSL has a **dedicated team of dental surgeons** that provides support and treatment to all hospitalised patients. The aim is to address AML associated dental problems and side effects that may impact care continuity

What is it?

- Dental surgeons connect with patients throughout the course of treatment to evaluate the patient's condition, share instructions for oral hygiene, and provide medications and treatment to reduce the risks of mucositis and xerostomia

How does it work?

- Dental surgeons conduct pre-treatment evaluations to assess the presence of infection in the mouth, and provide detailed guidance on oral hygiene
- They also contribute to each patient's pre-BMT multidisciplinary assessment with prescribing physicians, nurses, and psychologists in attendance, and maintain touchpoints throughout the treatment to **monitor infection, mucositis, and xerostomia**
- They provide **lubricating gels to reduce dryness** from xerostomia and **perform laser or surgery** as needed to treat mucositis and infections

What are the potential benefits?

- Benefit for patients: Frequent consultations to evaluate dental health enable **timely treatment and alleviation of side effects**
- Benefit for the AML team: Integration of dental professionals in the MDT facilitates **better management of side effects and improve care continuity**

> "The rate of mucositis is very low, and the severity is not high. Mucositis is an indicator of impact on the patient's health
>
> Dental surgeon

Spotlight intervention – Clinical research partnerships

Overview

- RDSL aims to **encourage and expand clinical research for AML** through continued investment, sponsorships, and partnerships with academic institutions

What is it?

- RDSL has partnered with the Brazilian registry for AML and made a significant investment to **enhance internal laboratory capabilities.** They continue to fund research through IDOR* to **bolster their position in clinical research for AML**

How does it work?

- RDSL collaborates with pharmaceutical companies to conduct clinical research and have been chosen as a research partner to **carry out a number of clinical research studies in the past year**, including three AML studies
- They have made a significant **investment to establish an advanced laboratory** equipped with biobanking and sample processing capabilities to drive and expand onco-haematology research in São Paulo
- RDSL continues to **drive clinical research through its research unit IDOR*** and enrolls eligible patients in clinical research. There are **130+ patients currently enrolled in ongoing clinical studies**

What are the potential benefits?

- Benefit for patients: Close collaboration with industry **offers the opportunity to take part in clinical studies and increased access to alternative treatment options**
- Benefit for the AML team: Quality clinical research increases the **centre's reputation and** provides **continued opportunities for learning and building expertise**

> "Rede D'Or has a network of 68 hospitals and a heterogenous group of patients that can significantly contribute to ongoing and future projects
>
> Haematologist

Spotlight intervention – National app for oncology

Overview

- RDSL has implemented the **'Oncologia D'Or Patient'** app that is used to document medical records for all oncology patients

What is it?

- Oncologia D'Or Patient is an **interactive app** covering patients' medical records and acts as a **virtual communication channel** between patients and the medical team
- **How does it work?**
- The Oncologia D'Or Patient is used to document exam results, patient progress, prescriptions, treatment history, and is enabled with built-in **self-assessments for patients**
- The app allows **two-way communication between patients and nurses** where patients can reach out to the nursing team as needed to report any side effects or concerns, and ask questions
- The nursing centre monitors the patients and notifies the clinical nurses if required to schedule a teleconsultation with the prescribing physician

What are the potential benefits?

- Benefit for patients: An interactive tool that provides **virtual access to the medical team through chat or teleconsultation** and timely responses to concerns, discomforts, and side effects
- Benefit for the AML team: The app provides a digital link with the patient and **enables the nursing team to remotely monitor and follow up with patients,** and schedule teleconsultations

> "It is an interactive app, the patient can report symptoms, there is a nursing centre that follows up and monitors the patient and notifies the clinical nurse
>
> Clinical nurse

Klinka Hematologii i Transplantacji Szpiku, Poznań Medical University (PMU), Poznań, Poland

Site visited by KPMG June 28th 29th, 2022

Centre overview

Centre summary

Centre type: Publicly funded tertiary hospital. AML centre is part of the Poznan Medical University, which offers access to other departments and services

Catchment area: The centre is based in Poznań, Poland, and treats patients from across the Wielkopolskie voivodeship (Great Poland) Province (with a population of nearly 3.5 million people)

Funding: PMU is funded by the public healthcare system

Services: Onco-haematology services, advanced clinical laboratory (cytogenetics and microbiology), bone marrow transplant (BMT), allied health services, and palliative care

AML Patient population: 80 AML cases and 125 total bone marrow transplants per year (the majority of which are done for AML patients)

Key strengths in delivery of AML care

Advanced BMT unit: The BMT unit is well-equipped and organised. The team meets weekly to discuss patient cases and plan the transplant schedule for the week. There is a stem cell bank on site, and a dedicated coordinator works to find a donor match for each patient

Robust infection control policies: Infection control is a top priority for AML patients, and strict protocols are in place to enhance infection control (including hand hygiene, sanitised scrubs, PPE, and a specially-trained cleaning team)

Focus on clinical research: Strong focus on research, with participation in studies through the Polish Adult Leukaemia Group (PALG) and other channels. The haematologists and clinical team evaluate the design of each study when deciding if it is a good fit for the centre or not (based on their patient pool)

Key challenges faced in delivery of AML care

Limited awareness of AML in the general population: There is limited awareness of AML and a prevailing stigma associated with cancer amongst the general population. Patients are hesitant to reveal or discuss their diagnosis openly within their communities

High workload within the laboratory and clinical teams: The laboratory and clinical teams are working close to capacity. It is difficult to attract new recruits to a field with high demands on time, training, and personal resilience

Resource and funding limitations: Funding for expansion of the haematology department (including expanding the ward, addition of new beds, and procurement of modern equipment), and access and reimbursement for novel treatment options is limited

Acute Myeloid Leukaemia (AML) in Poland

Healthcare system overview

Structure: The Polish healthcare system is primarily driven by the Ministry of Health, which is responsible for public health policies, governance of the healthcare sector, development and monitoring of guidelines, and management of major expenses. Private facilities mostly provide outpatient care, while the majority of inpatient care is managed in the public system. (1),(2)

Poland offers free public healthcare, and every resident* has the right to accessible health supported by the National Health Fund (NHF). Many people also have private health insurance, and the country has high out-of-pocket expenditure (~22%).(1),(2)

Insurance and funding: The NHF finances healthcare services for holders of public health insurance. The NHF also negotiates and signs contracts with healthcare providers (HCPs), monitors the execution of contracts, and manages contract accounting.(1)

AML care is mainly delivered in secondary care through publicly funded hospitals. Primary care physicians (PCPs) are responsible for conducting initial investigations and referring patients to specialised care (as needed). The government has recently launched several pilot programs to enhance the role of primary care and coordination between primary and secondary care.(2),(3)

Reimbursement for conventional AML treatment is covered, however novel therapies is possible under public reimbursement post approval.(2)

Guidelines and societies

Guidelines: Diagnosis and management of AML in adults: 2017 European Leukemia Net (ELN) recommendations, National Comprehensive Cancer Network (NCCN) guidelines

Professional bodies: Polish Society of Haematologists and Transfusiologists (PTHiT, Polskie Towarzystwo Haematologów i Transfuzjologów), Polish Adult Leukemia Group (PALG)

Patient association groups (PAGs): The Polish Cancer Patient Coalition (PKPO, Polska Koalicja Pacjentów Onkologicznych)

Statistics

	Poland	World		Poland	World
Cancer incidence(4)	267 **	201 **	Patient : Physician ratio(7),(8)	417	556
AML incidence(5),(6)	41**	30**	% GDP spend on healthcare(9),(10)	7.2	10
Public healthcare spend (% of all health expenditure)(11)				72.6	60

Sources:(1) European Committee of the Regions; (2) State of Health in the EU, Poland; (3) Assessing Recent Efforts to Improve Organization of Cancer Care in Poland, 2022; (4) World Health Organisation Global Cancer Observatory, 2020; (5) Haematology in clinical practice; (6) American society of clinical oncology; (7) The World Bank Databank; (8) Data bank – global; (9) Statista; (10) WHO, global spending on health, (11) Country Economy

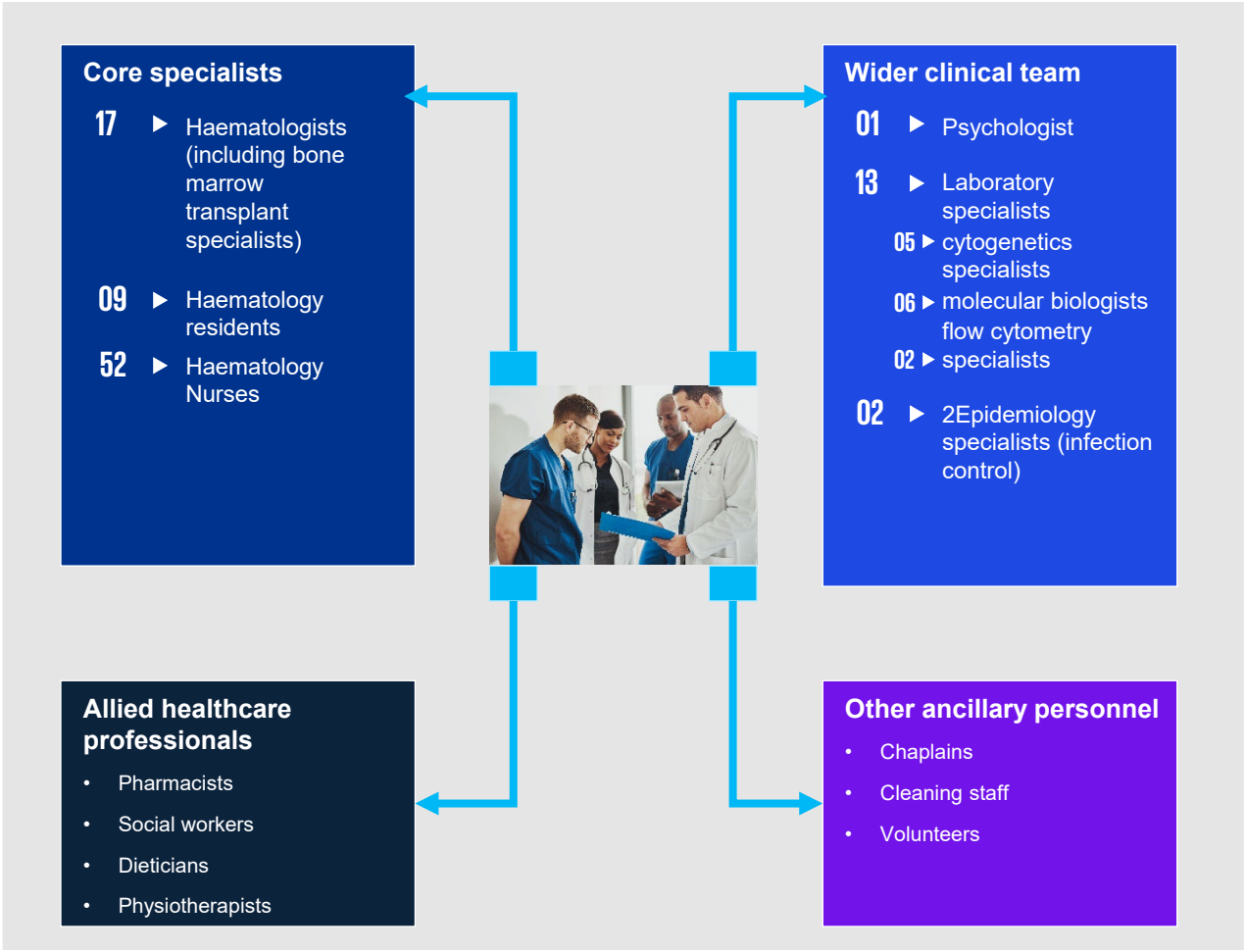
* Public healthcare is accessible to all Polish citizens, people staying temporarily in the country, residents of European Union countries and the European Economic Area; **Per 1,000,000 individuals

The centre and AML unit

The centre	
Centre type	• Publicly funded tertiary hospital (reference centre for AML in Poland)
Size	• 69 beds (12 in the day care centre, and 15 dedicated to bone marrow transplant patients)
Setting	• Inpatient, outpatient, and ambulatory
Catchment area	• Primarily provides care to patients coming from the Wielkopolskie voivodeship (Great Poland) region (which has a population of 3.5 million people)
Affiliation & accreditations	• Certified bone marrow transplant centre for more than 30 years • Accredited by the Polish Ministry of Health, Ministry of Science and Higher Education, and Polish Accreditation Committee

The AML unit	
Patient cohort	• 16,000 patients seen per year in the hospital (~50 chemotherapy patients per day), and 100-125 transplants per year (70% of these are for AML)
Team	• Multidisciplinary team including haematologists, bone marrow transplant specialists, physiotherapists, pharmacists, psychologists, nutritionists, and laboratory specialists
Services offered	• Comprehensive onco-haematology services including detection, diagnosis, treatment, palliative support, and rehabilitation
Guidelines used	• Diagnosis and management of AML in adults: 2017 European Leukemia Net (ELN) recommendations, National Comprehensive Cancer Network (NCCN) guidelines
Facilities on site	• Pathology, radiology, chemotherapy clinic, bone marrow transplant (BMT) clinic, and advanced clinical laboratory equipped to perform cytochemistry and molecular testing

The team



Governance and processes

Team meetings

Team meetings are conducted with the core specialists on Mondays and Thursdays to align on patient treatment plans, transplant referrals, and discharge decisions. These meetings are supplemented with a short ‘stand-up’ briefing each morning to align on immediate tasks

There is an additional weekly meeting to discuss patient cases from across Poland and their eligibility for bone marrow transplant

Pharmacy

Pharmacists dispense medications, explain prescriptions to patients, and support medication preparation for clinical trials

Laboratory staff

The laboratory staff follow stringent protocols to complete testing according to set timelines, and support timely diagnosis and treatment decisions (including antibiotic selection for infections)

Roles and responsibilities of the team

Haematologist and BMT specialist

- Delivers specialist care in oncology and haematology
- Leads multi-disciplinary (MDT) discussions on patient treatment plans, bone marrow transplant (BMT) planning, and collaboration with the lab
- Attends to patients on the ward, in the outpatient clinic, and in the ICU
- Follows up with patients to monitor progress and symptoms post treatment

Cytogeneticist (laboratory specialist)

- Follows guidelines and protocols to complete testing according to set timelines, and support timely diagnosis and treatment decisions
- Collaborates with the clinical team to plan which tests are required for each patient, and carry out testing and analysis accordingly
- Classifies patients as high, intermediate or low risk based on the results of their tests; this informs prognosis and clinical treatment decision

Haematology nurse

- Establishes first contact with patients and supports initial consultations
- Supports patients at each stage of treatment; monitors vital signs, collects blood samples, assists with dental hygiene, maintains infection control measures, and escalates clinical concerns to the treating physician
- Participates in haematology and AML-specific training organised by national nursing organisations and local nursing teams

Pharmacist

- Dispenses oral drugs, explains how and when they should be taken, and highlights the importance of adherence to treatment
- Prepares leaflets for oral drugs with a summary of key information and side effects
- Raises suspected adverse side effects and any patient concerns with the treating physician
- Manages the supply and stock of medications

Infection control specialist

- Delivers training on prevention of hospital-acquired infection
- Detects signs of infection and monitors at-risk patients on a regular basis
- Diagnoses infection and coordinates measures to keep infected patients isolated
- Ensures decontamination of the ward, including the water supply, once an infected patient has been isolated
- Selects antibiotics based on microbiology results and monitors patients' responses

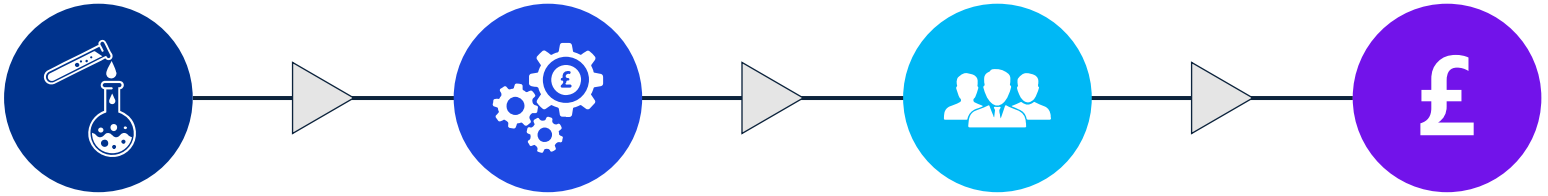
Psychologist

- Supports patients and families in addressing challenges associated with AML throughout the patient pathway
- Helps patients work through the shock of initial diagnosis, fear of death, financial concerns, and social isolation
- Facilitates conversations to discuss concerns and suggests relaxation and visualisation techniques to improve anxiety and stress

