



# Haematology Cancer Clinical Guidelines

Haematology Expert Advisory Group (EAG)  
on behalf of Northern Cancer Alliance

<b>Title:</b>	Haematology Cancer Clinical Guidelines
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**Version History:**

<b>Date:</b>	10.04.18	<b>Version:</b>	V17 – section 6	<b>Review Date:</b>	November 2019
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## Document Control

Version	Date	Summary	Review Date
V17			

**Date Agreed:** Haematology EAG members agreed the Guidelines on:  
Emailed to group on 12.04.18 for formal endorsement at the next meeting

**Review Date:** November 2019

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# GUIDELINES FOR MANAGEMENT OF ACUTE LYMPHOBLASTIC LEUKAEMIA

## Overview

The Alliance Expert Advisory Group recommends that all adult patients with acute lymphoblastic leukaemia (precursor B-lineage and T-lineage ALL) are invited for entry into the UKALL 14 trial if eligible.

The main inclusion criteria of UKALL14

1. age  $\geq 25$  and  $\leq 65$
2. newly diagnosed, previously untreated ALL (a steroid pre-phase of 5-7 days is acceptable and can be started prior to registration)

The main exclusion criteria of UKALL14

1. known HIV infection
2. pregnant or lactating women
3. blast transformation of chronic myelogenous leukaemia
4. mature B-cell leukemia i.e. Burkitt's disease t(8,14)(q24;q32) and all disorders with amplification of c-myc e.g. t(2;8)(p12;q24),t(8;22)(q24;q11)

Patients of age between 18 and 24 must be referred to the Teenage and Young Adult MDT and should be considered to be entered into UKALL2011 study

For patients who are not entered into these trials, the following protocols are recommended as the standard of care.

- UKALL 2011 for 24 years and under (discuss at the Teenage and Young Adult MDT), and
- UKALL 14 "standard treatment" arms for adults of age  $\geq 25$  and  $\leq 65$
- UKALL60 for adults  $>60$  if unfit for UKALL14 study – treatment pathways are dependent on cytogenetics, co-morbidities and performance status

NHS England has nationally approved PEG-asparaginase instead of L-asparaginase for induction ALL therapy

## 1. Adults 16-24 years - UKALL2011 trial

Refer to UKALL2011 for guidance on treatment schedules, supportive care and details of MRD testing.



UKALL2011 Protocol v3.0 01-Oct-2013.pdf

[UKALL2011 Protocol](#)

Latest Resources/Other

All patients aged  $> 10$  are classified as NCI high risk and will receive regimen B.

MRD monitoring is done at day 29 and further treatment is stratified based on MRD results at day 29 or tumour volume if LBL. Patients with MRD risk (>0.005%) and MRD No results but slow early responder on day 8 marrow will be switched to regimen C.

Allogenic transplantation is not recommended in patients with CR1 independent of cytogenetics.

## 2. Adults 25-60 years as well as adults >60 fit enough to be considered for an allograft - UKALL14 trial

It is recommended to refer to the UKALL 14 protocol for treatment schedules MRD testing and supportive care.



1 UKALL14 Protocol v7 0 09.09.15 CLEAN.pdf

[UKALL14 Protocol 09.09.15 CLEAN](#)

Latest Resources/Other

- Patients who are not entered into the UKALL14 trial, should receive treatment according to the “standard” arms of the UKALL 14 protocol.
- See the treatment algorithm for adults with acute lymphoblastic leukaemia : age  $\geq$  24 years. (UKALL 14 standard treatment arm).
- Refer to the UKALL 14 protocol for details of phase 1 induction; phase 2 induction, intensification, consolidation and maintenance therapy.
- Patients with **Philadelphia positive disease (Ph<sup>+</sup> ALL)** should also receive continuous daily imatinib, orally, starting at 400mg daily, aiming to escalate to 600mg daily within 2 weeks, if tolerated. This should be continued until transplant wherever possible.
- **Important:** Patients with Philadelphia positive ALL should not receive PEG-asparaginase at any timepoint.
- Patients who achieve complete remission have risk assessment at the end of phase 2 of induction. Any one of the factors below makes the patient **high-risk**.
  1. Age over 40 years
  2. WBC  $\geq$ 30 x 10<sup>9</sup>/L (precursor-B),  $\geq$ 100 x 10<sup>9</sup>/L (T-lineage)
  3. Cytogenetics – any one or more of the abnormalities below
    - t(4;11)(q21;q23)/MLL-AF4
    - low hypodiploidy/near triploidy (30-39 chromosomes / 60-78 chromosomes)
    - complex karyotype (five or more chromosomal abnormalities)
    - Philadelphia chromosome t(9;22) (q34;q11)/BCR-ABL1 (detected by cytogenetic or molecular methods)
  4. High Risk Minimal Residual Disease (MRD) post phase 2 of induction.
- If the MRD result is not available (failed or specimen not sent) patient should be considered standard risk in the absence of any other high risk features.

