NCCP NATIONAL HAEMATO-ONCOLOGY ADULT PATIENT PATHWAY: ACUTE MYELOID LEUKAEMIA (AML)

Version	Date	Amendment	Approved By
1	11/12/2023		NCCP Haemato-oncology Clinical Leads Group
2	13/09/2024	Amendments made to Sections 1-3 and 5-9. Addition of new sections (Section 4 and 10). Amendment of pathway diagram in Appendix 1. Addition of Appendix 2 (abbreviations).	NCCP Haemato-oncology Clinical Leads Group

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1 Background

Acute myeloid leukaemia (AML) is an uncommon and heterogeneous clonal haematopoietic neoplasm (1). It represents approximately 24% of all leukaemias in Ireland with over 130 people diagnosed with AML in Ireland every year (2). AML incidence is age dependent, rising markedly in patients aged 60 years and older and is higher in males than in females. The median age at diagnosis is approximately 70 years (3).

Overall, AML can be cured in approximately 30–45% of patients who are fit enough to withstand intensive chemotherapy (1). The prognosis and long-term survival rates of patients less than 65 years have incrementally improved with time, largely based upon improved supportive care and increased utilisation of allogeneic haematopoietic cell transplantation (alloHCT) (3). For those who are cured, there is a modest increased risk of secondary cancers and cardiovascular disease due to the adverse effects of treatment (1).

The heterogeneity of AML extends not only to the disease phenotype, but also to the many molecular aberrations that are associated with leukaemogenesis, making the diagnostic and treatment monitoring pathway particularly specialised and targeted to the AML sub-type (1). Recent advances, including insights into the clinical value of genomic abnormalities for diagnosis and prognosis, the clinical significance of inherited predisposition to AML, technological advancements in the quantitative assessment of measurable residual disease (MRD), the development of a range of novel therapeutic agents, and developments in alloHCT, have significantly influenced clinical practice (4).

Acute haematological malignancies such as AML require complex treatment and are resource intensive (5). In line with Recommendation 24[1] of the National Cancer Strategy 2017-2026, such treatment should be delivered in a limited number of centres with appropriate facilities in place (5).

[1] National Cancer Strategy 2017-2026; Recommendation 24: The NCCP will develop appropriate MDT, centralisation and treatment arrangements to meet the diverse needs of patients with haematological cancers.

2 Scope

In line with the Strategy's Recommendation 24[1], the purpose of this pathway is to define referral, tumour conference and treatment pathways for new and relapsed adult patients[2] diagnosed with AML. The following are not within the scope of the document:

- Patient pathways for children (0-16 years)
- Patient pathways for adolescents and young adults (AYA) (16-25 years) where there is an agreed national pathway under the AYA programme.
    - Strategies for the provision of SACT[3] services for children and adolescents and young adults with cancer are being managed in a separate work stream within the NCCP.
- Details of clinical trials
- Specific laboratory guidelines for diagnosis of haematological malignancies

It is important to note that this document has been developed as a pathway and not a clinical guideline. As such, it does not provide treatment guidelines or recommendations.

The document has been informed by published literature as well as local and international practice. The pathway is not designed to be exhaustive, but should act as a guide.

3 Referral pathways

The Acute Myeloid Leukaemia Patient Pathway is illustrated in Appendix 1.

1. Patients with acute leukaemia should be referred immediately to a haematologist for assessment (9). Referral policies should be available to promote prompt and appropriate referral (10).

[2] Strategies for the provision of SACT services for children and adolescents and young adults with cancer are being managed in a separate work stream within the NCCP.

[3] SACT (systemic anti-cancer therapy) involves systemic treatment for cancer; involving parenteral and oral anti-cancer therapies, including but not limited to chemotherapy, targeted therapies and immunotherapies.