Additional team members

- **Physiotherapist:** Helps patients with physical rehabilitation, providing exercises to build strength and maintain activity
- **Microbiologist:** Collaborates with the infection control specialist to identify infectious agents and inform antibiotic selection
- **Social worker:** Coordinates financial and social support for patients

Challenges faced in AML care delivery



High workload within the laboratory and clinical teams

- The laboratory and clinical teams are working close to capacity
- Healthcare professionals may not have capacity to participate in additional training and educational activities
- It is difficult to attract new recruits to a field of complex diseases with such high demands on time, training, and personal resilience

Low AML awareness in the general population

- There is not a high level of awareness of AML amongst the population overall, and this is difficult to address given the prevailing stigma associated with cancer in Poland
- Patients are hesitant to reveal or discuss their diagnoses openly within their communities

Limited network of AML patient support in Poland

- Patient support and advocacy groups can be helpful in educating and providing social support to patients with AML, but there is not an established network for AML patients in Poland
- AML is an aggressive disease, and patients do not always have time to research and access support from external groups following their diagnosis

Resource and funding limitations

- Funding for expansion of the haematology department (including expanding the ward, addition of beds, and modern laboratory equipment) is limited
- Currently, there are not enough beds to accommodate the number of patients who need intensive treatment and one-day chemotherapy
- The department continuously engages with the health ministry and the centre's management to secure funding and expand access to novel therapies

Overview of AML patient pathway

Awareness and symptom recognition

- The centre actively supports **events to raise** awareness about AML in the community (such as the charitable bike ride for AML in Poznań)

Diagnosis, classification, and prognosis

- Patients are usually referred to the centre via **regional hospitals or through specialist outpatient care** after initially presenting to primary care
- Testing is conducted through **dedicated on-site labs, which have protocols in place for timely testing** (including blood tests, bone marrow culture, flow cytometry, and karyotyping)
- **Diagnosis is typically made within 2-3 days**
- Nurses, psychologists, physiotherapists, and transplant coordinators are all involved in patient care from early stages following diagnosis

Treatment (intensive + non-intensive) and relapse care

- Laboratory staff assign high, medium and low risk status to each patient based on initial test results. This status determines the **urgency of each case**
- Treatment is **initiated within 24 hours of arrival in most cases**
- The clinical team has created a detailed algorithm (process map) of steps to be followed in the management of patients with AML
- **Core specialists** meet twice a week to align on the treatment plan for each patient. These meetings focus on patient test results, response to treatment, suitability for transplant, and planning the transplant schedule and logistics
- **Over 55% of patients are on intensive treatment**, while others remain on non-intensive
- Patients are evaluated based on age, **ECOG index score** (Eastern Cooperative Oncology Group), and **SONAR index score** (for transplant complications) to **guide treatment intensity**
- Cardiologists conduct echocardiograms and ECGs to confirm patients' eligibility for intensive treatment
- Patients may be **offered enrollment in clinical studies** if they are eligible candidates

Remission

- Following transplant, patients attend clinic once a week for chemotherapy, once a month for morphology testing, and once every three months for bone marrow testing
- Each patient's complete blood count is checked monthly, and patients are **followed up for two full years after remission**
- Patients who are confirmed to be in remission are managed based on ELN (European Leukemia Net) guidelines and MRD (minimal residual disease). They are **monitored every 6 weeks through molecular markers**

Palliative care

- Palliative care is offered to patients who have exhausted treatment options – **approximately 20% of AML patients receive palliative care**
- **Outpatient palliative care** is managed in collaboration with primary care, with transfusions conducted in local hospitals
- Community palliative nurses conduct **2 visits per week,** and daily contact is maintained by telephone
- The centre has a general **palliative ward, which has a dedicated care team**

Interventions and good practices across the care pathway

Advanced BMT services ★

The centre has a nationally recognised BMT unit that works collaboratively with the wider MDT. They connect at weekly meetings to discuss potential transplant patients and agree on the transplant schedule and logistics. There is a dedicated transplant coordinator who organises the unit and helps to find suitable donor matches.

Personalised psychology services

Psychologists support patients and families in addressing the challenges associated with AML throughout the patient pathway. The psychologists also follow up with patients post treatment if needed.

Access to EMR (IT system)

Patients and their families have online access to their electronic medical record (EMR), including test results and treatment history. The full MDT also has access to the EMR and can coordinate referrals, prescriptions, and patient updates on the system.

Specialised haematology nurses

Nurses are trained in haematology and blood transfusions, and are fully involved in clinical care. As primary contacts for patients, they monitor symptoms and treatment side effects and escalate any concerns. They maintain practical infection control measures (e.g. changing towels daily) and keep symptom logs for inpatients.

Integrated pharmacy services

Pharmacists dispense prescriptions and provide patients with information on usage, dose, side effects, and the importance of treatment adherence. They are the first point of contact for reporting prescription side effects, and they raise any adverse events with the prescribing physician.

Protocol-based care delivery

The centre has established protocols for diagnostic testing, treatment, and infection control. Team roles and responsibilities are clearly defined, as are target timelines. This approach drives timely, efficient care, and helps to minimise the risk of infection for immunocompromised patients.

Access to clinical trials ★

The centre is involved in multiple clinical trials (across phases) through the Polish Adult Leukaemia Group (PALG). This provides access to novel therapies that would not otherwise be accessible to most patients. The head of the haematology department is heavily involved in trial design and participation.

Dedicated laboratory staff ★

A dedicated haematology laboratory team collaborates with the medical team and follows specific protocols and guidelines to support timely diagnosis and treatment decisions. They conduct testing within set timelines and communicate with the clinical team by phone to avoid any delays.

Volunteering programme

A volunteering programme provides support for elderly patients and patients with limited mobility. Volunteers help patients with shopping, errands, and companionship. The programme was particularly beneficial during the Covid-19 pandemic.

Focus on infection control ★

Infection control is critical for AML patients, and the department has implemented strict guidelines to reduce the risk of infection for all patients. Measures are taken to regularly monitor patients for signs of infection, isolate any infected patients, limit the spread of infection, and treat infections with effective and appropriate agents.

Multi-disciplinary care services

The centre provides multidisciplinary care with haematologists, nurses, BMT specialists, laboratory staff, social workers, physiotherapists, psychologists, pharmacists and nutritionists all involved in patient care.

Keys: Awareness and symptom recognition; Diagnosis, classification and prognosis; Treatment and relapse care; Remission; Palliative care; ★ Spotlight intervention

What are the next steps for the centre?

Using Next Generation Sequencing (NGS) for diagnostic testing

Objective

Use NGS to enhance AML diagnosis and classification.

What is the rationale?

Currently, bone marrow biopsy, karyotyping, and molecular testing are used to confirm AML diagnosis and plan treatment, which can be very time consuming. NGS is a faster sequencing method and is expected to significantly change AML diagnostics, as mutations detected by molecular analysis can impact prognostic stratification and treatment decisions. Detection of mutations has influenced recent updates to AML disease classification by WHO.(1)

How to implement it?

NGS is an advanced and a sophisticated method and will require an initial phase of training for the laboratory staff. The haematology department has raised the request with the centre's management to obtain NGS and hopes to implement it in the haematology lab soon.

Expanding available space

Objective

Expanding physical space of the department and providing beds for more patients.

What is the rationale?

Space is a key challenge in the department, with more beds needed and more space added in between existing beds. Expanding the available space would help to enhance infection control and allow more patients to be treated in the inpatient and day unit settings.

How to implement it?

The centre is under discussions with the health authority and the University administration regarding an expansion of the department. This would require an investment to fund the refurbishment and purchase new beds and equipment.

Sources:(1) Next Generation Sequencing in AML—On the Way to Becoming a New Standard for Treatment Initiation and/or Modulation, NIH, 2019

Spotlight intervention – Advanced BMT services

Overview

- PMU has a **well-organised bone marrow transplant (BMT) unit**, which works with the wider multidisciplinary care team to identify eligible patients, find donor matches, perform transplants, and provide follow-up care

What is it?

- Established BMT unit with dedicated BMT specialists, residents, nurses, and a transplant coordinator that works closely with the AML MDT

How does it work?

- The team is highly organised with **clear alignment of roles and responsibilities**. The transplant coordinator manages the transplant schedule and works with the team to ensure that the unit runs smoothly
- There are **two meetings every week to discuss AML transplant cases.** The first meeting includes the transplant coordinator and stem cell bank colleagues to plan logistics with the lab, and the second meeting is focused on discussing patient eligibility for transplant
- Additionally, **a forum is conducted once a week where AML patients from across Poland are discussed** and considered for transplant if eligible
- The transplant process involves the search for a donor match, a checkup to see if the disease is in remission, conditioning chemotherapy started 7-10 days before transplant, inpatient transplant and recovery, and discharge if there are no adverse events

What are the potential benefits?

- **Benefit for patients:** Regular team meetings **ensure access to transplant for eligible patients, no delays, and transplant coordination enhances the efficiency of the transplant process**
- **Benefit for the AML team: Structured care delivery with defined roles and responsibilities** increases work efficiency, and allows the team to offer a high number of transplants

> “The bone marrow transplant unit is well established and a leading centre in Poland. They have a dedicated care team with a strong focus on patients
>
> Haematologist

Spotlight intervention – Dedicated laboratory support

Overview

- Developed **a dedicated haematology lab that follows set protocols and works collaboratively with the clinical team** to support timely diagnosis and treatment decisions

What is it?

- The department has dedicated haematology laboratory staff members to support the diagnosis, risk rating, and treatment decisions for AML patients

How does it work?

- Haematology laboratory staff follow a **protocol-driven approach to ensure timely results to support diagnosis and treatment decisions**, which is essential for AML patients given the nature of the disease. There are defined timeline targets for each test, e.g. each bone marrow culture must be completed within 24 hours
- The clinical team directs the type of testing to be conducted for each sample. **Coordination between the clinical team and the lab team via cell phones helps to avoid delays in communication**
- Karyotyping is used for diagnosis, with MPM-1 and FLT-3 gene results completed within 48 hours, and total karyotype results available in 2-3 weeks. T**he lab classifies patients as low, intermediate, or high risk** and this impacts the clinical team's treatment decisions

What are the potential benefits?

- **Benefit for patients:** Timely testing leads to **faster diagnosis and treatment initiation** for patients, which is critical given the nature of the disease
- **Benefit for the AML team:** The protocol-driven approach for testing and diagnosis establishes **clear targets and timelines for the team**. Strong communication and collaboration between the lab and clinical team supports **integrated care delivery**

> "There is good cooperation between the clinical team and the lab
>
> Cytogeneticist

Spotlight intervention – Focus on infection control

Overview

- Infection control is critical in AML patient management, and infection control specialists outline **strict guidelines to help prevent and contain the spread of infection**

What is it?

- The haematology department is **supported by infection control specialists, nurses, and a dedicated cleaning team** to minimise the risk and spread of infection amongst AML patients

How does it work?

- The department has implemented and follows clear **guidelines for management of infection**, and there is a trained cleaning team dedicated to the haematology department
- Infection control specialists are responsible for **detecting signs of infection and monitoring at-risk patients on a regular basis**
- **If an infection is identified, the patient is isolated**, and the ward (including the water supply) is decontaminated by the specially-trained cleaning team. **Antibiotics are chosen based on microbiology results**, and nurses manage patient care in isolation
- Twice a year there is a meeting with the microbiology team, haematology team, and transplant team to **discuss the department's infection profile and review the antibiotic regimen**
- Oher initiatives introduced to reduce infections include **hand hygiene guidelines, single use products on the ward, personal protective equipment (PPE), sanitised short-sleeved scrubs provided by the hospital**, and regular staff training on infection control

What are the potential benefits?

- **Benefit for patients:** Regular check-ups and isolation of infected patients **reduces the risk of infection and improves patient outcomes**
- **Benefit for the AML team**: Implemented protocols, training, and collaboration with the microbiology **decreases patient complications**

> "We regularly monitor each patient's symptoms, ensuring isolation of infected patients
>
> Infection control specialist

Centre specific report: Poznań Medical University

Spotlight intervention – Access to novel therapies through clinical trials

Overview

- The haematology department is **focused on conducting research and is involved in various clinical trials** (both trial development and participation)

What is it?

- The department supports multiple clinical trials (across all clinical phases) to increase access to novel therapies

How does it work?

- The head of the Department of Haematology and BMT has been involved in a number of clinical AML studies. **The clinical team evaluate the design of each study** when deciding if it is a good fit for the centre or not (considering their patient cohort)
- The centre participates in studies through the Polish Adult Leukaemia Group (PALG), Spanish Adult Leukaemia Group, and other channels. Currently there are 30 clinical trials ongoing in the haematology department, with four AML studies recruiting
- **Physicians work with the pharmacists, who coordinate preparation and transfer of medications** used in clinical trials (including investigational drugs)
- **Novel therapies can take up to 2-3 years to be included under public reimbursement post approval.**(1) **Clinical trials can provide access to novel therapies which are not yet reimbursed**, and the majority of eligible patients agree to participate in trials if given the opportunity

What are the potential benefits?

- **Benefit for patients:** Participation in clinical trials **allows patients access to novel therapies** which would not otherwise be accessible
- **Benefit for the AML team:** Involvement in research provides **continued learning experiences for the team, and the opportunity to stay current with the latest treatment options for AML**

Sources: (1) State of Health in the EU, Poland;

> Novel AML treatments are not always seen as a priority necessarily since the patient group is relatively elderly. Currently, novel therapies are only available through clinical trials
>
> Haematologist

Policlinico Sant'Orsola, Bologna, Italy

Site visited by KPMG, 30th June 1st July 2022

Centre overview

Centre summary

Centre type: Public hospital

Catchment area: The centre is located in central Bologna and receives patients from across the Emilia-Romagna region and Italy

Funding: Provides care for patients funded through the Italian public healthcare system, Servizio Sanitario Nazionale

Services: Haematology, bone marrow transplant (BMT), clinical pathology, translational research, clinical studies, radiology, allied healthcare services, and palliative care

Patient population: 80-100 AML patients per year

Key strengths in delivery of AML care

Reference centre: Sant'Orsola is both a national and international reference centre for AML, with experienced specialists, a high volume of AML patients, and the academic recognition of IRCCS(a) for clinical research in AML

Access to innovative therapies through clinical research: The physicians, laboratory staff, and data managers work closely on research projects and ensure enrollment of patients in numerous clinical studies. The centre's involvement in research increases access to many alternative and innovative therapies for AML patients

Humanised care: The care team understands the impact of AML on patients' lives and works sensitively to address the specific needs of each patient. Close and trusting relationships are built with both patients and caregivers throughout treatment and follow-up

Key challenges faced in delivery of AML care

Burden of care on regional reference centres: There is a need to increase collaboration between the network of reference centres and smaller centres to share AML standards of care, protocols, and guidelines. This will enable smaller centres to manage less complex AML patients

Complexity in diagnosis and treatment: AML patients require immediate diagnosis and treatment as they may be unstable and frail. It is operationally difficult to perform multiple tests and create personalised treatment plans with high accuracy. The treatment options can be limited due to patients' eligibility based on age and comorbidities

Dispensing prescriptions under tight timelines: Prescriptions need to be dispensed in a short turnaround time, but also need to undergo cost-effectiveness evaluation in line with summary of product characteristics (SmPC) guidelines. Ensuring necessary evaluations while dispensing drugs in a timely manner can be challenging in practice

Acute Myeloid Leukaemia (AML) in Italy

Healthcare system overview[1]

Structure: The national health service (Servizio Sanitario Nazionale; SSN) is responsible for basic healthcare benefits and providing budget guidance to 19 regions and two autonomous provinces in Italy.

Insurance and funding: Healthcare services are covered by the SSN, which is largely funded through central and regional taxation. The role of private health insurance is limited. Regions are responsible for the management of primary, secondary and tertiary care, public health, and social care. Depending on the availability of funds, each region can provide additional services that are not covered in the national statutory benefit package, "essential levels of care" (LEAs), as set by the Ministry of Health (Ministero della Salute).

The quality of care and services provided is not always consistent across different regions, resulting in significant cross-regional patient travel, notably for tertiary care. Tertiary hospitals manage their own budgets (within regional guidelines), independent of the 140+ local health authorities (ASLs).

Primary care is provided by contracted self-employed and independent GPs and paediatricians, who refer patients to public or private tertiary hospitals for specialist care when needed. AML treatment and management of the disease is delivered by specialists both in public and accredited private hospitals.