TREATMENT ALGORITHM FOR ADULTS WITH ACUTE LYMPHOBLASTIC LEUKAEMIA : Age  $\geq$  24 years. (UKALL 14 Standard Treatment Arm)

Refer to the UKALL 14 protocol for details.

Steroid pre-phase (5-7 days); dexamethasone 6 mg/m<sup>2</sup>/day orally for 5-7 days



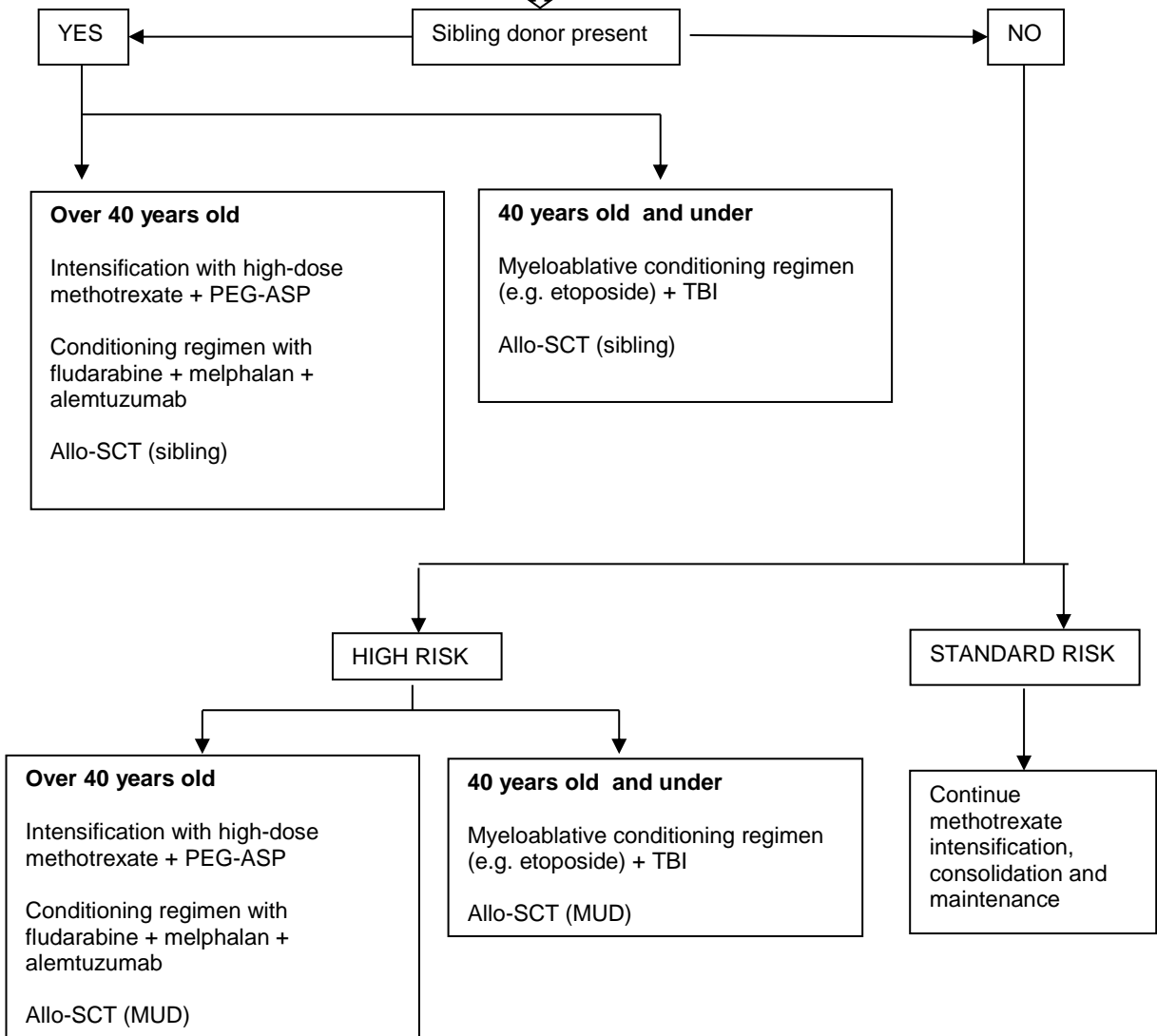
Phase 1 induction (4 weeks) : pegylated asparaginase (PEG-ASP) + standard phase 1 induction therapy