2. An efficient triage, transfer and workup process is critical when results from a blood test or bone marrow assessment / tissue biopsy indicate that a patient may have acute leukaemia (11).
    a. Immunophenotyping of samples needs to consider the future management of minimal residual disease (MRD) monitoring.
3. These patients should be urgently referred to an emergency department[4] or directly to a haemato-oncology inpatient unit which treats AML.
4. All new and relapsed patients should be referred to the tumour conference for confirmation of diagnosis, prognosis and management plan, taking into account their performance status, needs and co-morbidities.
5. Patients should be considered for treatment on clinical trials if an appropriate trial is available.
6. Planning for an allogeneic stem cell transplant should begin at the time of diagnosis in conjunction with the transplant centre. Patients should be human leukocyte antigen (HLA)-typed at the time of diagnosis.
    a. Patients considered for haematopoietic stem cell transplantation need to be referred early in their treatment (as soon as is practical and at the latest after recovery from cycle 1 induction) to a Joint Accreditation Committee of the International Society for Cellular Therapy (ISCT) and the European Society for Blood and Marrow Transplantation (EBMT) (JACIE)-accredited centre.
7. A joint approach with consultant geriatricians and palliative care teams may be appropriate in older patients / patients with poor prognosis disease (1).
8. Patients who fail to respond to first-line therapy, lose response or experience disease progression may be discussed with a centre offering a clinical trial for relapsed patients, especially if they progress through second-line treatment (1).

[4] NCCP SACT Model of Care, Recommendation 24: Type 3 SACT hospitals and non-SACT hospitals with an emergency department should have processes in place for the assessment, rapid referral and transfer of patients to an acute SACT hospital in a timely manner.

3.1 Tumour conferences

A standard SOP guidance for haemato-oncology tumour conferences[5] has been developed by the NCCP. This document may be adopted and adapted as appropriate to local processes.

1. Tumour conferences should take place for (1):
   a. all new patients with AML in order to confirm the diagnosis and treatment plan
   b. all patients with a restaging assessment of response to treatment
   c. all patients for whom an allogeneic stem cell transplant is a consideration
   d. all patients where a new line of therapy needs to be considered

2. As per the NCCP Haemato-oncology Tumour Conference - Standard Operating Procedure Guidance[5], the following information should be available to inform the tumour conference discussion:
   a. demographic information (patient's name, date of birth and health care record number)
   b. the Primary Consultant or delegated representative should present the rationale for discussion and patient history
   c. patient-related staging information images (e.g. pathology, radiology) must be available at the conference and suitable technical equipment must be provided for the presentation of the visual material
   d. other relevant reports and clinical information
   e. patient views and preferences, if known
   f. the question being posed for the tumour conference

[5] NCCP Haemato-oncology Tumour Conference - Standard Operating Procedure Guidance. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/tumour-conference-sops/haemonc-tumour-conference.pdf

3. Information to be documented prior to or during the tumour conference may include:
    a. referring physician and / or GP
    b. performance status
    c. an indicator of co-morbidities (e.g. co-morbidity score)
    d. any other relevant history
    e. details of fertility preservation if available
    f. pertinent positive and negative findings on physical examination (splenomegaly, rashes, etc)
    g. availability of a clinical trial/research study and if the patient is eligible
    h. management and treatment plan
    i. clinical nurse specialist/designated contact person
    j. named consultant
    k. See Section 4 (Investigations and diagnosis) for further information to be documented

3.1.1 Tumour conference considerations

1. Patients with AML should be discussed at a tumour conference within two weeks of diagnosis. In some cases, it may be safe to wait for genetic test results before initiating treatment, whilst in others, treatment may have commenced prior to the tumour conference discussion, based on clinical urgency (1).
2. Where there is a need for urgent treatment, new patients should be commenced on an appropriate therapy and scheduled for discussion at the next tumour conference.
3. The GP should be informed of the tumour conference outcome in line with NCCP guidance.
4. Location of tumour conferences:

    In line with the National Cancer Strategy 2017-2026, the NCCP are developing appropriate MDT, centralisation and treatment arrangements to meet the diverse needs of patients with haematological cancers. Once these arrangements are agreed patients should be discussed at the appropriate tumour conference within these agreed arrangements.