Guidelines and societies[3]

Guidelines: European society of medical oncology (ESMO) and European Leukemia Net (ELN)

Professional bodies: Italian Society of Hematology (SIE), Italian Society of Experimental Hematology (SIES), and the Italian Group for Bone Marrow Transplantation (GITMO), European Society for Blood and Marrow Transplantation (EBMT)

Patient association groups (PAGs): Leukemia Patient Advocates Foundation and Associazone Italiana Contro Leucemie Linfomi e Mielloma (AIL)

Statistics

	Italy	World		Italy[5],[7]	World[6],[8]
Cancer incidence[4]	292*	201*	Patient: physician ratio	125	556
AML incidence[2],[3]	35*	30*	% GDP spend on healthcare	9.5	10
Public healthcare spend (% of all health expenditure)				76	60

Sources: (1) The Commonwealth Fund; (2) American society of clinical oncology; (3) The economist ; (4) World Health Organisation Global Cancer Observatory, 2020; (5) The World Bank Databank, (6) Data bank – global, (7) Statista, (8) WHO, global spending on health,

* Public healthcare is accessible to all Polish citizens, people staying temporarily in the country, residents of European Union countries and the European Economic Area; **Per 1,000,000 individuals

The centre and AML unit

The centre	
Centre type	• Public hospital
Size	• 1,515 total beds in the centre, with ~42-43 beds dedicated for haematological cancer patients
Setting	• Inpatient and outpatient units
Catchment area	• The centre is located in central Bologna and receives patients from across the Emilia-Romagna region and Italy
Affiliation & accreditations	• Accredited by Joint Commission International (JCI), affiliation with the School of Medicine and Surgery of the Alma Mater Studiorum – University of Bologna, collaboration with Italian Association for Leukemia, Lymphomas, and Myeloma (AIL, Associazone Italiana Contro Leucemie Linfomi e Mielloma), and recognised as a Scientific Institute for Research, Hospitalization and Healthcare (IRCCS, Istituto di Ricovero e Cura a Carattere Scientifico) through ministerial listing

The AML unit	
Patient cohort	• 80-100 AML patients per month
Team	• Medical team is made up of haematologists, haematology nurses, clinical laboratory staff, pharmacists, and data managers
Services offered	• Comprehensive oncology services including diagnosis, treatment, palliative care, and innovative therapies through clinical studies
Guidelines used	• Gruppo Italiano Malattie Ematologiche dell'Adulto (GIMEMA) and Regional Group of Oncological Drugs (GREFO)
Facilities on site	• Facilities include clinical pathology and laboratory equipped to perform cytogenetic testing, proliferative molecular analysis, and translational research, radiology, chemotherapy, and BMT

The team

Core specialists

- 12 ▶ Haematologists
- 04 ▶ BMT specialists
- 20 ▶ Haematology residents

Wider clinical team

- 50 ▶ Haematology nurses
- 3 ▶ Psychologists

Allied health professionals

- Pharmacists
- Physiotherapists
- Dieticians

Other ancillary personnel

- Translational research scientists
- Data managers
- PhD candidates and postdoctoral fellows

Governance and processes

Team meetings

Weekly AML meetings involving physicians, study coordinators, and lab-based researchers are held to align on patient treatment plans. Data managers and physicians also conduct a monthly meeting to discuss and agree patient allocation to clinical studies.

A weekly meeting is held with the home care assistance team to discuss outpatients.

Patient records

Patient's medical records are documented primarily on paper. There is a portal to record clinical details (e.g. management, prescriptions, and any treatment complications) for patients enrolled in clinical studies.

Pharmacy

The pharmacy liaises with both clinical and research teams including physicians, nurses, and translational laboratory specialists. They are responsible for dispensing drugs and tracking inventory levels with nurses in the wards, recording side-effects and adherence to treatment, and managing the 'investigational drug service' for experimental drugs.

Roles and responsibilities of the team

Haematologist

- Coordinates activities across the centre and handles all institutional responsibilities for haematology
- Attends to hospitalised patients in the ward and outpatients at the day hospital
- Leads the clinical research laboratory alongside other laboratory specialists to drive molecular research focused on the tumour microenvironment in AML

Haematology nurse

- Provides nursing care for inpatients and outpatients at the hospital
- Provides guidance to patients on hygiene standards to minimise the risk of infections
- Schedules training sessions with physicians to increase the understanding of new therapies and molecules across the medical team
- Organises training for new nursing staff

Pharmacist

- Dispenses and administers prescriptions to patients
- Provides guidance on medication usage, dosage, and potential side-effects
- Collaborates with the clinical team to identify suitable drug treatment for each patient, and prepares oral and intravenous therapies for administration
- Works jointly with physicians and AIFA(a) to obtain approval for therapies currently under development for patients who are not responding to conventional therapies
- Ensures administration of anti-collateral drugs to patients to manage side-effects

Research lab specialist

- Liaises with laboratory teams (e.g. morphology, cytogenetics, immunology), medical team, and data managers to discuss outcomes and ensure alignment for patients enrolled in clinical studies
- Interfaces with the clinical research team and nurses to ensure specimens for the study are retrieved on time
- Performs analytical tests to characterise the markers in AML patients (defined by ELN[b] or WHO[c] that are used as parameters for diagnosis, therapy selection, and prognosis
- Drives translational research oriented towards cell biology, HSCs[d], and tumour microenvironment to understand each patient's response to drugs and chemotherapy

Data manager

- Manages new and ongoing clinical studies end-to-end
- Ensures biological samples are retrieved and required data is recorded in a timely manner
- Works jointly with clinicians and study coordinators to identify eligible patients based on the enrolment criteria for each study
- Organises and schedules appointments for each patient, and coordinates appointments with other clinics to minimise the number of visits to the centre for patients travelling long distances

Psychologist

- Supports patients and families in addressing challenges associated with AML throughout the patient pathway
- Helps patients work through the shock of initial diagnosis, fear of death, financial concerns, and social isolation
- Facilitates conversations to discuss concerns and suggests relaxation and visualisation techniques to improve anxiety and stress

Additional team members

- PhD candidates and postdoctoral fellows: Collaborate with residents and physicians in the medical team to create a close working relationship and ensure management of trial and non-trial activities for AML patients enrolled in clinical studies

Notes: (a) AIFA: Agenzia Italiana del Farmaco – the Italian medical agency, (b) ELN: European leukaemia network, (c) WHO: World health organisation, (d) HSCs: Haemopoietic stem cells

Challenges faced in AML care delivery

Burden of care on regional reference centres

- As a regional reference centre, Sant'Orsola receives a large volume of AML patients from smaller centres, and is typically responsible for all aspects of AML patient care
- There is a need to increase collaboration between the regional reference centres and smaller centres to share AML standards of care, protocols, and guidelines. This will enable smaller centres to manage less complex AML patients, and reference centre to focus more on initial diagnosis, complex cases, and clinical studies

Extensive procurement process for laboratory equipment

- Lab specialists are required to deliver results, within 24-48 hours in emergency cases. Access to innovative technology (e.g. next generation sequencing, NGS) to increase sensitivity, specificity, and turnaround time of assays is limited due to the complexity in obtaining new instruments
- The requirement to hold a European-level tender for the procurement of high value instruments and reagents and the lengthy approval process are some of the major barriers

Fragmentation in multidisciplinary team (MDT) meetings

- Weekly meetings do not always include the full nursing team due to scheduling conflicts and the perception that attendance may increase overall workload
- Effort may be duplicated as information from the weekly team meetings must be passed on from attendee (head nurse) on to the rest of the nursing team

Dispensing prescriptions under tight timelines

- Prescriptions need to be dispensed quickly, but also need to go through cost effectiveness evaluation in line with the summary of product characteristics (SmPC) guidelines
- Managing the necessary evaluations for each prescription while dispensing medication in a timely manner can be challenging in practice

Complexity in diagnosis and treatment

- AML patients may be unstable and frail, and they might require immediate diagnosis and treatment. It can be operationally difficult to perform multiple tests and create personalised treatment plans with high accuracy
- There can be further clinical limitations in creating a personalised and effective treatment plan based on patients' age and comorbidities

> The center will have to implement changes that allow effective management of patients, who from year to year are increasing in number, also in consideration of the reference role played by the centre

Overview of AML patient pathway

Awareness and symptom recognition

- **Awareness campaigns** are carried out in **collaboration with AIL[(a)]** to increase patients' general understanding of results, diagnosis, and treatment options

Diagnosis, classification, and prognosis

- Patients presenting with AML-associated symptoms (e.g. bleeding, haemorrhage, fever) are either referred in by **primary care**, or presented to the emergency room directly
- Complete blood count results are ordered in either setting
- **Bone marrow aspiration** is performed, and samples are sent for cytogenetic testing, immunophenotyping, and proliferative molecular analysis
- **Genetic tests** are performed to understand if the patient has a **familial predisposition**. This will inform donor eligibility down the line
- Patients are **classified as 'fit', 'unfit', or 'frail'** based on their age and geriatric score
- Physicians conduct **pre and post-test counselling** sessions to explain the suggested treatment protocol and the prospects of a transplant

Treatment (intensive + non-intensive) and relapse care

- Treatment intensity is decided according to **clinical parameters**, including the presence of relevant comorbidities. The Ferrara score is used to assess fitness for chemotherapy and non-intensive therapies
- **A number of specialists** including anesthesiologists, infectious disease specialists, cardiologists, and microbiologists are involved in the care early on to **limit the risk of infections and cardiotoxicity**
- Approximately half of the patients begin **risk-based chemotherapy**, and patients who test positive for FLT3 mutations are also started on targeted inhibitor therapy
- Patients that undergo chemotherapy are **periodically reevaluated** to assess if they are 'fit' for transplant
- High-risk patients who are classified as 'fit' are immediately **referred for allogenic bone marrow transplant (BMT)**
- ~5-10% of patients aged over 80 years are not prescribed any treatment, while some patients classified as 'unfit' do undergo conventional chemotherapy
- Patients are also **offered enrollment in clinical studies as appropriate** after diagnosis, without waiting for the failure of conventional therapeutic options

Remission

- Follow-ups occur **weekly (for transplant patients) or biweekly (for patients who do not undergo transplant)** followed by monthly, quarterly, and yearly check-ups
- Patients who undergo BMT receive **consolidation therapy**
- Patients who achieve **molecular remission** may not require further induction therapy
- Although rare, young patients who undergo autologous transplant are first started on **intensive chemotherapy**, and stem cells are collected for reinfusion
- If relapse occurs, **diagnostic investigations are repeated**, and patients are reassessed before initiating relapse treatment

Palliative care

- **End of life care** is advised only for patients who become unresponsive to all available treatment options
- **Home-based palliative care** is offered to provide pain management, monitor lab results, and offer additional support (e.g. transfusions)
- Many patients remain under the care of the haematologist until the end as it is more of an **interventional culture**

Notes: (a) AIL: Associazone Italiana contro leucemie Linfomi E Mielloma

Interventions and good practices across the care pathway

Recognised as an IRCCS(a) centre

Sant'Orsola runs numerous clinical studies and is a specialised centre for research in transplantation and integrated medical and surgical management of oncological diseases. The institute was recognised as an IRCCS[(a)] in this specialty in 2020 through a ministerial listing.

Translational research

Haematologists lead the translational research laboratory with other laboratory specialists to conduct research oriented towards cell biology, haemopoietic stem cells, and investigational drugs. The aim is to drive molecular research to understand the immunological microenvironment and mechanisms that drive leukaemia.

Genetic screening of high-risk patients

Sant'Orsola has set up a medical genetics service to perform genetic analysis for high-risk patients and their family members. The evaluation aims to identify certain common mutations seen in leukaemia and understand the presence of a familial predisposition.

Adherence monitoring ★

Pharmacists act as a point of contact for patients once the treatment is prescribed. They provide detailed information on drug dosage, possible side-effects, and indications for ancillary support. Treatment adherence is monitored regularly.

Home therapy in collaboration with AIL[(b)] ★

Sant'Orsola collaborates with AIL(b) to provide home therapy for many patients, including AML patients. AIL(b) has signed an agreement with the public healthcare system, Servizio Sanitario Nazionale (SSN), and is able to perform transfusions, administer therapies, and conduct counselling sessions for patients at home.

Management of complications ★

Pharmacists are actively involved in the management of any therapy-related complications. They work closely with physicians to help manage side effects, and report adverse events to the health authorities as needed. This collaboration is facilitated by the hospital's digital platform.

Integrated care ★

Haematologists collaborate with primary care physicians who review and approve patients for home care through AIL(b). Weekly meetings are conducted between the home care association and Sant'Orsola, and reports from each home visit are circulated to ensure transparent communication between the teams.

Access to innovative therapies ★

Sant'Orsola is recognised as an established centre and is often approached to take part in clinical studies, and physicians actively seek studies that may offer benefit to patients. The centre is able to provide increased access to innovative therapies through participation in numerous clinical studies.

Management of clinical studies ★

Data managers and clinical coordinators work with physicians, pharmacists, nurses, and laboratory specialists to ensure enrollment of eligible patients in studies, collection and analysis of biological specimens, and administration of drugs. They also track patients' clinical progress and any adverse event as they undergo treatment.

Keys: Awareness and symptom recognition; Diagnosis, classification and prognosis; Treatment and relapse care; Remission; Palliative care; ★ Spotlight intervention

Notes: (a) IRCCS: Istituti di Ricovero e Cura a Carattere Scientifico, (b) AIL: Associazone Italiana contro leucemie Linfomi E Mielloma

Interventions and good practices across the care pathway

Management of trials database

Data managers are required to capture and track data on patients' enrollment, clinical history, demographics, and trial results in a database provided by the pharmaceutical companies for each study. Timely enrollment of adequate number of patients from the centre is required to ensure inclusion in each study and any resulting publications.

Interdisciplinary care ★

Patients are monitored and cared for by a team of various specialists including anesthesiologists, infectious disease specialists, cardiologists, and microbiologists. The aim is to prevent and proactively manage infection, comorbidities, and any complications arising from treatment.

Investigational drug services

Sant'Orsola has created an investigational drug service led by pharmacists. They manage interactions with pharmaceutical companies and conduct pre-monitoring visits for experimental drugs (which are increasingly common at the centre). Pharmacists also assist physicians in raising requests for non-conventional therapies.

Collaboration between data managers and physicians

Physicians and data managers conduct weekly meetings to discuss patients, align on treatment protocols, plan activities, and address any concerns (e.g. timelines). A monthly meeting is organised where case studies are presented, and data managers share clinical data and any guidelines updates.

Open patient communication ★

Physicians and clinical staff communicate openly with patients throughout treatment and build strong relationships. This helps to monitor each patient's condition throughout treatment, increases treatment adherence and clinic attendance, and contributes to an improved patient experience overall. Patients enrolled in clinical trials submit feedback regularly through questionnaires, which help guide clinical decisions.

Patient database

Sant'Orsola maintains a database to record patient details. Patients are grouped based on their specific pathology, and parameters relevant to each patient's clinical needs (e.g. the presence of sepsis, drug toxicity, comorbidities, mobility, etc.). The data informs the specific needs of each patient and enables personalised and tailored care.

Prescription management

Pharmacists evaluate each prescription in line with summary of product characteristics (SmPC) guidelines to assess if a drug is both appropriate and cost-effective. They regularly review expenditure to ensure drug availability within the annual budget.

Patient support

AIL(a) and ADMO(b) conducts seminars to bring together AML patients through an open forum. The aim is to encourage the patients to share their experiences with the treatment and concerns associated with the disease.

Support houses for accommodation

AIL(a) has established 'Casa AIL', a support housing network with 15-16 double occupancy rooms dedicated for Sant'Orsola's patients. The set-up enables free accommodation near the hospital for patients and families who live far from the centre.

Keys: Awareness and symptom recognition; Diagnosis, classification and prognosis; Treatment and relapse care; Remission; Palliative care ★

Notes: (a) AIL: Associazone Italiana contro leucemie Linfomi E Mielloma, (b) ADMO: Associazione Donatori di Midollo Osseo

What could further drive excellence in care at the centre

Enhance psychological support

Objective

Enhance psychological support available for AML patients.

What is the rationale?

AML patients can feel overwhelmed and anxious following diagnosis given the severity of the disease and the initial uncertainty around prognosis. Psychological support is an important aspect of care throughout the patient journey, and support should be made available from the early stages of care.

How to implement it?

Setting up consultations with psychologists from the start of the patient journey (e.g. diagnosis) to ensure support is provided and a trusting relationship can be built. Currently, psychological support is primarily offered to patients who do not respond well to treatment, as part of end-of-life care.

Developing infrastructure for remote consultations and communication

Objective

Developing infrastructure for remote consultations and communication.

What is the rationale?

