Pan Birmingham NHS
Cancer Network

Guidelines for the Management of Acute Myeloid Leukaemia in Adults (AML)

Version History

Version	Date	Summary of Change/Process
2.0	08.05.08	Endorsed by the Governance Committee
2.1	14.02.11	Circulated at NSSG meeting
2.2	28.04.11	With Juliet Mills changes for resubmission at the next NSSG
2.3	15.06.11	Approved by the Haematology NSSG Chair
2.4	29.07.11	Reviewed and updated by Fiona Clair, Haematology NSSG Chair
3.0	03.08.11	Reviewed and endorsed by Governance Committee

Date Approved by Network Governance	**August 2011**

Date for Review	**August 2014**

Changes between version 2 and version 3

- Additional information on Cytogenetics, FISH and molecular testing for Flt-3 (mutations of c-kit, RUNX-1, NPM-1, CEBP-A may also be considered but are not core funded) included.
- Additional information on Improving outcomes guidance requires this to be done within an integrated diagnostic service and to produce a finalised integrated report. The diagnosis should be reviewed at a haematology MDT for treatment planning.
- Updated information on current national clinical trials (AML 16 and 17).

1. This Guidance has been produced to support the following:

a) The management of patients suspected of having AML
b) The management of patients diagnosed with AML

2. Guideline Background

2.1 In Pan Birmingham Cancer Network two hospitals are designated transplant centres for haematological malignancies - University Hospital Birmingham Foundation Trust and Heartlands Hospital (part of Heart of England Foundation Trust [HEFT]). These two hospitals treat patients with haematological malignancies at BCSH levels I-IV. In addition to this Good Hope Hospital (part of HEFT) practises to level 1 and Worcester Hospital and Sandwell and West Birmingham Hospitals NHS Trust Sandwell site practise to level 2.

2.2 The Haematology Network Site Specific Group has agreed to continue to follow the BCSH Guidelines on the diagnosis and management of acute myeloid leukaemia (2005). This is a summary – please see reference[1] for full version of these guidelines.

Guideline Statements

3. Referral

3.1 Patients with a blood count / film reported as suggestive of acute leukaemia the should be referred **immediately** to the local haematology team.

3.2 Patients with a combination of the following should undergo an urgent blood count and film, erythrocyte sedimentation rate (ESR) and plasma viscosity or c-reactive protein (+/- clotting screen):

- Fatigue
- Drenching night sweats
- Fever
- Weight loss
- Breathlessness
- Bruising / bleeding
- Recurrent infections
- Lymphadenopathy
- Splenomegaly

3.3 Patients should be referred using in the 2 week wait form (appendix 1) to their local haematology service.

4. Investigation and diagnosis

4.1 Patients suspected of having acute leukaemia should urgently undergo the following:

a) Bone marrow aspirate and trephine biopsy (unless peripheral blood blast count is high). The trephine should be assessed with immunohistochemistry.
b) Immunophenotyping with extended panels to include multi-colour flow cytometry and to identify leukaemia associated phenotypes (LAP) which may be monitored for minimal residual disease.
c) Cytogenetics, FISH and molecular testing for Flt-3 (mutations of c-kit, RUNX-1, NPM-1, CEBP-A may also be considered but are not core funded).

4.2 Patients with neurological symptoms will require CT/MRI and lumbar puncture at diagnosis.

4.3 The marrow and blood samples for diagnosis should be reported by a specialist haematopathologist (histologist or haematologist) trained in leukaemia morphology. The diagnosis of leukaemia is reliant on highly-specialised immunology, haematology, histopathology and genetic services, these components parts should be integrated to produce a diagnosis as per WHO criteria. Improving outcomes guidance requires this to be done within an integrated diagnostic service and to produce a finalised integrated report. The diagnosis should be reviewed at a haematology MDT for treatment planning.

5. For all patients

5.1 Local, Network and BCSH guidelines should be followed for the management of the following treatments and care:

a) Blood and blood product support
b) The use of growth factors
c) Neutropenia – prevention and treatment

These can be found here: http://www.birminghamcancer.nhs.uk/staff/clinical-guidelines/haematological-cancer

5.2 Tumour lysis should be prevented / detected early and managed proactively. This should include careful monitoring of U's and E's, potassium and urine output as well as adequate hydration, allopurinol; and rasburicase where the white cell count (WCC) is >100. Leucopheresis should be considered in patients who do not have APL but when the WCC is greater than 100.