5. All AML patients should have their care discussed in a complete[6] tumour conference attended by members involved in the diagnosis, treatment, or care of a particular patient, and all the clinicians in the tumour conference should regularly treat patients with AML.
6. For a resilient service, there should be adequate resources and supports in place for tumour conferences. Please refer to the NCCP Haemato-oncology Tumour Conference SOP Guidance[5] for details of requirements.
7. Required attendees at the tumour conference should include[5]:
    a. Two Consultant Haematologists
    b. Clinical nurse specialist (CNS) / other nurses
    c. Consultant Histopathologist / Haematopathologist where indicated
    d. Non-consultant hospital doctors (NCHDs) in Haematology with cancer service rotations
    e. Tumour conference coordinator
    f. Data manager
    g. Administrative support
    h. Consultant Radiologist, where indicated.
    i. Consultant Radiation Oncologist, where indicated
8. Desirable attendees may include other relevant disciplines, as appropriate, depending on the nature of the cases to be discussed.
9. Individual clinicians are responsible for discussing the tumour conference recommendations with their patients, who should have the opportunity to be informed of the outcome of the tumour conference (12).

[6] A complete tumour conference is defined as a tumour conference that follows (as appropriate) the NCCP standard operating procedure for haemato-oncology tumour conferences and provides a recommendation on the patient's treatment plan.

4 Investigations and diagnosis

The following tests may be carried out, as appropriate, as part of investigation and diagnosis (1):

a. full blood count (FBC), haematinics, liver function tests (LFTs), urea and electrolytes (U&E), glucose, lactate dehydrogenase (LDH), urate
b. coagulation screen
c. C-reactive protein (CRP)
d. blood group and antibody screen
e. renal, liver and bone profile
f. hepatitis B virus (HBV) [HBV sAg, HBV sAb, HBV cAb], hepatitis C virus (HCV), human immunodeficiency virus (HIV), cytomegalovirus (CMV) serology [IgG] and additional screening as clinically indicated
g. pregnancy test (if relevant)
h. urinalysis
i. human leukocyte antigen (HLA) screen of patients and siblings in patients where a stem cell transplant (SCT) is being considered
j. bone marrow aspirate and trephine histology
l. bone marrow aspirate immunophenotyping
m. molecular and cytogenetic analysis at diagnosis and relapse
n. relevant imaging (e.g. computed tomography (CT) staging). For patients with features suggestive of central nervous system disease, consider magnetic resonance imaging (MRI) / CT head / spine +/- lumbar puncture.
o. echocardiogram (ECHO) study
p. electrocardiogram (ECG)
q. risk score

5 Patient information / support

Patient information / support should be provided in line with the recommendations of the NCCP Oncology Medication Safety Review Report[7] and the NCCP SACT Model of Care[8] (6, 7).

The Psycho-Oncology Multi-Disciplinary Teams are located in the main cancer treatment centres. The focus of the Psycho-Oncology service is to provide psychosocial and psychological support to cancer patients who are experiencing significant levels of distress due to their cancer diagnosis.

There are a variety of community cancer support centres and services located nationally, ranging from support groups to full-time professional organisations. Further information on the patient supports available can be found at this link: www.hse.ie/survivorship.

6 Treatment

1. Aggressive haematological malignancies such as AML are potentially curable with intensive chemotherapy[9] (10).
2. Patients diagnosed with acute haematological malignancies such as AML who are treated with intensive chemotherapy should be cared for in a designated number of centres[10] capable of accepting patients on transfer within 24 hours of diagnosis (5, 7).
3. Treatment for AML follows strict protocols. Patients are considered for clinical trials if available / appropriate (Refer to Section 0: Research / Clinical Trials).
4. Treatment regimens for individual patients will be decided as per tumour conference.
5. Where circumstances allow, less intensive treatments and supportive care can be provided closer to the patient's home in cooperation with the treatment centre.
6. There is a NCCP Myeloid Clinical Advisory Group in place. Their role includes overseeing the development and review of national chemotherapy regimens and developing, reviewing and approving clinical guidelines for new drugs and new indications for existing drugs that are in the HSE reimbursement approval process.