Phase 2 induction (4 weeks) : standard phase 2 induction therapy



Patients in complete remission : risk assessment performed on all patients at this point.



## SCHEDULE OF TESTING FOR MINIMAL RESIDUAL DISEASE (MRD) FOR RISK ASSESSMENT

	<b>Specimens for local assessment</b>	<b>Specimens to be sent to central laboratory**</b>
<b>At Diagnosis</b>	Cytogenetics/molecular assessment of BCR-ABL and MLL on bone marrow.	Bone marrow 3-5ml in EDTA (OR peripheral blood 30-50ml in EDTA if WCC > 30x 10 <sup>9</sup> /L). BCR-ABL status will also be checked.
<b>At recovery* post Phase 1</b>	Bone marrow aspirate for remission assessment locally.	Bone marrow from biopsy: 3-5ml in EDTA for MRD assessment (IgH/TCR rearrangements for Ph-ALL, BCR-ABL for Ph+ALL)
<b>At recovery* post Phase 2</b>	Bone marrow aspirate for remission assessment locally.	Bone marrow from biopsy: 3-5ml in EDTA for MRD assessment (IgH/TCR rearrangements for Ph-ALL, BCR-ABL for Ph+ALL)

\*Recovery is defined as neutrophils >0.75 x 10<sup>9</sup>/L, platelets >75 x 10<sup>9</sup>/L.

\*\*All samples should be sent by courier or by 1st class post to arrive the same day or overnight to the following address:

Minimal Residual Disease Laboratory  
URGENT UKALL14 STUDY SAMPLE (FAO Adele Fielding, Rachel Mitchell or Krisztina Alapi)  
UCL Cancer Institute  
Paul O’Gorman Building  
72 Huntley Street  
London UK  
WC1E 6DD

MRD Lab email: [ALLMRDlab@ucl.ac.uk](mailto:ALLMRDlab@ucl.ac.uk)