Although AML care needs to be largely delivered in person, there are opportunities to reduce the amount of travel required for some touchpoints between patients and the care team. Implementing remote consultations would help minimise travel for patients, and make interactions with the care team easier.

How to implement it?

Introducing technology, tools, and dedicated time for a small number of remote consultations. For patients who have access to a computer or smart device, video consultations may be possible, and telephone consultations can be considered where this is not an option.

Spotlight intervention – Management of complications and adherence monitoring

Overview

- Pharmacists play an **integral role in the care pathway** and provide support in many aspects of treatment

What is it?

- Pharmacists collaborate with clinicians, laboratory specialists, and patients. They support with the **management of complications and adherence monitoring**

How does it work?

- Pharmacists evaluate each **prescription** and ensure all necessary details required to raise requests for prescribed drugs are documented
- They **maintain direct contact with the prescribing physician** to track and record any change in dose or frequency before dispensing the drug
- They **provide detailed information** on each medication's dosage, use and side-effects, and provide anti-collateral drugs to reduce side-effects
- They **ask a series of questions at various touchpoints during the treatment** to understand patients' experience with the drug and any side-effects, and **verify adherence**
- They act as a **point of reference for patients** and are actively involved in monitoring complications and side-effects, and they notify the treating physician as appropriate

What are the potential benefits?

- **Benefit for patients:** Frequent touchpoints with the pharmacist **enables effective management of side-effects and ensures smooth treatment journey for patients**. Patients have an accessible point of contact in between appointments with their treating physician
- **Benefit for the AML team:** Close collaboration with pharmacists enables **adherence monitoring and triage of priority drug side-effects or adverse reactions**

> "The role of the pharmacist must also be rethought; evolving from a simple drug dispenser into a clinical pharmacist
>
> Pharmacist

Spotlight intervention – Home therapies in collaboration with AIL(a) and integrated care

Overview

- **Sant'Orsola collaborates with the 'AIL(a)'**, a patient advocacy group to provide home-based care and support for it's AML patients

What is it?

- **'AIL(a)'** has an agreement with the public healthcare system, Servizio Sanitario Nazionale (SSN) and is **approved to deliver home-based care in Italy**
- **Sant'Orsola collaborates with 'AIL(a)' to provide therapies and counselling support** to its AML patients at home

How does it work?

- **Haematologists provide documentation to patients to raise requests** for home care through primary care physicians
- **Primary care physicians approve the requests for home-based care** and maintain direct contact with home care associations throughout treatment
- **Weekly meetings are conducted** with members from the home care association and the medical team at Sant'Orsola **to ensure alignment on each patient's care**
- **Emails and visit reports** are shared digitally to ensure transparency in communication across teams
- **AIL(a) ensures the administration of transfusion and drug therapies**, and provides **counselling support** for patients at home

What are the potential benefits?

- **Benefit for patients:** Administration of care and counselling support at home **minimises the need for patients to travel to the centre**, and allows them to remain in the comfort of their homes
- Benefit for the AML team: Collaboration with AIL(a) enables the management of some of the patients at home resulting in **reduced hospitalisation and patient load at the centre**

Notes: (a) AIL: Associazone Italiana contro leucemie Linfomi E Mielloma

> "The intravenous infusions must be done for five consecutive days for elderly patients; therefore, clinicians try to have the treatment delivered at home through the support of AIL(a) and minimise the travel for the patients as much as possible
>
> Pharmacist

Spotlight intervention – Management of clinical studies and access to innovative drugs

Overview

- Sant'Orsola **participates in a number of clinical studies** and has established dedicated teams and services to enable close management of ongoing and new projects

What is it?

- Sant'Orsola is recognised as an IRCCS[(a)] centre and runs numerous clinical studies in partnership with pharmaceutical partners to drive research on innovative therapies
- It has **created a dedicated centre for investigational drug service**, and established a **team of clinical coordinators and data managers** for clinical studies

How does it work?

- Clinical study coordinators and data managers work closely with physicians to **identify eligible patients to be enrolled in clinical studies** based on the defined criteria
- Data managers collaborate with pharmacists, nurses, and laboratory specialists to **schedule appointments, coordinate the collection and analysis of biological specimens, and ensure administration of drugs**
- The clinical studies **are also open to patients outside the Sant'Orsola**. Physicians from other centres can liaise with the centre to have their patients enrolled in a study if appropriate
- **Principal investigators monitor and record adverse effects** and notify clinical teams and pharmaceutical sponsors of any adverse events

What are the potential benefits?

- **Benefit for patients:** Extensive clinical research at the centre offers the opportunity to participate in clinical studies and **access to alternative treatment options, including innovative therapies and drugs**
- **Benefit for the AML team:** The team **is at the forefront of clinical research and** is kept abreast of innovation in AML treatment. Once new treatment modalities become available as part of day-to-day clinical care, the **team is already upskilled** from their participation in the studies

Notes: (a) IRCCS: Istituti di Ricovero e Cura a Carattere Scientifico

> "Doctors are heavily invested in clinical research, and closely collaborate with pharmaceutical partners. The hospital is considered as a center of excellence for research because they manage to stratify patients relatively well with respect to the currently active clinical trials
>
> Data manager

Spotlight intervention – Translational research

Overview

- Sant'Orsola has a **dedicated translational research lab** equipped to perform research on cell biology, haemopoietic stem cells, and investigational drugs

What is it?

- The lead haematologist works jointly with a laboratory specialist, four postdoctoral fellows, and a few PhD students in the translational research lab. The laboratory team **aims to dive into molecular research to understand the immunological microenvironment and mechanisms in leukaemia**

How does it work?

- The current research is focused on **cell biology, hematopoietic stem cells, and the impact of chemotherapy on the immune system**
- As patients themselves are not enrolled in these research studies, the laboratory team use **samples from the patients that have previously been diagnosed or treated** at the centre, after obtaining their consent
- The laboratory team liaises with the medical team that carries out clinical research projects as well as laboratory staff, and nurses to retrieve specimens for their research
- They collect and maintain data for each active line of research and **share their insights with other professionals at meetings and conferences**

What are the potential benefits?

- **Benefit for patients:** Extensive in-house research benefits the AML community and patients overall, aiming to identify new treatment approaches for AML and other pathologies
- **Benefit for the AML team:** Collaboration with the translational research team provides a ground for cross-functional knowledge sharing on innovation in AML

> "There is a significant amount of investment in both improving care and research. The centre provide accessibility to patients and specimens with a open-minded view on research, a practice that's not very common in every centre in Italy
>
> Laboratory specialist

Spotlight intervention – Interdisciplinary care and open patient communication

Overview

- The **medical team collaborates with healthcare professionals across specialties to** ensure timely management of complications, improve treatment adherence, and provide holistic care

What is it?

- **Prescribing physicians and nursing team jointly work with a team** of specialists including cardiologists, microbiologists, and infectious disease specialists
- The team conducts **interdisciplinary assessment of patients**, ensures timely **management of complications**, and **enables enhanced communication between patients and the clinical team**

How does it work?

- **Cardiologists** evaluate the presence of cardiovascular risk factors in patients planned to undergo treatment with cardiotoxic therapies
- **Microbiologist and infectious disease specialists assess patients** to identify infection and any potential risks to the treatment
- **Prescribing physicians and clinical staff maintain frequent touchpoints** throughout the treatment to assess patients' response to therapies, associated impact on appetite, and their psychological and emotional well-being
- **Physician and nurses connect regularly with patients** to understand their evolving condition, and ensure timely clinic attendance

What are the potential benefits?

- Benefit for patients: Regular touchpoint with various specialists and clinical team enables **timely reporting and solutioning of treatment-associated complications**
- Benefit for the AML team: Interdisciplinary evaluation and close working relationship amongst HCPs **allows the team to make better treatment decisions and improve quality of care delivered**

> "Patients feel good because they can communicate to any difficulty to the medical team, not only on the clinical aspect but also on the emotional level. This creates a basis of a very trusting relationship between the patient and the clinical team
>
> Head nurse

Notes: (a) IRCCS: Istituti di Ricovero e Cura a Carattere Scientifico

Institute of Hematology and Blood Diseases Hospital, Tianjin, China

Site visited by KPMG 27th June 2022

Centre overview

Centre summary

Centre type: Non-profit, public hospital

Catchment area: The centre provides care to patients primarily coming from Northeast regions of the country including Heilongjiang, Jilin and Liaoning, Shaanxi, and Henan. Some patients also come from Eastern and Western provinces (e.g. Anhui, Shandong, Jiangsu, Inner Mongolia) in China

Funding: The centre is primarily publicly funded

Services: Clinical haematology, bone marrow transplant (BMT), advanced clinical laboratory, radiology, and allied healthcare services

AML Patient population: 35 AML patients per week and 2,000 AML patients per year

Key strengths in delivery of AML care

Well-defined protocols and guidelines: The centre has adopted care protocols that outline clear guidance across the care pathway and the roles and responsibilities of each team member. Guidelines are regularly reviewed to ensure that they are up to date with the latest developments in AML care

Patient-centered care: The centre has a strong focus on patient education and engagement throughout each step of the patient journey. This has resulted in high level of trust and confidence in care, with a large volume of patients travelling from across the region to access treatment at the centre

Remote communication: The medical team uses multiple channels (e.g. an official IM app, calls, and texts) to connect with patients undergoing treatment and those enrolled in clinical trials. This facilitates a real-time digital link between the team and patients for communication, education, and guidance

Key challenges faced in delivery of AML care

Limited supply of blood transfusion products: There is a gap in supply and demand for blood transfusion products in the region, and it is becoming increasingly difficult to keep up with the growing demand

Prolonged inpatient days: The capabilities to manage post-treatment AML care outside specialised haematology centres are limited, resulting in longer inpatient days and waiting times at the centre

Increased patient volume and limited capacity: The medical team and inpatient ward is running at capacity due to the growing number of AML patients at the centre. AML incidence in China is amongst one of the highest globally[1,2]

Sources: (1) GlobalData, (2) Acute Myeloid Leukemia landscape in Asia-Pacific

Notes: (a) AML: Acute myeloid leukaemia

Acute Myeloid Leukaemia (AML) in China

Healthcare system overview

Structure: The Chinese central government formulates national healthcare legislation, policy, and administration to ensure every citizen has access to basic healthcare services. These laws and policies are implemented by local government at prefecture, county, city, and town levels[1]

Insurance and funding: Employed individuals must enroll in employment-based insurance programs, funded primarily via employer and employee payroll taxes. Urban-rural residents without formal jobs including self-employed people, elderly, and children are offered basic medical insurance through subsidised premiums, partly covered by central and local government funds. Financial assistance through a publicly-funded 'safety net' is offered to individuals who are not able to afford premiums for publicly financed health insurance or out-of-pocket spending. Employers and high-income individuals may purchase private insurance to cover deductibles, co-payments, and high-cost healthcare services not covered through public insurance[1]

Primary care services are provided by rural doctors, community health workers, and family doctors in clinics and hospitals. Referrals from primary care are not mandatory to see a specialist, with a few exceptions in certain localities. Regional hospitals refer patients with certain diseases (including AML) for inpatient specialist care on a case-by-case basis[1]

Guidelines and societies

Guidelines: Chinese guidelines for diagnosis and treatment of adult acute myeloid leukaemia (2017) and Center for International Blood and Marrow Transplant Research (CMBTR) guidelines

Professional bodies: Chinese Journal of Hematology, Chinese Children Cancer Group (CCCG) , and Chinese Children Leukemia Group (CCLG)[2]

Patient association groups (PAGs): There aren't any AML PAGs at the national level in China. Many patients gather in smaller groups regionally and within their respective treatment centres

Statistics

	China	World		China	World
Cancer incidence[3],[6]	201 *	201 *	Patient: Physician ratio [7],[9]	556	556
AML incidence[4],[5]	51*	30*	% GDP spend on healthcare[8],[10]	7.1	10
Public healthcare spend (% of all health expenditure)				72	60

Sources: (1) The Commonwealth Fund; (2) Treatment of childhood cancer in China: (3) Current cancer situation in China (4) Acute Myeloid Leukemia landscape in Asia-Pacific (2021) (5) American society of clinical oncology; (6) World Health Organisation Global Cancer Observatory, 2020; (7) The World Bank Databank, (8) Data bank – global, (9) Statista, (10) WHO, global spending on health,

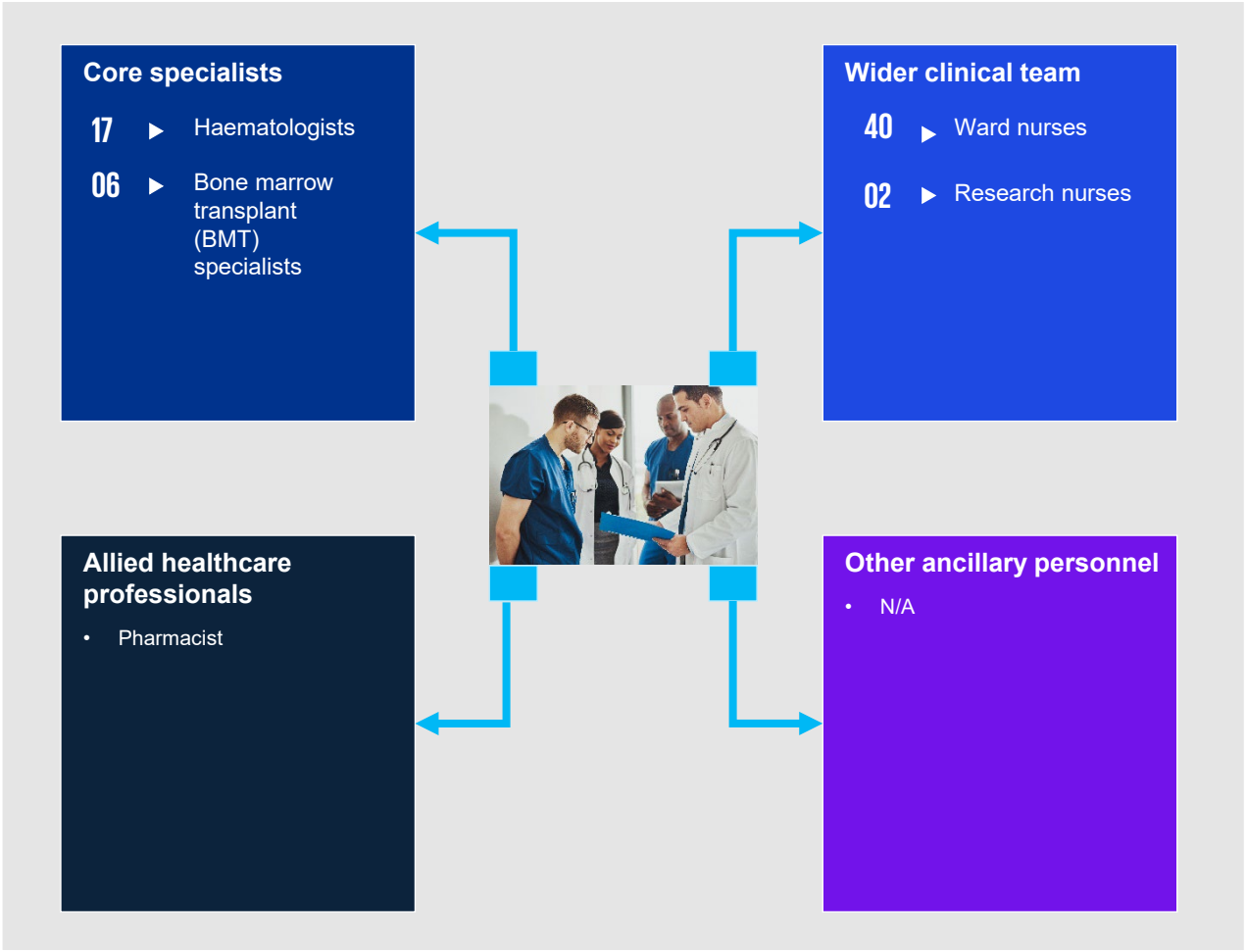
*Per 1,000,000 individuals, **excluded out of pocket expenditure and includes health spend funded by ffinanced by the central and local governments, publicly funded health insurance, private health insurance

The centre and AML unit

The centre	
Centre type	• Non-profit, public hospital
Size	• 700 total beds at the centre with ~240 beds dedicated to AML inpatients and bone marrow transplant (BMT) patients
Setting	• Inpatient and outpatient
Catchment area	• The majority of patients come from the Northeastern region including Heilongjiang, Jilin and Liaoning, Shaanxi, and Henan province. Some patients also come from Eastern and Western provinces (e.g. Anhui, Shandong, Jiangsu, and Inner Mongolia) in China
Affiliation & accreditations	• Recognised as the Base of National Key Discipline on Blood Diseases by Ministry of Education, Clinical Trial Base of New Drugs for Blood Diseases by the State Drug Administration, Member of the World Federation of Hemophilia, and Publisher of the Chinese Journal of Hematology