5.3 Consider using hydroxycarbamide to reduce a high WCC if there is a delay in starting intensive chemotherapy e.g. patient awaiting transfer to another hospital.

5.4 Echocardiogram to assess LV function may be required if intensive induction with anthracyclines is considered.

5.5 Arrange for central venous access if intensive induction is considered.

5.6 Where active treatment is not recommended patients may find a second opinion reassuring and this should be supported.

6. De novo\secondary AML

6.1 All patients fit enough to receive intensive treatment should be offered one of the national AML trials, either AML 17 or the intensive arm of AML 16. The decision to offer AML17 or AML 16 is based on age, performance status and patient wishes. Older (>60) or less fit patients who are suitable for intensive treatment are usually recommended to go into AML 16.

6.2 Patients opting for non-intensive chemotherapy (and not entered into clinical trials) should be offered low dose cytarabine or may be eligible for azacitidine (as per NICE TA218).

6.3 Patients unable to tolerate chemotherapy should be offered best supportive care including transfusion support and hydroxycarbamide.

7. Acute promyelocytic leukaemia (APL)

7.1 ATRA should be started as soon as APL is suspected.

7.2 Leucopheresis should be avoided.

7.3 Platelet count should be maintained at >50 with platelet transfusions.

7.4 ATRA syndrome should be treated promptly with dexamethasone 10mg bd until symptoms resolve.

7.5 Diagnostic work up should include cytogenetic and molecular analysis.

7.6 Patients with *PML-RARA* positive APL, deemed suitable for intensive therapy, should be treated with concurrent ATRA and anthracycline based chemotherapy for induction, followed by anthracycline-based consolidation therapy.

7.7 Eligible patients should be offered entry into the AML 17 study.

7.8 Patients should undergo molecular monitoring after treatment to guide further therapy.

7.9 For relapsed disease, ATRA should not be used as single agent therapy due to significant possibility of acquired secondary resistance and arsenic trioxide (ATO) should only be used in patients with confirmed *PML-RARA* positive APL.

8. Pregnancy

9.1 AML in pregnancy should be managed jointly between the haematologist and the obstetrician with full involvement of the mother.

9.2 Chemotherapy in the first trimester should be avoided if possible. The option of terminating the pregnancy should be discussed with the mother. If termination is refused and the mother's life is at risk, chemotherapy should be started.

9.3 Where appropriate consideration should be given to early induced labour between cycles of chemotherapy.

9. Transplantation and management of relapse

9.1 Allogeneic transplantation is a highly effective mechanism of reducing the risk of disease relapse but is associated with significant morbidity. It should therefore be offered to patients with high risk AML in the first remission who have an HLA identical donor. In patients lacking a sibling donor an unrelated transplant may be considered. Standard risk patients should be offered allo-transplantation as part of a clinical trial. Allogeneic transplantation is not indicated in good risk patients in 1st CR.

9.2 HLA-matched sibling allogeneic transplantation improves outcome in patients in second CR and should be considered the treatment of choice for younger patients who are in second remission.

9.3 Allogeneic transplants performed using reduced intensity conditioning regimens have the capacity to produce long term disease free survival in a substantial proportion of patients with AML in 1st or 2nd CR. Consequently a reduced intensity allograft, using a sibling or matched unrelated donor, should be considered in older patients with AML in 1st CR (normal or high risk) or 2nd CR, preferably in the context of a clinical trial.

9.4 Younger high risk patients, or those beyond first remission, may be considered for a halpo-identical or cord blood transplant in the context of a clinical trial.

9.5 The role of autografting in the management of AML is contentious but autologous transplantation may be of benefit in patients with AML in 2nd CR who lack a suitable allogeneic donor.

9.6 Salvage chemotherapy to achieve a second CR should be considered if the patient has a transplant option available and is in good performance status. Regimens may be previous induction regimen if CR is >12months or with a more intensive salvage with high dose cytarabine.