[7] NCCP Oncology Medication Safety Review Report; Recommendations 29-32, 36, 37
[8] NCCP SACT Model of Care; Recommendations 1 and 2
[9] Intensive chemotherapy is defined as that which is anticipated to result in severe neutropenia of 0.5 x10^9 /L or lower for greater than 7 days, in addition to other potential organ toxicities, co-morbidities and frailty.
[10] The centralisation of haemato-oncology strategy is in development

6.1 Summary of main considerations in the treatment of AML

1. Appropriate specimens should always be taken before therapy is started.
2. AML may be a curable disease in young and older fit patients. It becomes harder to treat as the patient ages. Fewer patients are cured as age advances and therapeutic complications become increasingly common (1).
    a. All patients should be treated with age-appropriate therapy.
    b. All patients should be treated with therapy adjusted to performance status and AML risk stratification.
    c. For AYA patients, there should be engagement with the relevant AYA centre once the pathways are established. AYA patients can be discussed at the relevant local tumour conference but they must also be referred to the National AYA multidisciplinary team meeting (MDM) once the pathways are established.
3. As the disease is rare and treatment is complicated, there are many areas where best practice is not defined.
4. Experienced specific supportive care and expertise is required.
    a. Acute haematological malignancies such as AML require complex inpatient care, comprehensive multidisciplinary team (MDT) availability at all times and ideally single high efficiency particulate air-filtered (HEPA) rooms. Admission facilities and day units that are separate from the general hospital emergency department are desirable. Access to other key services, especially intensive care, radiology and laboratory medicine (including transfusion medicine) on both an emergency and elective basis is required (5).
        - The hospital should also participate in clinical trials for patients with AML where available.
    b. Centres caring for patients who are receiving high-intensity chemotherapy should provide high-intensity (non-transplant) chemotherapy for induction or re-induction of remission to a minimum of 10 patients per year who have new or relapsed haematological malignancies and who are at risk of more than 7 days of neutropenia of 0.5×10^9 /litre or lower (10).

5. Adherence to the detail and timing of scheduled treatment strategies is important. Minimising therapeutic delays has a positive impact on outcomes.
6. Recognising complications of therapy quickly and being aware of which complications require treatment cessation and which do not are also vital.
7. Allogeneic bone marrow transplant is a common element of patient management (4). Patients identified as transplant eligible at presentation should be referred to a specialist centre for consideration of allogeneic transplantation at the earliest opportunity (13).

7 End of treatment information

End of treatment is defined as the end of the patient's therapy plan and / or when there are any significant changes in treatment (1). The tumour conference outcome form and clinic letters will serve to communicate new lines of treatment to the GP (1).

7.1 Treatment summary and care plan

The National Cancer Strategy 2017-2026 recommends that all hospitals should offer patients a patient treatment summary and care plan as part of their support (5). A treatment summary provides a summary of the cancer treatments received by the end of the primary treatment and planned follow-ups. The aim is to provide information not only to the patient, but also to the GP about possible consequences of cancer and its treatment, signs of recurrence and other important information.

A care plan is the agreed plan between the patient and healthcare professional about how the identified areas of concern will be addressed. This may cover provision of information, onward referral for specialist assessment and intervention, or patient-related matters such as engagement with employer / human resources department regarding graduated return to work options.

7.2 End-of-treatment consultation

An end-of-treatment consultation should be offered to every patient. This should include an end-of treatment holistic needs assessment and associated written care plan, and should also include the discussion and provision of a comprehensive treatment summary.

The NCCP SACT Model of Care states that on completion of SACT, relevant information must be given to each patient, the patient's GP and any other primary care facility that the patient is linked with (7).

8 Follow-up arrangements

Patients on treatment will generally need inpatient admission for their induction treatment, and often for parts of their additional cycles of therapy. When discharged, frequent monitoring is required and is dependent on the therapeutic phase of treatment and the degree of supportive care required (1).

The NCCP SACT Model of Care (2022) recommends that an individual follow-up care plan should be provided to each patient (7).

