LCA Haemato-Oncology Clinical Guidelines

Acute Leukaemias and Myeloid Neoplasms

Part 5: Myelodysplastic Syndromes

April 2015
Contents

1. Introduction ..........................................................................................................................4
2. Referral Pathways from Primary Care..................................................................................5
3. Investigation and Diagnosis ..................................................................................................7
   3.1. Pathology .......................................................................................................................13
4. Risk Stratification ................................................................................................................14
5. Patient Information/Support .................................................................................................16
6. Treatment ..............................................................................................................................17
   6.1. Low or intermediate-risk MDS ......................................................................................17
   6.2. High risk MDS ................................................................................................................18
   6.3. Chronic myelomonocytic leukaemia (CMML) ...............................................................19
   6.4. Fertility ..........................................................................................................................19
7. Management of Disease and Treatment-related Complications ........................................20
   7.1. Anaemia ........................................................................................................................20
   7.2. Severe neutropenia .........................................................................................................20
   7.3. Neutropenic sepsis .........................................................................................................20
   7.4. Severe thrombocytopenia ...............................................................................................21
   7.5. Haemostasis and thrombosis .........................................................................................21
   7.6. Transfusional iron overload .........................................................................................21
8. Supportive Care .....................................................................................................................23
   8.1. Anaemia ........................................................................................................................23
   8.2. Transfusions ..................................................................................................................23
   8.3. Haemostasis and thrombosis .........................................................................................23
   8.4. Infection prophylaxis .................................................................................................23
9. Treatment Summary and Care Plan ....................................................................................24
   9.1. Treatment summary and care plan ..............................................................................24
10. Follow-up Arrangements ....................................................................................................25
11. Rehabilitation and Survivorship ........................................................................................25
   11.1. Psychological impact ....................................................................................................25
12. Research/Clinical Trials ......................................................................................................26
13. End-of-life Care ...................................................................................................................26
1. Introduction

This guidance should be read in conjunction with the British Committee for Standards in Haematology (BCSH) myelodysplastic syndrome (MDS) guideline¹ and the European Leukaemia Net (ELN) guidelines on myelodysplastic syndromes.²

The myelodysplastic syndromes (MDS) are a group of clonal stem cell disorders characterised by qualitative and quantitative defects in haemopoiesis that predispose individuals to anaemia, life-threatening bleeds and infection concomitant with a risk of transforming to acute myeloid leukaemia (AML).

The incidence of MDS is 4–5 per 100,000, but it increases with age such that the incidence is 30 per 100,000 in those aged over 70; and 40 per 100,000 in those aged over 80. Some 10% of MDS are secondary, most often due to radiotherapy or chemotherapy for cancer; with increasing numbers of patients surviving chemotherapy, the incidence of therapy-related MDS may also be set to increase.

Cytogenetic abnormalities are present in 40–50% of patients and are of value both in confirming the diagnosis and indicating the risk of disease progression. More recently, molecular abnormalities that commonly occur have been identified and their prognostic value is being clarified. Thus, several prognostic indices incorporating these features have been developed in order to guide optimal management.
2. Referral Pathways from Primary Care

A blood test (FBC) should be performed in elderly patients presenting with symptoms of anaemia, infection or bruising/bleeding. At specialist centres, a blood film and bone marrow aspirate and trephine (BMAT) with cytogenetics can be undertaken to assess for a clonal abnormality. Where a BMAT is declined by a patient, peripheral blood cytogenetics/FISH may be informative.

Patients with suspected MDS should be referred to a haematologist for assessment. It may be appropriate for patients with severe neutropenia, thrombocytopenia or blasts in peripheral blood to be referred via the 2 week wait pathway (often picked up on a routine blood test via the laboratory) (please see Appendix 1: 2 Week Wait Referral Forms).

All new patients should be referred to the MDT for confirmation of diagnosis, prognosis and management plan taking into account their performance status, needs and co-morbidities. A joint approach with elderly care physicians and palliative care teams may be appropriate (see Annex 3).

The following patients should be brought to the MDT:

- all new patients with MDS in order to confirm the diagnosis and treatment plan
- all patients where a new line of therapy needs to be considered
- all patients with a restaging assessment of response to treatment (e.g. hypomethylating agents or immunosuppression)
- all patients in whom an allogeneic stem cell transplant is a consideration.

Information to be captured and documented prior to or during the MDT includes:

- demographic information
- referring physician and GP
- performance status
- an indicator of co-morbidities (e.g. co-morbidity score)
- any relevant history
- pertinent positive and negative findings on physical examination (spleenomegaly, rashes, etc)
- FBC, haematinsics, LFTs, U&E, LDH, urate, reticulocyte count, DAT, AIS, SPEP, peripheral blasts, promonocytes, serum erythropoietin, transfusion dependency
- bone marrow aspirate and trephine histology (i.e. cellularity, megakaryopoiesis, presence of ALIPs, presence of reticulin, lymphoid aggregates and mast cells)
- bone marrow aspirate immunophenotyping, if relevant
- cytogenetic status (FISH del5q, 7q- and t8)
- specific diagnosis/category of MDS
- relevant imaging (e.g. US abdomen or CT chest)
- risk score (at least IPSS)
- availability of a clinical trial/research study and whether the patient is eligible
- management and treatment plan
- key worker/clinical nurse specialist (CNS)
- named consultant/treating team.