The AML unit	
Patient cohort	• 35 AML patients per week and 2,000 AML patients per year
Team	• Medical team including experienced haematologists, BMT specialists, specialised nurses, and pharmacists
Services offered	• Comprehensive oncology services including support in detection, diagnosis, and treatment
Guidelines used	• Chinese guidelines for diagnosis and treatment of adult acute myeloid leukaemia (2017) and Center for International Blood and Marrow Transplant Research (CMBTR) guidelines
Facilities on site	• Facilities include radiology, chemotherapy, BMT, and clinical laboratory equipped to perform routine biochemical tests, cytogenetics, karyotyping, HLA typing, FISH, and flow cytometry

The team



Governance and processes

Team meetings

Haematologists organise multidisciplinary seminars to discuss treatment plan for complex cases with BMT specialists and microbiologists on a case-by-case basis

Patient records

A cloud-based system is used to document patients' medical records at the centre. Records detail treatment decisions and prescribed medications (including efficacy and side effects) after each consultation. Paper documents are also available to facilitate record sharing with primary care and other hospitals

Pharmacy

The pharmacy team is responsible for dispensing drugs as well as ensuring sufficient supply and inventory levels of all medications. The team supports physician consultations to provide patients with guidance on medications and side effects

Roles and responsibilities of the team

Haematologist

- Delivers specialist care in oncology and haematology
- Attends to inpatients on the ward and outpatients in the day hospital
- Follows up with patients to monitor progress and symptoms post treatment
- Coordinates activities across the centre and handles all institutional responsibilities including the development of protocols and guidelines for AML treatment

BMT specialist

- Evaluates the patients' eligibility for bone marrow transplant
- Attends all AML patients during the first treatment cycle, including relapsed patients
- Collaborates with haematologists to formulate the BMT plan for each patient
- Performs BMT procedure for eligible patients
- Closely monitors patients following BMT to assess the need for additional treatment and follow up

Ward nurse

- Monitors clinical observations (e.g. blood glucose, blood pressure and oxygen saturation), documents results for these parameters, and administers chemotherapy infusion
- Administers treatment according to prescribing physicians' instructions and explains drug efficacy indicators (e.g. tumor burden) and dietary precautions to patients
- Works with prescribing physicians to manage drug complications and adverse effects including gastrointestinal and systemic reactions
- Manages ward supplies and the distribution of relevant drugs and medical devices

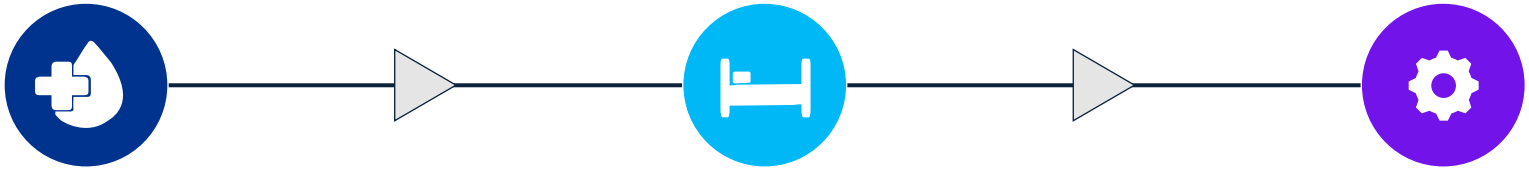
Pharmacist

- Manages the supply and inventory level for all the drugs related to AML
- Supports physician consultations to provide patients with guidance on medications and side effects
- Documents medical records related to medications used, efficacy, and side effects in the cloud-based system
- Maintains contact with patients through virtual communication channels (e.g. chat groups on an official IM app) to ensure treatment adherence

Research nurse

- Manages clinical trial data and enrollment of patients in ongoing clinical trials
- Maintains records of all complications faced by patients enrolled in the clinical trials, and reports any adverse events
- Connects virtually with patients enrolled in clinical trials to collect data on symptoms, adverse effects, and patients' overall wellbeing

Challenges faced in AML care delivery



Limited supply of blood transfusion products

- There is a gap in demand and supply for blood transfusion products in the region and it is becoming increasingly difficult to meet the growing demand for blood products
- The insufficient supply of transfusion products can lead to critical challenges in patient safety

Prolonged inpatient days

- Patients stay at the centre for prolonged periods due to limited capabilities to manage post-treatment care for AML outside specialised haematology centres (this may include blood transfusion support and enhanced infection control)
- Prolonged patient stays can result in a delay in releasing capacity for new patient admissions and an increase in waiting times at the centre

Increased patient volume and limited capacity

- The medical team and inpatient ward is running at capacity due to the growing number of AML patients at the centre. AML incidence in China is amongst one of the highest globally with ~30,000 new AML cases in 2021, and it is forecasted to reach 40,000 by 2029[1,2]
- Maintaining the target average consultation time for each patient is not always possible, and consultations may run beyond allocated time given each patients' needs
- There is a need to review the size of medical team and inpatient capacity at the centre to meet the growing needs

> Chinese patients have longer hospital stay period as they have to wait until several [prognostic] indicators meet a high standard compared to overseas regions to be discharged
>
> Haematologist

Sources: (1) GlobalData; (2) Acute Myeloid Leukemia landscape in Asia-Pacific

Overview of AML patient pathway

Awareness and symptom recognition

The centre **collaborates with the Tianjin Association against Cancer** to conduct awareness activities aimed at the general public

Diagnosis, classification, and prognosis

Patients generally **arrive at the centre with an initial diagnosis** from local hospitals

Haematologists evaluate patients in the outpatient clinic and order **routine blood tests** (e.g. complete blood count, comprehensive metabolic panel, HLA typing, and coagulation tests)

A bone marrow aspiration is performed for cytogenetic analysis, karyotyping, FISH, genetic testing, and flow cytometry

FISH and genetic mutation analysis results are critical for diagnosis and treatment decisions

Haematologists conduct pre and post-test counselling sessions to explain testing indications and results

Treatment (intensive + non-intensive) and relapse care

Treatment protocol is determined based on each patient's age, comorbidities, physical fitness, risk of potential complications (e.g. infection), and genetic analysis results

All patients under the age of 65 are put on **high-dose chemotherapy combined with targeted therapy** and patients over 70 years of age undergo **low-dose chemotherapy**

The targeted therapy is selected based on **molecular testing results**, performance status (PS) score, and presence of complications

Eligible patients **undergo bone marrow transplantation** based on HLA typing results

~90% of patients are enrolled in **clinical trials**

An **MDT discussion** is organised only for complex cases, to consult with haematologists, BMT specialists, microbiologists, and ICU specialists

Physicians communicate closely with the patients during treatment to **educate them on the disease, treatment, and side effects**

In case of relapse, patients are offered the **option of clinical trial enrolment**. Some patients may be put on targeted therapy combined with a chemotherapy regimen (that differs from their initial regimen)

Remission

~40%-50% of patients undergo **consolidation therapy** to complete remission

Nurses provide **detailed guidance about home care** including diet and activities of daily living, and indicators for in-person review at the time of discharge

Patients typically attend in-person checkups **every quarter**

Physicians maintain **regular touchpoints remotely** through telephone and an official instant messaging (IM) app

Research nurses monitor patients enrolled in clinical trial initially through **monthly check-ins**, and later followed by quarterly follow-ups

Palliative care

Patients eligible for palliative care are **transferred to a local tertiary hospital** for pain management

Interventions and good practices across the care pathway

Protocols and guidelines ★

The centre has developed well-defined protocols that serve as guidelines for healthcare professionals to diagnose, treat, and provide follow-up care for AML patients. The guidelines are regularly reviewed to ensure that they are up to date with the latest developments in AML care

Treatment feedback

Department leads, physicians, and nurses conduct quarterly seminars to gather feedback from patients and families. The team uses a scoring system to assess patients' experiences with the centre's education and awareness activities and inpatient care. Feedback informs potential improvements and changes in practice

Patient education

Physicians and nurses organise educational seminars, social media streaming, and broadcasts for patients and their families. The aim is to raise patient awareness on available therapies and provide guidance on daily care, diet, and address any concerns and complications

Remote communication ★

Physicians and nurses regularly connect with patients undergoing chemotherapy and those enrolled in clinical studies through phone calls and an official instant messaging (IM) app. They conduct these check-ins to assess each patient's condition, symptoms, adverse effects, and their overall wellbeing

Trainings for physicians and nurses

Physicians and nurses organise monthly and fortnightly seminars in addition to collaboration during their shifts. These meetings facilitate sharing of knowledge on important clinical cases, discussion on possible improvements in practice, and training for complication management of new treatments and therapies

Adherence monitoring ★

Physicians and pharmacists maintain direct contact with patients during treatment and follow-ups through personal texts and chat groups created on official IM app. The virtual communication channels allow the team to track and ensure treatment adherence

Access to innovative therapies ★

The centre is one of the leading research centres in China and often approached by pharmaceutical companies to participate in clinical trials. This enables increased participation in clinical trials and access to innovative therapies for patients treated at the centre

Digital medical records

The centre has established a cloud-based system to maintain patients' medical records. The system enables detailed documentation of treatment protocols and management of data (e.g. drugs' side effects and efficacy with different combinations) which is used to perform in-house research on drug tolerance

Complication and comorbidity management

Nurses monitor each patient's condition to identify signs of complications or comorbidities and highlight any concerns to physicians during daily rounds in the haematology unit. Physicians incorporate inputs from these visits to personalise the treatment plan based on each patient's evolving condition

Keys: Awareness and symptom recognition; Diagnosis, classification and prognosis; Treatment and relapse care; Remission; Palliative care; ★ Spotlight intervention

Interventions and good practices across the care pathway

Digital channel for post-treatment patient management

The medical team has a dedicated official instant messaging (IM) app that serves as digital link with the patients. The medical team uses this channel to regularly interact with patients, provide educational information on the disease, send reminders to take medication and order refills, and address any concerns or questions after discharge

Drug safety and efficacy research

Pharmacists conduct research to evaluate efficacy, safety, and risk levels of different drug combinations for patients with varying mutations. The team aims to use results from this research to tailor interventions for patient based on the treatment outcomes and risk categories observed in the study

Drug supply management

Pharmacists work closely with suppliers to track and maintain the inventory levels for relevant drugs. In the event of supply shortages with a current manufacturer, they identify an alternative manufacturer or drug substitute to maintain a steady supply of required drugs

Integration of pharmacists in care delivery

Pharmacists assist physicians during consultations and provide guidance to patients on medication usage, doses, and dietary precautions. This allows physicians to manage the time spent in each patient consultation and increase capacity for more outpatient clinic visits

Management of side effects

The prescribing physician and nursing team work together to manage treatment-associated side effects (e.g. gastrointestinal and systemic reactions). The team follows defined protocols to manage treatment complications and side effects

Multidisciplinary meetings ★

MDT meetings are organised on a case-by-case basis. Treating physicians discuss the case and treatment approach with microbiologists, BMT specialists, and intensive care specialists at the centre. The team may consult with pulmonologists and infection specialists from other centres if needed

Keys: Awareness and symptom recognition; Diagnosis, classification and prognosis; Treatment and relapse care; Remission; Palliative care; ★ Spotlight intervention

What are the next steps for the centre?

Expand the size of the medical team and department

Objective

Expand the size of the medical team and space available in the department

What is the rationale?

The patient load is consistently growing at the centre, with the inpatient ward and medical team often running at capacity. The centre is not always able to provide separate rooms for each patient, which can increase the risk of infection. Since the medical team is managing a high volume of patients, maintaining patient education activities can be challenging with the number of physicians and nurses available at the centre. There is a need to increase the number of beds and review the size of medical team to distribute workload and maintain the high standard of care

How to implement it?

The centre has planned to double its inpatient capacity through a new site that is under development. The new site will enable increase capacity while maintaining high infection control standards. The number of physicians and nurses can be increased to enable adequate time for dedicated patient education and reduced workload on individual HCPs

Develop psychological support services

Objective

Develop psychological support services

What is the rationale?

The current capability to offer psychology support to patients has been limited at the centre. Active engagement with patients to address their psychological and emotional needs throughout diagnosis, treatment, remission, and palliative care can have positive impact on treatment adherence and overall wellbeing

How to implement it?

Collaborate with psychologists at the centre and look to increase the support available to patients

Spotlight intervention – Multidisciplinary meetings

Overview

- The medical team **involves various specialists both from within and outside the centre to ensure multidisciplinary evaluation** on a case-by-case basis

What is it?

- The treating physician collaborates with a number of specialists within and outside the institute to outline the treatment approach for critical and/or complex patient cases

How does it work?

- Each case is evaluated individually to assess the need for multidisciplinary consultation
- Treating **physicians consult with the BMT team**, **microbiologists, and infection control specialists** for patients who are at a higher risk of infections and are planned to undergo BMT
- **Pulmonologists and infection control specialist from other leading centres** are also invited to discuss the treatment plan, if necessary

What are the potential benefits?

- **Benefit for patients:** Multidisciplinary evaluations **enable better management of disease, a personalised treatment plan, and holistic care**
- **Benefit for the AML team:** MDT discussions conducted on a needs basis **improve efficiency** and allow for more flexibility

> [The MDT discussions on a case-by-case basis] maximise efficiency for physicians and enable personalisation of treatment plan with a compact group of specialists
>
> Haematologist

Spotlight intervention – Remote communication and adherence monitoring

Overview

- The centre has **implemented multiple channels to maintain remote communication** with patients and track treatment adherence

What is it?

- The **medical team maintains touchpoints with patients** through texts, phone calls, and an **official instant messaging (IM) app** during treatment and follow-ups

How does it work?

- **Physicians maintain direct contact with patients** through personal texts and chat groups created on an **official IM app**
- Physicians connect **with patients between chemotherapy sessions** to track patients' evolving symptoms and response to treatment
- Physicians and pharmacists **send reminders to patients to take medications and order refills** through the IM app
- **Additionally, research nurses connect with patients enrolled** in clinical studies **through phone calls** to collect data on any adverse events, side effects, symptoms, and their overall wellbeing

What are the potential benefits?

- **Benefit for patients:** Frequent virtual touchpoints with the medical **team leads to a better understanding of the disease and treatment.** Patients are able to report any question or concerns, and **receive prompt and appropriate answers and guidance**
- **Benefit for the AML team:** The virtual communication channels provide a constant digital link with patients and allow the team to **remotely contact and monitor patients, and ensure treatment adherence**

> "Patients at the centre have good compliance in general, and there have been very few cases of discontinuation of follow-up treatment or attendance at follow-up visits
>
> Haematologist

Spotlight intervention – Protocols and guidelines

Overview

- The medical team follows a **standard care protocol for the diagnosis and treatment of AML**

What is it?

- The medical team including haematologists, nurses, and pharmacists follow the well-defined protocols for the delivery of care for AML patients

How does it work?

- The **centre lead and director are key members** involved in developing and regularly updating the protocols based on the latest developments in AML global practices
- The **protocols define clear roles and responsibilities for each healthcare professional** including nurses, physicians, and pharmacists
- The **guidelines provide specific parameters (e.g. type of assays used) to confirm diagnosis**, classify patients, define the treatment approach, manage complications, guide eligibility for clinical trial enrollment, and outline discharge and follow-up

What are the potential benefits?

- **Benefit for patients: Well-defined and regularly updated protocols ensure consistent, evidence-based treatment and management**
- **Benefit for the AML team**: Use of protocols by all the healthcare professionals in the team **enables systematic management of patients and minimises the duplication of efforts in care delivery**

> “The centre has a well-established protocol to maintain service quality even without face-to-face meetings. There are clear regulations for the diagnosis and treatment path, therefore the pandemic had very little effect on the centre’s operations
>
> Haematologist

Spotlight intervention – Access to innovative therapies

Overview

- Institute of Hematology and Blood Diseases Hospital is **a research-oriented centre**, and it is highly focused on increasing access to innovative therapies

What is it?

- The centre is one of the leading centres specialised in haematology in the region. It is often **approached by pharmaceutical companies to participate in clinical trials**

How does it work?

- Up to **~90% of patients qualify for enrollment in relevant clinical trials** and real-world data (RWD) studies
- Patients are **selected based on the inclusion and exclusion criteria** defined in the trials
- The medical team conducts **a detailed briefing session to familarise each patient** with the trial, required documentation, and consent forms before enrollment into a clinical trial
- **Dedicated research nurses jointly work with physicians** to monitor patients enrolled in trials, maintain a detailed record of any complications, and notify treating physicians of any concerns

What are the potential benefits?