Patients may have shared follow-up care between a specialist site and the local treating hospital. These arrangements must be clearly outlined so that the patient knows where to attend in an emergency and understands the pathways of communication between the sites. These arrangements must be documented in PPPGs **(Refer to local policy).**

Patients who have completed SACT will be followed up according to Table 1 below (1), which can be modified according to the patient's individual risk.

Specialist treatments, for example SCT and chimeric antigen receptor T-cell (CAR-T) therapy, may require a different follow-up schedule.

Table 1: Suggested follow-up of patients with AML post chemotherapy

Year 1 & 2	3 monthly
Year 3-5	3-6 monthly, depending on disease risk
Year 5	6 monthly
Year 6 onwards	Discharge to GP

The National Cancer Strategy 2017-2026 recommends that primary care services should be supported by hospital-based care with specialist haemato-oncology nurse-led clinics, using remote follow-up where appropriate (5).

9 Research / clinical trials

All patients should be considered for a clinical trial wherever possible (1). This is in line with the National Cancer Strategy 2017-2026 and the NCCP SACT Model of Care (2022) (5, 7). The National Cancer Information System (NCIS) will support the gathering of cancer clinical trial activity.

For patients with long distances to travel to the trial centre, the option of shared care may be considered (1)[11]:

- Care may be transferred to the local unit for the maintenance phase of care if clinically appropriate and allowed for within the trial protocol / ethics approval.
- For those centres wishing to participate in shared care, clear documentation of shared care arrangements must be undertaken with communication to centres, the GP and the patient.

10 End of life care

For older patients and in those with poor performance status and / or high-risk disease, discussions regarding prognosis and treatment options should also include discussions on end-of-life care. These are to facilitate transitions between active disease-modifying therapy to clinical trials, or supportive care only at the time of disease progression / non-response. Care may be required from specialist palliative care teams.

11 Data requirements

Accurate data collection is essential to monitor outcomes and the collection of this information, particularly clinical data, remains the responsibility of the members of the tumour conference with support from a data manager. NCCP standardised haematology tumour specific datasets should be used where available.

[11] Patients diagnosed with acute haematological malignancies such as ALL who are treated with intensive chemotherapy should be cared for in a designated number of centres capable of accepting patients on transfer within 24 hours of diagnosis

As per Recommendation 14 of the NCCP SACT Model of Care (2022), all SACT services should have a data and information management strategy document (7). The implementation of NCIS will support many aspects of data and information management in hospitals. Where possible, a shared patient record should be in place to facilitate the sharing of patient records between hospitals and primary care (7). Data managers, tumour conference co-ordinators and other staff should be in place at designated cancer centres to facilitate this (5).

The National Cancer Registry Ireland (NCRI) collects, collates and analyses data on cancer incidence, staging, treatment and survival. Mortality data is collected and published by the Central Statistics Office (5).