10. Follow-up

10.1 Follow-up should be in the haematology clinics at appropriate intervals e.g. 3 monthly when in complete remission after completion of all courses of induction & consolidation chemotherapy. Patients should be advised to report promptly to their GP for an urgent FBC if they develop any signs or symptoms that might indicate disease relapse.

10.2 Patients who have been recruited into a clinical trial will be followed up as per the protocol.

11. Palliative care

Early links should be made to the palliative care team where the treatment intent is not curative or where the patient has symptoms that are difficult to manage.

12. Clinical trials

12.1 Wherever possible, patients who are eligible should be offered the opportunity to participate in National Institute for Health Research portfolio clinical trials and other well designed studies.

12.2 Where a study is only open at one Trust in the Network, patients should be referred for trial entry. A list of studies available at each Trust is available from Pan Birmingham Cancer Research Network.
Email: PBCRN@westmidlands.nhs.uk .

12.3 Patients who have been recruited into a clinical trial will be followed up as defined in the protocol.

13. Patient information and counselling

13.1 All patients, and with their consent, their partners will be given access to appropriate written information during their investigation and treatment, and on diagnosis will be given the opportunity to discuss their management with a clinical nurse specialist who is a member of the relevant MDT. The patient should have a method of access to the haematology team at all times.

13.2 Access to psychological support will be available if required. All patients should undergo a holistic needs assessment and onward referral as required.

Monitoring of the Guideline

Implementation of the guidance will be considered as a topic for audit by the NSSG in 2012\2013

References

1 Milligan et. al. 2005 Guidelines *for the Management of Acute Myeloid Leukaemia in Adults*. BCSH 2005 www.bcshguidelines.com
2 NICE 2005 Referral Guidelines for Suspected Cancer www.nice.org.uk
3 2011 National Comprehensive Cancer Network Guidelines for AML (US): version2.2011

Authors of versions 1 and 2

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Approval Signatures

Pan Birmingham Cancer Network Governance Committee Chair

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Signature  Date August 2011

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Signature  Date August 2011

Network Site Specific Group Clinical Chair

Name: Fiona Clark

Signature  Date August 2011

Appendix 1 – 2 week wait referral form

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URGENT REFERRAL FOR SUSPECTED HAEMATOLOGY CANCER

If you wish to include an accompanying letter, please do so. **On completion please FAX to the number below.** (Version 2.0)

These forms should only be used for suspected cancer and in conjunction with the NICE Referral Guidelines for Suspected Cancer, June 2005

Patient Details	**GP Details (inc Fax Number)**
Surname Forename D.O.B. Gender Address Postcode Telephone NHS No Hospital No Interpreter? Y / N First Language:	**Date of Decision to Refer** **Date of Referral** **GP Signature**

Relevant information: (Check as appropriate)

Symptoms/Signs:

Fatigue	☐	Drenching night sweats	☐	Fever	☐
Weight Loss	☐	Generalised itching	☐	Recurrent infections	☐
Bruising	☐	Breathlessness	☐	Lymphadenopathy	☐
Bone Pain	☐	Alcohol-induced pain	☐	Persistent unexplained splenomegaly	☐

Additional Lymphadenopathy Features:

Lymph nodes increasing in size	☐	Lymph nodes greater than two cm in size	☐
Persistence for six weeks or more	☐	Widespread nature	☐
Associated splenomegaly, night sweats or weight loss	☐		

Investigations:			
ESR	_____	Full Blood Count	_____
Blood film	_____	Clotting screen	_____
X-ray	_____	Liver/Bone profile	_____
Urea & Electrolytes	_____	Immunoglobulin/paraprotein	_____

Clinical Details:

History/Examination/Investigations……

Medication ……

For Hospital Use

Appointment Date Clinic Attending

Was the referral appropriate Yes No (if no please give reason)

HAEMATOLOGY CLINICS WITH RAPID ACCESS FACILITIES

Hospital	Tel	Fax
City and Sandwell	**0121 507 5805**	**0121 507 5075**
Good Hope	**0121 424 5000**	**0121 424 8952**
Heartlands and Solihull	**0121 424 5000**	**0121 424 8952**
Queen Elizabeth (UHBFT)	**0121 627 2485**	**0121 460 5800**
Walsall Manor	**01922 721172 ext 7110 or 7785**	**01922 656773**

ENDORSED BY THE GOVERNANCE COMMITTEE