- **Benefit for patients:** Patients have **increased access to advanced and innovative therapies** for AML available in the region
- **Benefit for the AML team:** Strong focus on research and collaboration with pharmaceutical companies provides **a better understanding of new treatments and clinical adoption**

> "As one of the largest AML centres in China, cutting-edge clinical trials in AML are conducted at the centre and there are more options for treatment
>
> Haematologist

Yamagata University Hospital, Yamagata, Japan

Site visited by KPMG July 11th 2022

Centre overview

Centre summary

Centre type: Public tertiary hospital

Catchment area: Primarily provides care to patients coming from four key regions in Yamagata prefecture: Murayama, Shonai, Okitama (Oitama), and Mogami. The centre also receives international patients

Funding: Yamagata University Hospital is primarily funded by the public healthcare system through the universal health coverage (UHC)

Services: Medical oncology, haematology, pathology, haematopoietic cell transplantation, radiology, allied healthcare services, and palliative care

AML Patient population: 25-30 new AML patients per year (2-3 patients per month). 2,000-3,000 patients per year in the haematology department as a whole

Key strengths in delivery of AML care

Specialised transplant centre: The centre is a specialised transplant centre and also performs HSC[(a)] transplants between non-related donors (which is unique in the prefecture)

Specialised onco-haematology HCPs: The centre has a dedicated team of HCPs including certified haematology nurses and specialised oncology pharmacists. These HCPs are integral to care delivery and have consistently contributed towards the centre's improved patient outcomes (e.g. increased survival, enhanced QoL[(b)])

Collaboration with local affiliate hospitals: The centre collaborates with local affiliate hospitals and allocates a dedicated haematologist to work at each. This facilitates information sharing and a smooth referral process for patients

Elder patient care and contribution of nurses: The centre cares for many elderly patients who need care to maintain ADL[(c)] and QoL[(b)] and discharge to home. Nurses contribute to support their QOL[(b)] care

Key challenges faced in delivery of AML care

Longer ALOS[(d)] in tertiary hospitals: There is a limited number of local hospitals in Yamagata prefecture, which limits post-discharge care options for patients. Some critical patient stays at the centre are therefore prolonged, resulting in longer ALOS[(d)] and limited capacity for new patients

Limited transfusion capabilities in local hospitals: Few centres are equipped to provide the post-discharge care required in BMS(e) cases (e.g. transfusions), which can delay recovery. Patients often travel back to the tertiary centre for transfusions. This is an added burden for patients and increases the patient load at tertiary centres like Yamagata University

Limited reimbursement for novel drugs: The high out-of-pocket cost of high-cost novel drugs can be unaffordable for many patients (particularly the elderly), resulting in financial burden

Notes: (a) HSCs: Haemopoietic stem cells, (b) QoL; Quality of Life, (c) ADL: Activities of daily living, (d) ALOS: Average length of stay, (e) BMS: Bone marrow suppression

Acute Myeloid Leukaemia (AML) in Japan

Healthcare system overview

Structure: Japan offers universal health coverage through the statutory health insurance system (SHIS), funded primarily through public taxes and a social insurance premium. All residents are required to enroll either through employment or residence-based plans. Residents pay a 10-30% co-payment for all health services and pharmaceuticals with the benefit from the cap on co-payment burden(1)

Insurance and funding: The SHIS provides universal health coverage to ~99% of its population through employment and residence-based government funded health insurance plans. A separate social assistance programme provides additional coverage for healthcare costs for unemployed and low-income individuals. National government has developed regulations for insurers and providers to set SHIS fee schedule. There is an annual out-of-pocket cost for the covered citizens to pay, for health care and long-term services based on age and income(1)

Primary care is delivered mostly through private physician-owned clinics, with a small proportion of clinics owned by public agencies, government, and non-profit organisations. Historically, clear separation between primary and specialist care settings has not been defined. However, patients are encouraged not to make self-referrals to large hospitals. The government has implemented national programmes to incentivise HCPs and encourage appropriate referral and coordination between primary and specialist care(1)

Tertiary hospitals in each prefecture deliver initial treatment for AML, with post-treatment care delivered at local hospitals in each region(1)

Guidelines and societies

Guidelines: Japan Adult Leukemia Study Group (JALSG) treatment protocol

Professional bodies: Japanese Society of Haematology (JSH), Japanese Paediatric Leukaemia/Lymphoma Study Group (JPLSG)

Patient association groups (PAGs): Japan Cancer Society (JCS), The Japanese Association of Supportive Care in Cancer (JASCC)

Statistics

	Japan	World		Japan	World
Cancer incidence(2)	285**	201 **	Patient : Physician ratio(5),(6)	400	556
AML incidence(3),(4)	56**	30**	% GDP spend on healthcare(7),(8)	8.2	10
Public healthcare spend (% of all health expenditure)(9)				83.4	60

Sources:(1) The commonwealth fund (2) World Health Organisation Global Cancer Observatory, 2020; (3) Precision medicine and novel molecular target therapies in AML; (4) American society of clinical oncology; (5) The World Bank Databank; (6) Data bank – global; (7) Statista; (8) WHO, global spending on health, (9) Country Economy

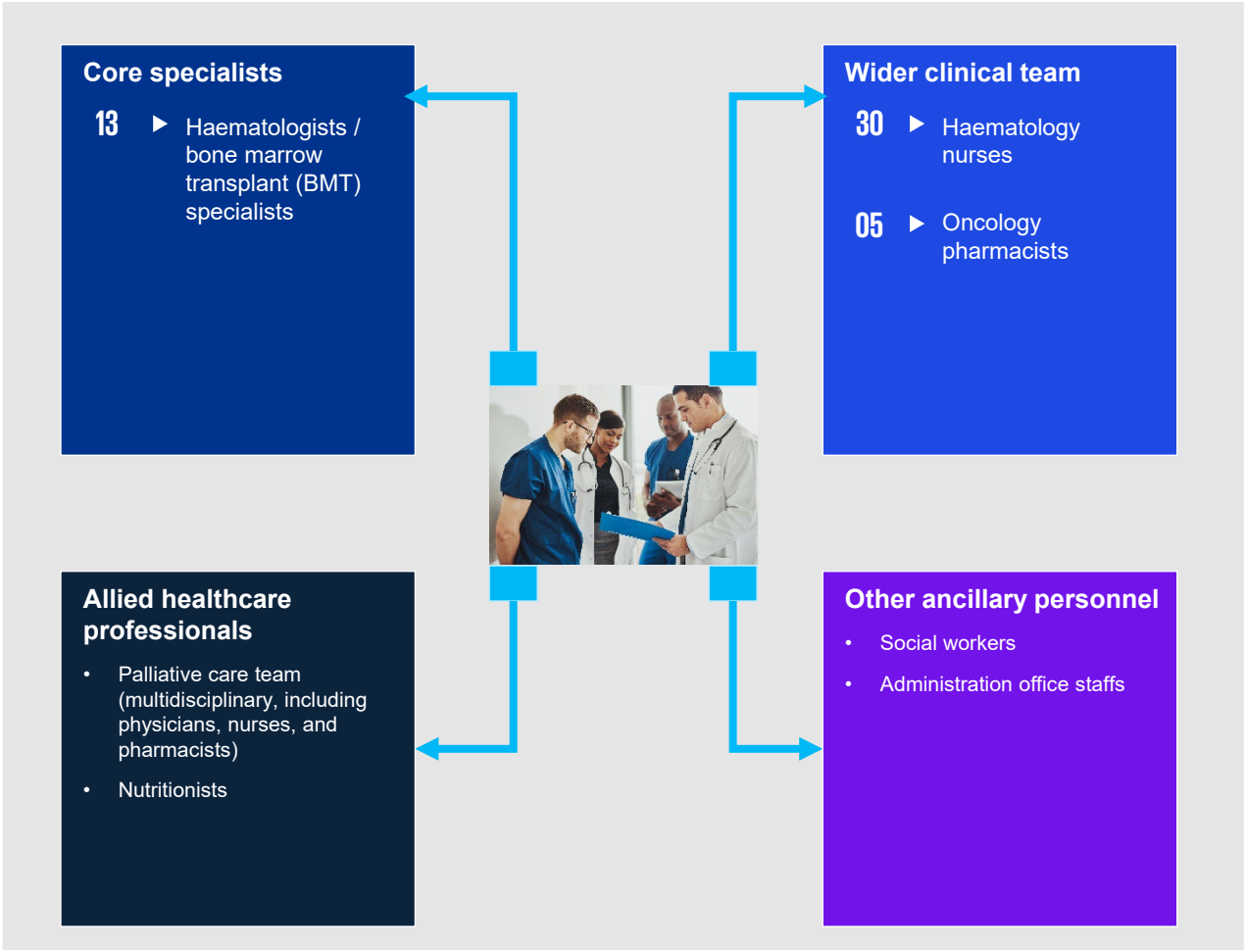
**Per 1,000,000 individuals

The centre and AML unit

The centre	
Centre type	• Public - teaching hospital (national university corporation), tertiary
Size	• 637 beds in total, 39 beds for haematology disease and transplants
Setting	• Inpatient, outpatient, and ambulatory
Catchment area	• Primarily provides care to patients coming from four key regions in Yamagata prefecture: Murayama, Shonai, Okitama (Oitama), and Mogami
Affiliation & accreditations	• Certified by International Organisation of Standardisation (ISO 90001), affiliation with the National University, and recipient of the highest standard certification in 3rdG:Ver.2.0 from the Japan Council for Quality Healthcare

The AML unit	
Patient cohort	• 25-30 new AML patients per year (2-3 patients per month) • 2,000-3,000 patients per year in the haematology department as a whole
Team	• Multidisciplinary team including haematologists, certified nurses, specialised pharmacists, palliative care physicians, nutritionists, and social workers
Services offered	• Comprehensive haematology services including detection, diagnosis, treatment, palliative support, and rehabilitation
Guidelines used	• Japan Adult Leukemia Study group (JALSG) treatment protocols, Japanese Society of Hematology - Practical Guidelines for Hematological Malignancies
Facilities on site	• Medical oncology, haematology, radiology, pathology, hematopoietic cell transplantation, chemotherapy, bone marrow transplant, heavy ion bean cancer treatment, allied healthcare services, and palliative care

The team



Governance and processes

Team meetings

A weekly MDT meeting is conducted with physicians, nurses, and pharmacists to align on treatment protocols

A monthly conference is organised with physicians, pharmacists, nutritionists, nurses and administrative staff to discuss complex cases and share knowledge

Patient records

Electronic medical records are used to document patients' medical histories and share details among physicians. nurses, and pharmacists involved in care

Pharmacy

Pharmacists specialised in oncology dispense therapies, and are directly involved in care delivery including chemotherapy regimen management, follow-up care, and training HCPs on new therapies

Roles and responsibilities of the team

Haematologist / BMT specialist

- Coordinates activities across the oncology and haematology department in the centre
- Delivers specialist care in oncology and haematology
- Attends to all the inpatients in the ward and outpatients in the outpatient clinic
- Performs BMT for eligible patients
- Collaborates with other specialists for the management of adverse events post-chemotherapy

Haematology nurse

- Specialises in haematology and is certified to administer chemotherapy drugs, blood transfusions, and provide long-term follow-up care
- Works jointly with physicians and transplant coordinators in the BMT ward to identify relevant donors
- Provides patients with guidance and educational information (e.g. pamphlets) about the disease
- Assists treating physicians during consultations in outpatient clinic
- Coordinates with patients to assess their willingness to receive palliative care

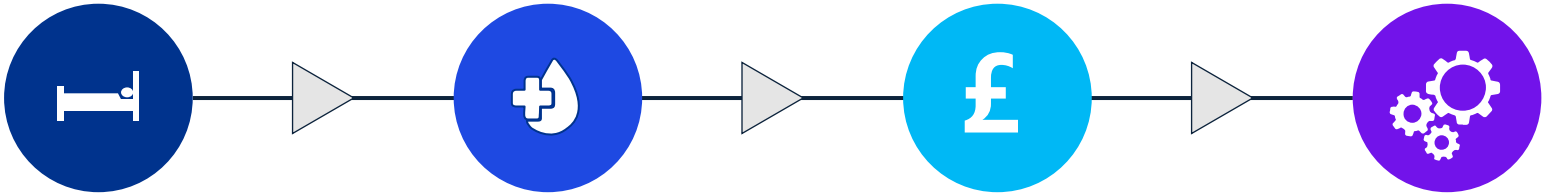
Oncology pharmacist

- Specialises in oncology and is dedicated to the haematology department
- Identifies patients at risk of stomatitis and ensures administration of appropriate medication to minimise the risk of treatment discontinuation
- Collaborates with other professionals to provide care to elderly patients in long-term follow-up care at the centre
- Assists the palliative care team during their daily visits in the haematology department

Additional team members

- **Nutritionist:** Provides guidance on diet management for inpatients undergoing treatment at the centre, and in follow-up care
- **Social worker:** Collaborates with other HCPs (e.g pharmacists) to facilitate early discharge and coordinates with local hospitals to ensure post-discharge care for patients. Also provides guidance to access high-cost drugs at subsidised prices through social assistance programmes (mainly for elderly and retired patients)

Challenges faced in AML care delivery



Longer ALOS[(a)] at tertiary centres

- There are a very few (only three) smaller hospitals equipped to provide post-acute care for AML patients in Yamagata prefecture, limiting post discharge care options
- Some critical and immunocompromised patients may require longer hospitalization, which impacts the efficiency of tertiary centres (e.g. Yamagata University) as it leads to longer waiting times for new patients

Limited transfusion capabilities in local hospitals

- Smaller hospitals providing post-discharge care are not always equipped to administer blood transfusions, which are required in bone marrow suppression cases. This can cause a delay in recovery
- Some patients travel long distances to tertiary centres (e.g. Yamagata University) for transfusions, which can be an additional burden for patients and lead to an increased patient load at the centre

Partial reimbursement for novel drugs

- Prescription drugs are partially covered and reimbursed via universal health coverage in Japan. However, there is an associated out-of-pocket cost for these drugs
- The out-of-pocket cost for novel drugs can be out of reach for some patients, including individuals who are retired or unemployed

Treatment for rapid clonal evolution and relapse cases

- Clonal evolution of AML is rapid and many cases face difficulty in treatment
- There is no set consensus on treatment for relapse cases across guidelines and protocols, and treatment decisions depends on each centre's discretion (apart from cases where special inhibitors are indicated)
- The centre tries to address this challenge by considering new medications and transplantation

> **"Ideally, we would like to help elderly patients return home directly, however if it is difficult, patients will be transferred to seek post-acute care in other smaller hospitals**
>
> **Haematologist**

Notes: (a) ALOS: Average length of stay

Overview of AML patient pathway

Awareness and symptom recognition

- Many AML cases are discovered at early stages, and **symptom recognition is widespread**

Diagnosis, classification, and prognosis

- GPs order routine **blood tests (e.g. CBC[(a)])** when patients first present with symptoms, and a **bone marrow biopsy** is later performed at the local hospitals
- Patients are usually referred to the centre **via local hospitals** after initial screening in primary care
- Post referral from regional affiliated hospitals, the centre repeats **routine blood tests (e.g. CBC[(a)]) and performs genetic screening to confirm diagnosis**
- **Access to universal health coverage** (UHC) enables a smooth referral and supports early screening in primary care

Treatment (intensive + non-intensive) and relapse care

- Treatment is outlined based on patients' physical status, complications, age, and genetic abnormalities, in accordance with the **JALSG (Japan Adult Leukemia Study Group) treatment protocol for first-line treatment**
- Most patients start on standard chemotherapy followed by **high intensity remission induction chemotherapy**
- **Transplant is usually offered to relapsed patients under 70 years old**. However, some the younger patients may be offered transplant as their first option. Typically, transplantation takes place within 6 months of diagnosis
- Patients also have an option of **HLA-haploidentical haematopoietic stem cell transplantation**
- Enrollment in clinical studies **is considered based on each patient's age, condition, and preference**
- A team of physician, nurses, transplant coordinators, and patients are involved in decision making, with **patient support and educational materials** provided throughout the treatment

Remission

- **Remission induction therapy** is given based on the patient's age, health status, and tolerability
- A longer hospitalisation of ~30-40 days is advised for patients facing **bone marrow suppression and transfusion-related risks**
- **Consolidation therapy is performed over 3-4 sessions i**n a year both at Yamagata University and local hospitals

Palliative care

- A dedicated team provides **palliative care based on patients' willingness and condition**
- The **specialised palliative team** helps patients with their physical and psychological stress