12 References

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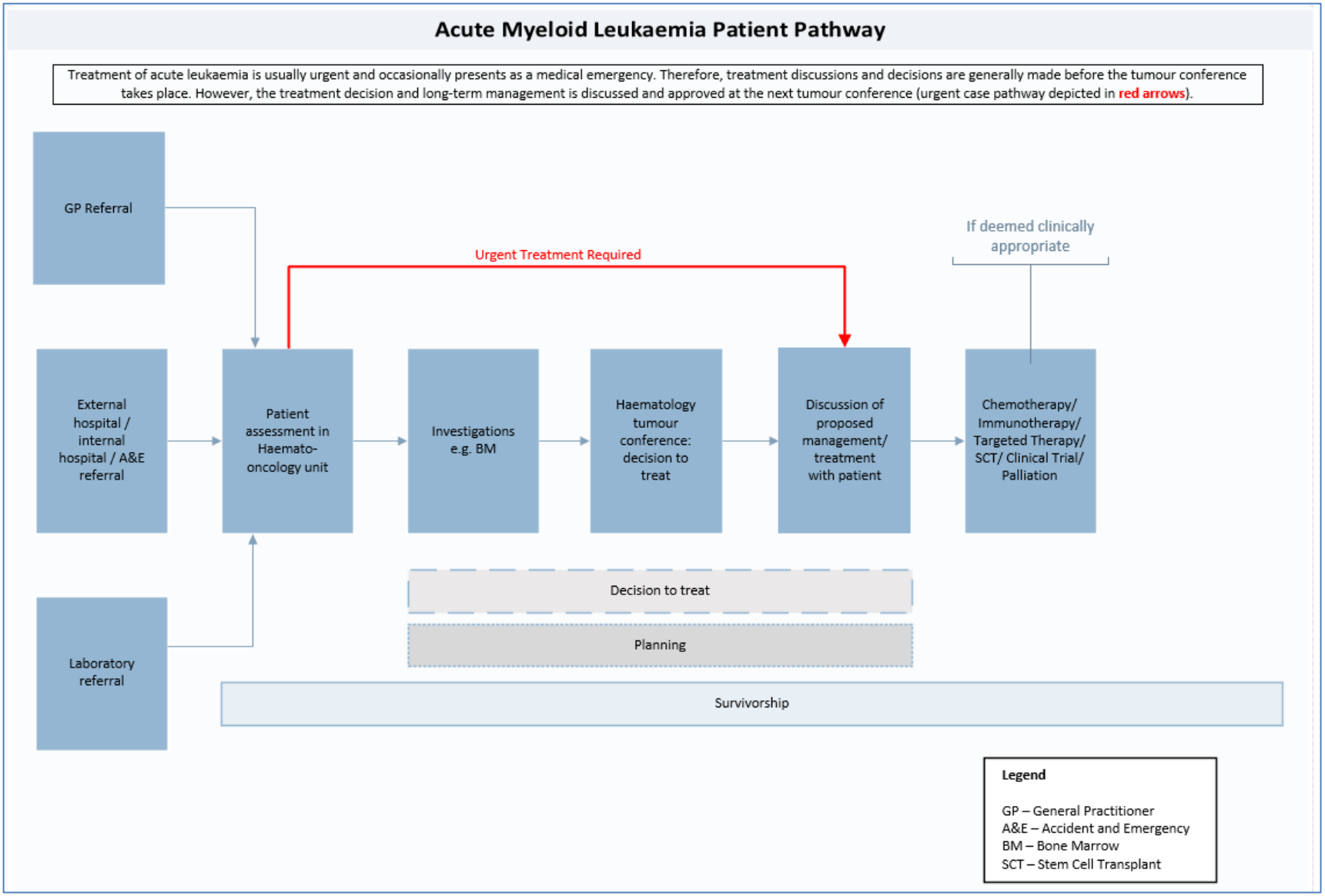
Appendix 1. Acute Myeloid Leukaemia Patient Pathway



Appendix 2. Abbreviation and Acronyms

The following abbreviations and acronyms have been used in this document:

Abbreviation/Acronym	Detail
A&E	Accident and emergency
alloHCT	Allogeneic haematopoietic cell transplantation
AML	Acute myeloid leukaemia
AYA	Adolescents and young adults
BM	Bone marrow
CAR-T	Chimeric antigen receptor T-cell
CMV	Cytomegalovirus
CNS	Clinical nurse specialist
CRP	C-reactive protein
CT	Computed tomography
ECHO	Echocardiogram
ECG	Electrocardiogram
FBC	Full blood count
GP	General practitioner
G6PD	Glucose-6-phosphate dehydrogenase
HBV	Hepatitis B virus
HCB	Hepatitis C virus
HEPA	high efficiency particulate air-filtered
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
IgH	Immunoglobulin heavy chain
JACIE	Joint Accreditation Committee of the International Society for Cellular Therapy (ISCT) and the European Society for Blood and Marrow Transplantation (EBMT)
LDH	Lactate dehydrogenase
LFTs	Liver function tests
MDM	Multidisciplinary team meeting
MDT	Multidisciplinary team
MRD	Minimal residual disease
MRI	Magnetic resonance imaging
NCHD	Non-consultant hospital doctors
NCIS	National Cancer Information System
NCRI	National Cancer Registry Ireland
SACT	Systemic Anti-cancer Therapy
SCT	Stem cell therapy
U&E	Urea and electrolytes