The MDT outcome form should be sent to the GP (by email, or preferably by fax) within 24 working hours of MDT discussion.

Patients with MDS IPSS-low and IPSS INT1 and INT2 may be managed at facilities with at least British Committee for Standards in Haematology (BCSH) Level 1 designation. MDS IPSS-high or complex patients may be referred to centres with at least BCSH Level 2 designation and with specific expertise, or which have available trials (see section 12: Research/Clinical Trials). Candidates for transplantation should be referred to a JACIE-accredited centre (see Annex 5). For complex MDS cases, a centre with a specific interest and expertise in MDS (e.g. King’s College Hospital NHS Foundation Trust) may be asked to review the case with the requesting site.
3. Investigation and Diagnosis

Investigations are aimed at excluding secondary causes of dysplasia or cytopenias, and tests to confirm the diagnosis of MDS and exclude other clonal stem cell disorders. Investigation of MDS is usually initiated with the findings of:

- a macrocytic anaemia (or persistent macrocytosis)
- unexplained neutropenia with a blood film that suggests dysplastic features (pseudo Pelger-Huët abnormality)
- unexplained thrombocytopenia (especially when not responsive to immunosuppressive therapy/ITP treatment)
- blasts in the peripheral blood
- a persistent unexplained monocytosis >1x10^9/L.

Appropriate investigations should exclude the following alternative causes:

- haematinic deficiency (vitamin B12, folate, selenium in appropriate patients)
- liver dysfunction
- thyroid dysfunction
- haemolysis
- autoimmune disorders
- viral infections such as HIV, HBV and HCV
- other primary cancers
- systemic inflammatory response syndrome (SIRS)/cytokine storm
- other causes of inflammation (e.g. concurrent infection).

A pertinent history should be taken including:

- smoking and alcohol intake history
- family history of thrombocytopenia, breast and other cancers, lymphoedema, pulmonary fibrosis or MDS/AML
- in younger patients, a family history of constitutional bone marrow failure such as Fanconi’s Anaemia, Schwachman Diamond Syndrome and Dyskeratosis Congenita should be sought
- prior exposure to chemotherapy particularly alkylating agents, topoisomerase inhibitors and radiotherapy (especially to the pelvis)
- occupational exposure to chemicals (e.g. benzenes)
- current medications (such as methotrexate, azathioprine, quinine)
- bleeding and infection history.
Physical examination of the patient should include the assessment of:

- abnormal skin, hair and nail changes/lesions (vasculitis, Sweet’s syndrome, E. nodosum/pyoderma gangrenosum lesions, café au lait spots, premature grey, etc)
- arthritis
- lymphoedema (Emberger syndrome)
- splenomegaly and lymphadenopathy.

In primary care, initial investigations that can be requested/performed are:

- FBC and blood film for morphologic assessment
- reticulocyte count
- DAT
- haematinics: vitamin B12 (if available, methylmalonic acid), red cell folate, ferritin
- haemoglobin electrophoresis
- thyroid function tests
- LDH and uric acid
- U&Es
- LFTs
- CRP and ESR
- serum protein electrophoresis (SPEP) with immunoglobulins (a paraprotein may occur with MDS)
- viral screen: HIV, hepatitis B and hepatitis C
- autoimmune screen.

More specialised tests which may be unavailable to GPs are:

- beta 2 microglobulin
- serum erythropoietin levels
- parvovirus if appropriate
- haptoglobins.

Investigations after referral to haematology:

- bone marrow aspirate and trephine (BMAT)
- peripheral blood film morphology
- PNH screen
- specific genetic tests where there is a suspicion of an inherited or acquired bone marrow failure syndrome.
The diagnosis of MDS is made based on the current World Health Organization (WHO) 2008 classification and morphologic assessment:

*To enable better evaluation of blasts, a haemogram of >500 cells that include >100 non-erythroid cells (where erythroid cells >50% of the count) is necessary for both peripheral blood films and aspirates. In performing a haemogram, due consideration must be given in identifying blasts, promyelocytes, monoblasts and promonocytes and examining >100 erythroblasts and 30 megakaryocytes. In cases where the diagnosis is difficult, i.e. normal / non-informative cytogenetics, no excess myeloblasts or ring sideroblasts, it may be appropriate to repeat the marrow (weeks to months apart) prior to confirming a diagnosis. An observation interval of 6 months is recommended in those with unilineage dysplasia, no increase in blasts (peripheral blood or bone marrow) and where ring sideroblasts <15%.*

The WHO classification requires the assessment of dysplasia in the following samples:

**Peripheral blood film**

It is recommended that at least 200 cells are examined. Features of dysplasia include:

- red cell anisocytosis, poikilocytosis, basophilic stippling
- myeloid nuclear hypolobation, pseudo Pelger-Huët anomaly, hypo- or degranulation
- the presence of myeloblasts
- platelet anisocytosis or giant platelets.