Notes: (a) CBC: Complete blood count

Interventions and good practices across the care pathway

Collaboration with affiliate hospitals

Yamagata University has cooperative arrangements with local hospitals affiliated in its network. The centre assigns one dedicated haematologist to work in each of these two affiliated hospitals full time. This facilitates a smooth referral process for patients that require advanced treatment at Yamagata University hospital

Education for terminal patients

The centre has developed educational documents to raise understanding of the disease and treatment for terminally ill elderly patients. Nurses work closely with the patients to understand their willingness and preference for long-term care e.g. staying at a local hospital, or returning home

Monthly knowledge sharing forum

The haematology team conducts a monthly conference with physicians, nurses, pharmacists, nutritionists, and administration office staff in attendance. The aim is to bring the team together, discuss case studies, and foster knowledge sharing amongst the professionals

Specialised transplant centre

The Yamagata University hospital is among a few specialised transplant centres that performs hematopoietic stem cell transplant between non-related donors. The medical team conducts rigorous training to educate the staff and provide personalised care

Palliative care ★

There is a dedicated palliative care team which includes physicians, nurses, and pharmacists. The nurses coordinate with patients early in the treatment process to understand their preferences for palliative care. The team conducts daily visits to provide support and address any patient concerns

Specialised outpatient clinic ★

The centre has established an outpatient clinic that offers weekly consultations for patients undergoing chemotherapy and those who have undergone BMT. It enables early identification of post-transplant complications (e.g. epidermal desquamation) and timely intervention

Specialised haematology nurses ★

The nurses at the centre are specially trained and certified in haematology care protocols (e.g. transfusions, chemotherapies, long-term follow-up care. The nurses are integrated in the patient pathway and play a key role in ensuring that patients are looked after, feel safe, and receive holistic care

Social services

Social support services are organised for patients by the nurses, when required. The social worker provides information on available subsidy schemes for high-cost drugs, and coordinates with local hospitals to ensure support following discharge

Dedicated oncology pharmacist ★

Specialised oncology pharmacists play an integral role in both inpatient and outpatient care. They dispense drugs, disseminate knowledge on new therapies, manage chemotherapy regimens, drug side effects, and patient comorbidities

Management of side effects

Pharmacists collaborate with the prescribing physicians to report and manage treatment-associated side effects. They discuss and modulate the treatment dosage or route of administration (e.g. switching to IV administration if oral therapy is not effective) to minimise the impact of side effects and support treatment continuity

Multidisciplinary team meetings

The medical team including treating physicians, nurses, and pharmacists connect weekly to discuss and align on treatment protocols for patients. This facilitates collaboration between team members and coordinated care for patients

Keys: Awareness and symptom recognition; Diagnosis, classification and prognosis; Treatment and relapse care; Remission; Palliative care; ★ Spotlight intervention

What are the next steps for the centre?

Recruit and educate the next generation of haematologists and haemato-oncology HCPs

Objective

Recruit and educate next generation of haematologists and haemato-oncology HCPs

What is the rationale?

The centre is amongst one of the few specialised centres that routinely perform transplants and other advanced haemato-oncology treatments (e.g. transplant between non-related donors) for patients with haematological diseases in the region. The field of haematology is an evolving domain with innovations and new evidence generated frequently. There is a need to expand the size of the medical team as well as ensure continuous education and training for all HCPs to provide specialised care for patients

How to implement it?

Haematology is an interesting and evolving field that could attract young residents and staff. As a specialised centre in haemato-oncology, Yamagata University can look to expand their recruitment activities and ensure that training and support remains an area of focus for incoming HCPs

Strengthen cell therapy treatment capability

Objective

Strengthen the cell therapy treatment capability

What is the rationale?

Yamagata University is the only specialised transplant centre in the region, and the team aims to provide advanced treatment including immunotherapies such as CAR-Ts[(a)] to patients. There are a few immunotherapies approved for lymphoma and myeloma patients with some promising clinical trials ongoing for AML. The ongoing trials demonstrate the necessity for infrastructure to support the administration of these advanced immunotherapies for AML, once they are approved[(1)]. The team will need a dedicated setup equipped to perform cell processing, apheresis to selectively collect T- cells, transfer them to CAR-T manufacturers in temperature-controlled shipments, and administer infusions once the T- cells have been tailored to each AML patient

How to implement it?

The team has planned to set up a dedicated space for cell preparation for CAR-T therapy at the centre and is in discussions with other departments to coordinate and launch the CAR-T cell preparation unit

Sources: (1): CAR T Cells for Acute Myeloid Leukemia: State of the Art and Future Directions

Notes: (a) CAR-Ts: Chimeric antigen receptor T-cells

Spotlight intervention – Dedicated oncology pharmacists

Overview

- Yamagata University hospital has a dedicated team of pharmacists specialised and trained in oncology care

What is it?

- Pharmacists are deeply **integrated across the patient pathway** and undertake a wide range of responsibilities across inpatient, outpatient, and palliative care units

How does it work?

- Pharmacists maintain touchpoints with patients undergoing chemotherapy or BMT to **assess the risk of stomatitis** and discuss treatment with prescribing physicians
- An **approval from the pharmacy department and pharmaceutical committee** is required to initiate any new regimen or therapy
- Pharmacists participate in multidisciplinary discussions and may provide suggestions on prescriptions. They are also **involved in disseminating knowledge on new therapies** (e.g. formulation changes, side effects, infusion reactions) to keep the wider HCP group updated
- **HCPs in the medical team collaborate with pharmacists to ensure early and smooth discharge** from hospital

What are the potential benefits?

- **Benefit for patients**: Frequent in-person communication and access to **specialised pharmacists provides comprehensive and consistent care, and effective management of treatment-associated side effects**
- **Benefit for the AML team**: Strong integration of specialised pharmacists within the care team **enables improved communication channels with the wider team**, patient management, and **enhanced knowledge sharing on new therapies** amongst HCPs

> [A dedicated] pharmacist oversees the haematology department on a full-time-basis, with other pharmacists providing support for follow-up to ensure seamless care
>
> Pharmacist

Spotlight intervention – Specialised haematology nurses

Overview

- The centre has a dedicated team of **specialised haematology nurses that are certified in the field of haemato-oncology**

What is it?

- The haematology team is supported by **~30 specialised haematology nurses**, many of which are professionally certified in chemotherapy nursing (4), LTFU[(a)] care (5), HCTC (Hematopoietic Cell Transplant Coordinator) (1), transfusion specialist nursing (4), and oncology care(1)

How does it work?

- **Nurses are integrated across the entire care pathway** from diagnosis, to treatment, psychological care, social support, follow-up, and palliative care
- They **conduct check-ins with patients** to ask a series of question during diagnosis and at the beginning of the treatment to **assess their willingness and preference for initiating palliative care**
- They regularly **communicate with both inpatients and outpatients to understand any concerns** (e.g. pain), evaluate patients' psychological condition, and organise social support if needed
- Additionally, nurses **ensure that all the hospitalised patients feel safe** and build a trusting relationship to allow them to share their concerns freely with them

What are the potential benefits?

- **Benefit for patients**: Specialised and dedicated team of nurses can provide clinical and psychological support, **allow the patients to raise any concerns about side effects or complications**, and feel safe throughout treatment
- **Benefit for the AML team**: Consistent and diligent nursing care has **contributed to the prevention of complications** (e.g. GVHD[(b)]), **and the delivery of improved clinical outcomes** (e.g. early regeneration of skin in case of epidermal desquamation, increased expected life expectancy from three months to a few years, with improved QoL[(c)])

Notes: (a) LTFU: long-term follow-up, (b) GVHD: Graft versus host disease, (c) QoL: Quality of life

> "Recently, we supported a patient whose life expectancy was estimated to be only three months. They actually lived 3-4 years with high-level of QoL. I believe this achievement is because of nurses' constant efforts
>
> Haematologist

Spotlight intervention – Specialised outpatient clinic

Overview

- The centre has established a specialised outpatient clinic for patients on chemotherapy and LTFU(a) care (e.g. patients who have undergone BMT)

What is it?

- The **outpatient clinic is run by the same treating physicians, certified nurses, and specialised pharmacists** who provide inpatient care to maintain consistency of care

How does it work?

- The outpatient clinic **offers consultations once a week for patients undergoing chemotherapy**
- The clinic **acts as a long-term follow-up care clinic for patients who have undergone transplant**. A team of ~5 LTFU(a) certified nurses provide support to these patients to **prevent GVHD**(b) and other infections or related diseases post transplant
- **Pharmacists also participate in outpatient clinics to understand the chemotherapy plan** with prescribing physicians and ensure appropriate administration of chemotherapies. They aim to **identify potential complications or side effects associated** with the treatment and provide appropriate solutions

What are the potential benefits?

- **Benefit for patients**: An outpatient clinic allows patients to **periodically connect with the same care team that delivered the inpatient care.** It enables better communication and care continuity
- **Benefit for the AML team**: The team is able to **build trust with the patients over time through both inpatient and outpatient services**, and ensures provision of long-term consistent care

> “Our strength is that HCPs in charge of inpatient ward are also involved in outpatient care, and staff can provide consistent care during hospital stay and follow-up as well
>
> Nurse

Notes: (a) LTFU: long-term follow-up, (b) GVHD: Graft versus host disease

Spotlight intervention – Palliative care

Overview

- The centre has an established **palliative care team that is brought in to provide support early in the patient journey** based on each patient's preference

What is it?

- The palliative care team **includes physicians, pharmacists, and nurses** who each play a key role in providing support and alleviating patients' symptoms

How does it work?

- Palliative care is **provided based on need and patient preference**. Nurses connect with patients and assess their preference for potentially initiating palliative care on an ongoing basis
- The palliative care team consisting of a physician, pharmacist, and 2-3 nurses conduct daily rounds in the haematology department
- The palliative care team and the medical nursing team work together to **assess each patient's need for psychological and financial support** and raise relevant requests

What are the potential benefits?

- **Benefit for patients**: Collaboration between palliative care and the medical team helps to ensure **patients' problems and concerns are identified and addressed, and that they have access to improved psychological support** throughout treatment
- **Benefit for the AML team**: **Early involvement and collaboration between the palliative care team and medical team facilitates improved patient management** and efficient information sharing between specialists across the two teams

> "Palliative care is necessary for patients with AML and [patients who] need transplant. Therefore, a special palliative care team is often involved
>
> Haematologist

Nippon Medical School Hospital, Bunkyo, Japan

Site visited by KPMG Sept 26th 2022

Centre overview

Centre summary

Centre type: Acute care, tertiary hospital

Catchment area: Primarily provides care to patients coming from central Tokyo

Funding: Nippon Medical School Hospital is primarily funded by the public healthcare system

Services: Medical oncology, haematology, pathology, bone marrow transplant, radiology, allied healthcare services, rehabilitation care, and palliative support

AML Patient population: Nearly 18,000 inpatients and 16,000 outpatients are seen per year in the haematology department

120 AML patients are seen per year (approximately 40 are new diagnoses)

Key strengths in delivery of AML care

Intensive care management: Nippon Medical School Hospital has an integrated intensive care unit (ICU) that works closely with the haematology department. This facilitates appropriate care for respiratory and kidney complications, which can occur during chemotherapy

Elderly patient care: The centre has a structured care plan that outlines the treatment and management of elderly patients. This patient cohort often experience age-related challenges including memory loss and mobility limitations

Open and effective communication between HCPs: Communication amongst the multidisciplinary care team is strong, and physicians conduct daily visits in the haematology ward. Nurses collaborate closely with treating physicians and other HCPs in the intensive care unit to facilitate informed transfers between departments as needed

Key challenges faced in delivery of AML care

Extensive drug approval pathway: The drug approval process in Japan is time intensive, and has been evolving over the past few years[(1),(2)]. Approval timelines are an area of focus in a number of therapeutic areas including haematology

Limited post-discharge care options: There are few post-discharge care options (e.g. local hospitals) available outside of the tertiary care setting. This limits the options available for patients who have ongoing care needs, especially amongst those patients who have poor performance status (PS) and activities of daily living (ADL) scores and need rehabilitation care

Limited coverage of genetic analysis: Genetic analysis is available to some patients through clinical trial programmes; however, it is not universally reimbursed through the public healthcare system. Genetic analysis can help inform tailored treatment decisions based on the mutation observed

Sources:(1) Evolving Landscape of New Drug Approval in Japan and Lags from International Birth Dates: Retrospective Regulatory Analysis, ASCPT, (2) Understanding the Japanese culture and approval process

Acute Myeloid Leukaemia (AML) in Japan

Healthcare system overview

Structure: Japan offers universal health coverage through the statutory health insurance system (SHIS), funded primarily through public taxes and a social insurance premium. All residents are required to enroll either through employment or residence-based plans. Residents pay a 10-30% co-payment for all health services and pharmaceuticals with the benefit from the cap on co-payment burden(1)

Insurance and funding: The SHIS provides universal health coverage to ~99% of its population through employment and residence-based government funded health insurance plans. A separate social assistance programme provides additional coverage for healthcare costs for unemployed and low-income individuals. National government has developed regulations for insurers and providers to set SHIS fee schedule. There is an annual out-of-pocket cost for the covered citizens to pay, for health care and long-term services based on age and income(1)

Primary care is delivered mostly through private physician-owned clinics, with a small proportion of clinics owned by public agencies, government, and non-profit organisations. Historically, clear separation between primary and specialist care settings has not been defined. However, patients are encouraged not to make self-referrals to large hospitals. The government has implemented national programmes to incentivise HCPs and encourage appropriate referral and coordination between primary and specialist care(1)

Tertiary hospitals in each prefecture deliver initial treatment for AML, with post-treatment care delivered at local hospitals in each region(1)

Guidelines and societies

Guidelines: Japan Adult Leukemia Study Group (JALSG) treatment protocol

Professional bodies: Japanese Society of Haematology (JSH), Japanese Paediatric Leukaemia/Lymphoma Study Group (JPLSG)

Patient association groups (PAGs): Japan Cancer Society (JCS), The Japanese Association of Supportive Care in Cancer (JASCC)

Statistics

	Japan	World		Japan	World
Cancer incidence(2)	285**	201 **	Patient : Physician ratio(5),(6)	400	556
AML incidence(3),(4)	56**	30**	% GDP spend on healthcare(7),(8)	8.2	10
Public healthcare spend (% of all health expenditure)(9)				83.4	60

Sources:(1) The commonwealth fund (2) World Health Organisation Global Cancer Observatory, 2020; (3) Precision medicine and novel molecular target therapies in AML; (4) American society of clinical oncology; (5) The World Bank Databank; (6) Data bank – global; (7) Statista; (8) WHO, global spending on health, (9) Country Economy