### **Adults > 60 years - UKALL60 trial**

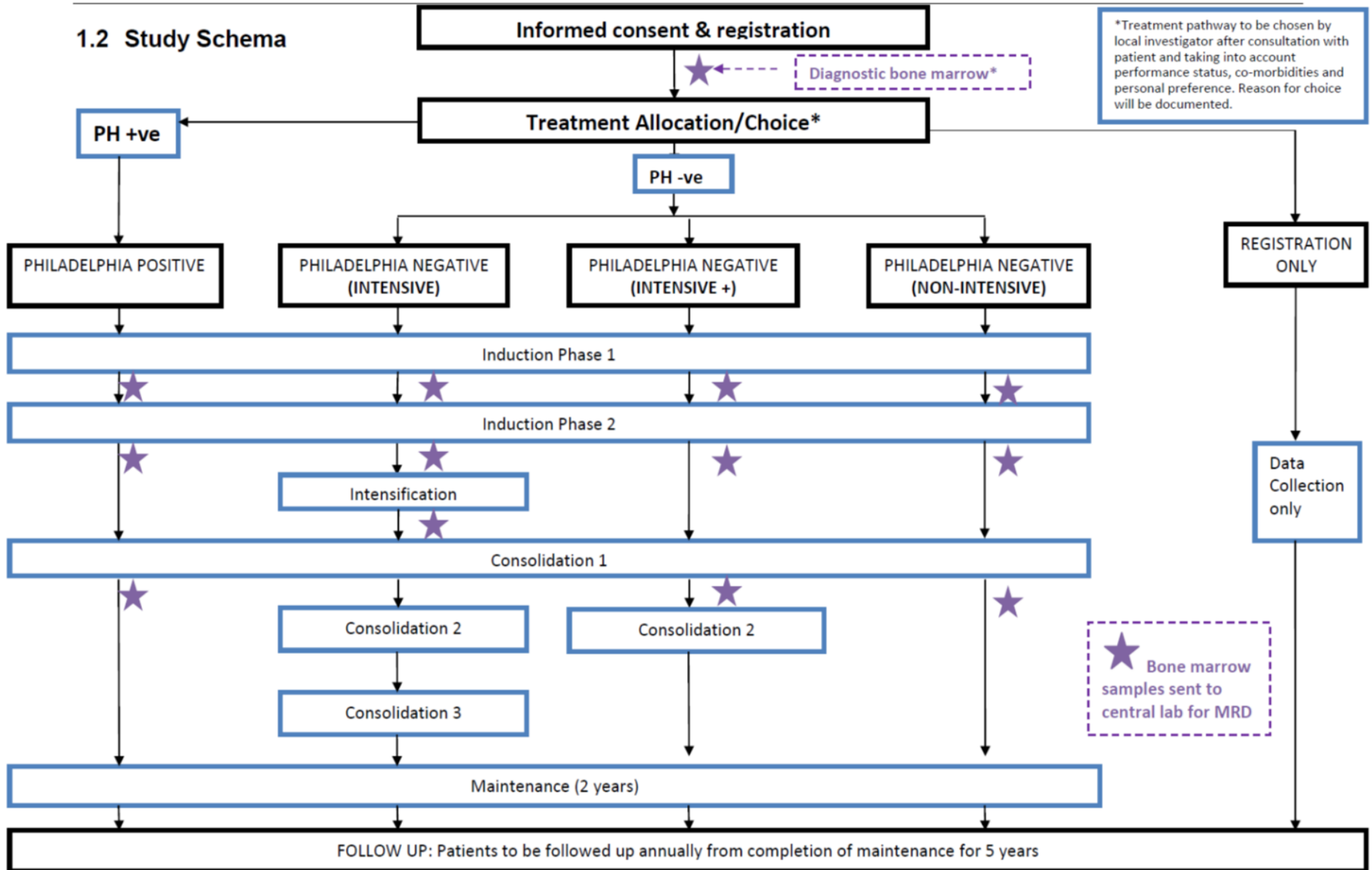
It is recommended to refer to the UKALL60 protocol for treatment schedules and supportive care.

[UKALL60 Protocol](#)

Latest Resources/Other

Four different treatment pathways are suggested depending on cytogenetics, co-morbidities and performance status of patient. The treatment pathway will be chosen by local clinician after discussion with patient.

1.2 Study Schema



All patients with Philadelphia positive ALL will be treated as per pathway A. Patients with Ph-neg ALL need to be carefully assessed and depending on clinical status can either be offered, an intensive arm (pathway B), an intensive + arm (pathway C) or a non-intensive arm (pathway D)

MRD assessment is experimental and should only be undertaken if patient is participating in the study. Intent is potentially curative but although remission is often achieved, relapses frequently occur and relapsing patients would not normally be offered salvage chemotherapy. This protocol can also be used for patients aged 60 or younger deemed unfit for standard arm of UKALL14.

#### **4. Relapsed ALL**

Patients treated on UKALL 2011 and UKALL14 and not transplanted owing to perceived 'low risk' may relapse. Other options for reinduction include FLAG-Ida, clofarabine (via CDF) and nelarabine (via CDF). Patients should proceed to transplantation if remission is achieved.