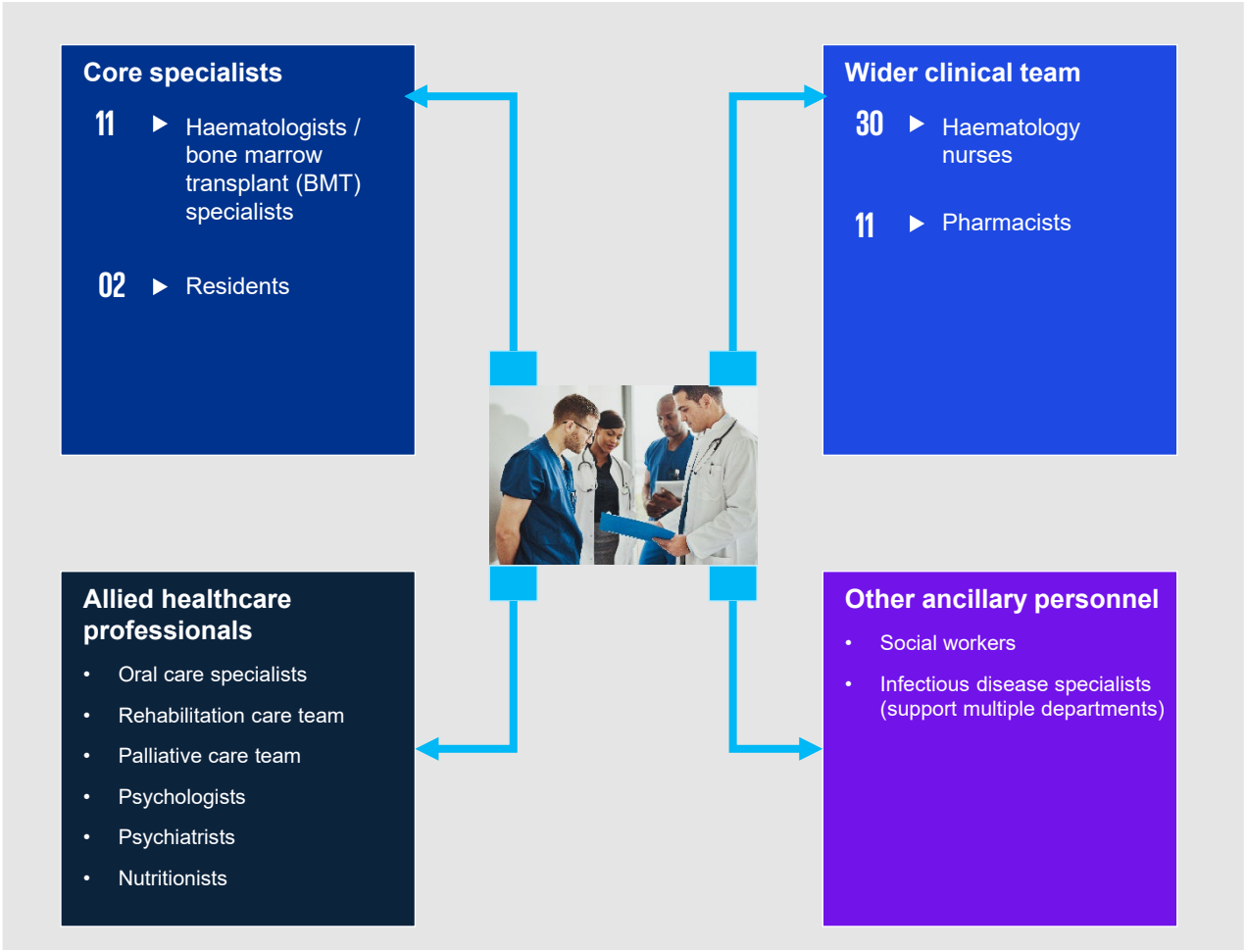
**Per 1,000,000 individuals

The centre and AML unit

The centre	
Centre type	• Acute care tertiary hospital
Size	• 850 total beds with ~40-50 beds dedicated to haematology and transplant patients
Setting	• Inpatient, outpatient, and ambulatory
Catchment area	• Primarily provides care to patients coming from secondary medical area, located in central part of Tokyo
Affiliation & accreditations	• Recognised as the first advanced critical care center by the Ministry of Health (MoH) and specified as the regional medical institution for cancer treatment

The AML unit	
Patient cohort	• Nearly 18,000 inpatients and 16,000 outpatients are seen per year in the hematology department • 120 AML patients are seen per year (approximately 40 are new diagnoses)
Team	• Multidisciplinary team (MDT) including haematologists, nurses, pharmacists, palliative care physicians, oral care specialists, physiotherapists, nutritionists, and social workers
Services offered	• Comprehensive haematology services including detection, diagnosis, treatment, rehabilitation care, and palliative support
Guidelines used	• Japan Adult Leukemia Study Group (JALSG) and Japan society of haematology (JSH)
Facilities on site	• Medical oncology, haematology, radiology, pathology, chemotherapy, bone marrow transplant, allied healthcare services, and palliative care

The team



Governance and processes

Team meetings

MDT meetings are conducted throughout the treatment process for the care team to discuss treatment approach, nutritional guidance, and social care concerns. The meetings are usually attended by treating physicians, nurses, and pharmacists

A separate MDT meeting is organised to discuss complex patient cases

Patient records

Electronic medical records are used to document and share patient information with the full care team

Pharmacy

Pharmacists dispense prescriptions including chemotherapy agents. They are also involved in monitoring adherence and providing patient follow-up

Roles and responsibilities of the team

Haematologist / BMT specialist

- Delivers specialist care in haematology and oncology
- Attends to all inpatients in the ward and outpatients in the outpatient clinic
- Performs bone marrow transplant (BMT) for eligible patients
- Leads multidisciplinary team (MDT) meetings
- Coordinates closely with the nurses to ensure transparent communication and alignment on treatment
- Manages and treats infections in AML patients

Haematology nurse

- Provides nursing care for inpatients and outpatients at the hospital
- Provides guidance to patients on home care
- Participates in MDT meetings
- Acts as the transplant coordinator and manages care before and after transplantation
- Educates patients' families and care givers on the management of AML

Haematology pharmacist

- Provides support in administration of remission induction and consolidation therapy for all inpatients
- Collaborates with physicians and nurses to align on chemotherapy regimen and help manage treatment side effects
- Provides follow-up support after discharge

Additional team members

- **Psychologist and psychiatrist:** Provide counselling sessions to address psychological concerns and improve patients' mental wellbeing
- **Dietitian:** Provides guidance on diet for all patients (including those undergoing BMT), and helps address concerns around appetite
- **Rehabilitation care team:** Dedicated physical and occupational therapists work with patients to maintain performance status (PS) and activities of daily living (ADL) throughout treatment
- **Palliative care team:** Composed of a pain management specialist and a specialised pharmacist who provide end of life care to terminally ill patients. The team also work with patients who have undergone BMT to alleviate pain and improve their psychological wellbeing

Challenges faced in AML care delivery

Limited coverage of genetic analysis

- Nippon Medical School Hospital conducts genetic analysis to outline personalised treatment for a number of AML patients through clinical research programmes
- However, the universal coverage for these advanced tests through public healthcare system is limited. Patients that do not undergo genetic analysis do not benefit from treatment personalisation based on type of mutation observed

Limited post-discharge care options

- There are limited post-discharge care options (e.g. local hospitals) for patients outside of tertiary centres such as Nippon Medical School Hospital
- This limits the options available for patients who have ongoing care needs, especially amongst those patients who have poor performance PS[(a)] and ADL[(b)] scores and need rehabilitation care

Extensive drug approval pathway

- The drug approval process in Japan is time intensive and has evolved in the past few years to streamline the process
- However, approval timelines are an area of focus in a number of therapeutic areas including haematology

> **Elderly AML patients sometimes have difficulty in maintaining PS[(a)] and ADL[(b)] during treatment**
>
> **Nurse**

Sources: (1) Evolving Landscape of New Drug Approval in Japan and Lags from International Birth Dates: Retrospective Regulatory Analysis, ASCPT, (2) Understanding the Japanese culture and approval process

Notes: (a) PS: Performance status, (b): ADL: Activities of daily living

Overview of AML patient pathway

Awareness and symptom recognition

- Nurses coordinate with patients' families and care givers to increase their understanding of AML management

Diagnosis, classification, and prognosis

- Patients who present with symptoms of leukaemia (e.g. fever, anaemia, and haemorrhage) are referred to the centre from **smaller local hospitals and other university hospitals**
- Following referral, the centre performs diagnostic tests including **blood tests, bone marrow aspiration, and microscopy** to confirm diagnosis
- **Genetic testing** is done to identify mutations seen in leukaemia and inform prognosis

Treatment (intensive + non-intensive) and relapse care

- Treatment is outlined based on patients' physical fitness, comorbidities, age, and cognitive ability, in accordance with the **JALSG[a] and JSH[b] treatment protocol**
- Patients who are **relatively fit and young are started on standard chemotherapy** for two months
- Patients who are more frail are put **on low intensity chemotherapy**
- Eligibility for bone marrow transplant (BMT) is based on each patient's **prognosis, age, and genetic analysis results** (applicable for patients enrolled in clinical research)
- **BMT** is usually offered to patients below 70 years of age, however, some older patients may also undergo transplant if they have a strong PS(c)
- Physicians conduct **pre and post transplant MDT meetings** with the oral care specialist, nutritionist, and pharmacist to discuss specific concerns and side effects

Remission

- After remission induction therapy, **consolidation therapy is performed over 3-4 sessions** at the centre
- An inpatient stay of ~30 days is advised for the first session of consolidation therapy, before patients are **transferred to the outpatient setting** for following sessions
- Patients attend **follow-up appointments every two months** for one year, and less frequently thereafter

Palliative care

- **Palliative care is provided to terminally ill patients** to help alleviate pain and improve their psychological wellbeing
- The palliative care team also helps in the **management of post transplant symptoms** (e.g. laryngeal and oral pain)

Interventions and good practices across the care pathway

MDT meetings ★

MDT meetings are conducted throughout the treatment process on a need basis, including at treatment initiation, pre and post BMT, and at the time of discharge. The team including physicians, nurses, and pharmacists gather to align on treatment plans and discuss any concerns to improve care delivery

Protocol-based care delivery

The AML care team has a structured approach to care delivery and defines care plans based on national guidelines and protocols. The team follows guidelines from the Japan Society of Hematology and Japan Society for Transplantation for treatment and transplant

Genetic analysis through clinical research

Nippon Medical School Hospital offers genetic analysis to AML patients through their clinical research programme. The medical team uses assay results to classify patients into groups, inform prognosis, and tailor the treatment approach to each patient accordingly

Haematologist trained as transplant specialist ★

The haematologists at the centres are specialised and trained to perform BMT, in addition to the delivery of specialised haematology care. The dual expertise of the haematologists allows greater flexibility in managing treatment plans and coordinating transplants

Rehabilitation care

There is a dedicated team of physical and occupational therapists for AML patients. The team aims to provide support to ensure adequate physical activity, maintain an optimal score for activities of daily living (ADL) and performance status (PS) throughout treatment

Fertility support

AML diagnosis and treatment can have a significant impact on fertility. Nurses connect with OBGYNs to discuss possible options for patients undergoing treatment

Integrated ICU ★

Nippon Medical School Hospital has an equipped intensive care unit. The ICU is closely integrated with the haematology department, which enables appropriate care for side effects (e.g. respiratory and kidney problems), often experienced by AML patients during chemotherapy

Adherence monitoring

A Patients who experience treatment-associated side effects (e.g. fatigue and oral health problems) or have trouble swallowing oral medication may have lower adherence rates. Physicians, nurses, and pharmacists collaborate to monitor and improve adherence

Dedicated haematology pharmacist ★

The pharmacist plays an integral role in chemotherapy regimen management for all inpatients. They collaborate with physicians for prescription management, ensure that correct dose of drug is administered, and carefully assess the prescription to avoid administration of contraindicated drugs

Elderly patient care

The care plan for elderly patients is carefully structured and outlined to ensure appropriate management of age-related challenges including memory loss and mobility limitations. The nurses address any social concerns to ensure psychological wellbeing of patients and provide guidance for care at home

Integration of nurses in care delivery

Nurses collaborate with treating physicians to align on the care plan for each patient, and coordinate with the ICU team when a patient's condition deteriorates. They provide close care to all inpatients and outpatients, and guidance on home care for families and care givers

Oral hygiene management

The centre has a team of oral care specialists who provides education and guidance on oral hygiene to patients planned to undergo BMT. The aim is to ensure good oral health and minimise any delays in transplant due to poor oral health

Keys: Awareness and symptom recognition; Diagnosis, classification and prognosis; Treatment and relapse care; Remission; Palliative care; ★ Spotlight intervention

What are the next steps for the centre?

Optimising the distribution of roles and responsibilities of HCPs

Objective

Optimising the distribution of roles and responsibilities of HCPs

What is the rationale?

Physicians in Japan are responsible for many different aspects of care and are often managing multiple responsibilities at the same time, resulting in long work hours. Further clarity in the distribution of responsibilities amongst HCPs (e.g. nurses and pharmacists) can enable greater flexibility and reduced ambiguity in day-to-day roles and responsibility for everyone

How to implement it?

The centre can look to structurally optimise the distribution of specific roles and responsibilities for each HCP including physicians, nurses, and pharmacists to drive collaboration, efficiency, and minimise ambiguity in day-to-day responsibilities

Enabling HCPs from other departments to provide care for AML patients

Objective

Enabling HCPs from other departments to provide care for AML patients

What is the rationale?

HCPs in other departments are often reluctant to provide care for haematology patients because these patients can have complex needs, and their care requires expertise in many aspects (infection control, circulatory management, nutritional guidance etc.). HCPs in other specialties are not consistently trained to provide the support necessary for AML patients, and this can complicate the management of comorbidities

How to implement it?

The team can contribute to the creation of educational material (e.g. digital content) which can be used to disseminate fundamental knowledge on AML to the wider team outside haematology. This will allow the haematology team to share the load of comorbidity management with teams from other departments more easily (as appropriate)

Spotlight intervention – Integrated ICU

Overview

- Nippon Medical School Hospital has an intensive care unit that works in close collaboration with the haematology department

What is it?

- The centre has a comprehensive ICU with ~20 ICU beds and is equipped to perform extracorporeal membrane oxygenation (ECMO), when needed
- Dedicated ICU specialists include cardiologists and nephrologists that are required to provide intensive care to patients (including those with haematological malignancies) with complex needs

How does it work?

- AML patients who experience respiratory or kidney complications during chemotherapy are taken to the ICU to provide specialised care (e.g. dialysis)
- Haematology nurses closely monitor such patients and report any concerns to treating physicians
- Once the patient becomes stable, they are transferred back to the haematology department where they are monitored by nurses

What are the potential benefits?

- **Benefit for patients:** An ICU integrated with the haematology department enables specialised care, and facilitates timely management of complications
- **Benefit for the AML team:** Collaboration between the ICU and haematology department facilitates transparent communication between HCPs and enables efficient delivery of specialised care

> “Critical care was delivered across different departments which have now been unified. Therefore, communication among nurses has become easier
>
> Nurse

Spotlight intervention – Haematologists trained as transplant specialists

Overview

- The **haematologists at the centre are trained to provide treatment and perform BMT** for AML patients

What is it?

- The dual role served by the haematologists at Nippon Medical School Hospital is consistent with expertise usually observed amongst haematologists in Japan

How does it work?

- The **centre invests in physicians' training and provide the resources** needed for haematologists to provide AML care and perform BMTs
- The training enables physicians to carefully **evaluate each patient's condition and needs individually** when deciding eligibility for BMT
- Physicians are able to **perform BMT for high-risk patients** when appropriate

What are the potential benefits?

- **Benefit for patients: Informed assessments of each patient's eligibility for BMT** and increased access to BMT
- **Benefit for the AML team:** The dual role served by the physician **provides increased capacity and flexibility to the team to perform BMTs** for large number of patients

> "90% of patients [who are eligible] for transplantation will access transplantation – the proportion seems higher [in Japan] than in overseas countries
>
> Haematologist

Spotlight intervention – Dedicated haematology pharmacist

Overview

- The **pharmacist at the centre plays an integral role** in various aspects of AML treatment

What is it?

- Pharmacist participates in **MDT meetings, discussions during daily visits with physicians, and other touchpoints** with nurses to effectively deliver care for AML patients

How does it work?

- A dedicated pharmacist is **involved in the remission induction and consolidation therapy** of all inpatients. They discuss the chemotherapy regimen for each patient with the treating physician and the haematology department director
- The pharmacist works closely with physicians to outline prescriptions and provide suggestions on **drug selection (e.g. to avoid drug-drug interactions) and intensity of chemotherapy**
- Additionally, the pharmacist collaborates with physicians and nurses to **provide support to patients experiencing side effects, monitor adherence, and assist with patient follow-up**

What are the potential benefits?

- **Benefit for patients:** Dedicated pharmacist enables **closer monitoring of patients, and identification and management of side effects**
- **Benefit for the AML team:** Pharmacist acts as an **advisor and provides expertise on the pharmacokinetics of drugs**

> “Pharmacists are so important for AML treatment, because they give us beneficial advice about effects and side effects of new drugs, and interactions of each drug
>
> Haematologist

Spotlight intervention – MDT meetings

Overview

- The centre has an **organised and structured schedule** to conduct multidisciplinary team meetings

What is it?

- The AML care team conducts **multiple multidisciplinary team meetings** based on patient needs throughout treatment

How does it work?

- The **physicians maintain touchpoints with allied health professionals, and the agenda of the MDT meeting varies based on the HCPs in attendance** (e.g. oral care specialist, nutritionist, social worker etc.)
- Haematologists, pharmacists, nutritionists, and oral care specialists conduct pre-transplant MDT meetings **to identify and address concerns** that may cause a delay in performing BMT
- **Dedicated pharmacist participates in MDT meetings** to discuss treatment compliance concerns, and caregiver support
- There are separate MDT meetings organised biweekly to discuss complex and critical cases

What are the potential benefits?

- **Benefit for patients:** Collaboration between various HCPs enables comprehensive and holistic care, and **timely identification of treatment concerns and complications**
- **Benefit for the AML team: Flexible schedule and agenda of MDT meetings reduces meeting burden**, and ensures that each member of the team only attends those that are most relevant to them

> “Working hours of HCPs in Japan are overwhelmingly longer than those in other countries. So, we are trying to minimize the hours by [conducting MDT on a need basis] ourselves
>
> Haematologist

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