**Bone marrow aspirate**

Dysplastic features should be present in >10% of the cells of the lineage in consideration to give a definition of MDS. The WHO classification stratifies patients based on the presence of dysplasia >10% of cells in any lineage. Multilineage dysplasia is defined as the presence of 10% dysplastic cells in at least two cell lineages and confers a poorer prognosis.

Features of dysplasia include:

- erythroid binuclearity, internuclear bridging, irregular nuclear edge, megaloblastoid changes, ring sideroblasts, cytoplasmic inclusions, cytoplasmic bridging, incomplete haemoglobinisation, fringed cytoplasm or vacuolisation
- myeloid bizarre nuclear shapes, pseudo Pelger-Huët anomaly, nuclear hypersegmentation, pseudo Chédiak-Higashi granules, cytoplasmic hypo- or degranulation, anisocytosis
- megakaryocyte large monolobular forms, small binucleated elements, dispersed nuclei, micromegakaryocytes and degranulation
- an excess of myeloblasts.

Features of dysplasia that are **diagnostic** of MDS are the presence of an acquired Pelger-Huët abnormality in the peripheral blood and presence of micromegakaryocytes in the bone marrow. The presence of circulating blasts of <1%, 1%, 2–4% or 5% alters the WHO classification, as does the presence of 5–10% and 11–20% blasts.

Iron stain with Prussian blue must be performed in order to identify the presence of significant numbers of ring sideroblasts (≥5 siderotic granules covering at least a third of the nuclear circumference in ≥15% of erythroid cells).
Flow cytometry

This is not currently used in standard practice and is not an essential test in MDS. In this context, it may be helpful in identifying dysplasia where no clear cytogenetic or clonal marker is present, in distinguishing refractory anaemia from refractory anaemia with multilineage dysplasia (scatter properties), and in enumerating myeloblasts, although all of the above should primarily be a morphologic diagnosis. If undertaken, this test is best performed at a centre with experience with the ELNET recommendations for MDS/AML.

Cytogenetics

G-banding and/or FISH analysis is usually done on a bone marrow aspirate sample, although it may also be undertaken on peripheral blood if marrow is not available.

At least 20 metaphases should be evaluated for non-random chromosomal abnormalities and reported. Interphase FISH is useful where conventional G-banding fails or is inadequate.

Selected recurrent chromosomal abnormalities are recognised as presumptive evidence of MDS (WHO 2008), even in the absence of definitive morphological features. These include the following anomalies (incidence):

- -5 or del(5q) (10–15%)
- -7 or del(7q) (10%)
- i(17q) or t(17p) (2–3%)
- del(12p) or t(12p) (1–2%)
- del(11q) (1–2%)
- -13 or del(13q) (1–2%)
- del(9q) (1%)
- idic(X)(q13) (1%)
- inv(3)(q21q26.2) (1%)
- t(6;9)(p23;q34) (1%)
- t(3;21)(q26.2;q22.1) (<1%)
- t(1;3)(p36.3;q21.2) (<1%)
- t(1;3)(p36.3;q21.2) (<1%)
- t(11;16)(q23;p13.3) (<1%)
- t(2;11)(p21;q23) (<1%).

Molecular genetics

Single nucleotide polymorphism (SNP) based karyotyping has a higher diagnostic yield of chromosomal defects compared with that of conventional metaphase cytogenetics and may be clinically useful. The detection of acquired somatic mutations has been made possible by high throughput sequencing techniques.
Commonly mutated genes in MDS (but not exclusive to MDS) include those of the spliceosome component:

<table>
<thead>
<tr>
<th>Gene mutation</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF3B1</td>
<td>25–30%</td>
</tr>
<tr>
<td>TET2</td>
<td>20–25%</td>
</tr>
<tr>
<td>RUNX1</td>
<td>10–20%</td>
</tr>
<tr>
<td>ASXL1</td>
<td>10–15%</td>
</tr>
<tr>
<td>SRSF2</td>
<td>10–15%</td>
</tr>
<tr>
<td>TP53</td>
<td>5–10%</td>
</tr>
<tr>
<td>U2AF1</td>
<td>5–10%</td>
</tr>
<tr>
<td>NRAS/KRAS</td>
<td>5–10%</td>
</tr>
<tr>
<td>DNMT3A</td>
<td>5%</td>
</tr>
<tr>
<td>ZRSR2</td>
<td>5%</td>
</tr>
<tr>
<td>EZH2</td>
<td>5%</td>
</tr>
<tr>
<td>IDH1&amp;2</td>
<td>2–3%</td>
</tr>
<tr>
<td>ETV6</td>
<td>2%</td>
</tr>
<tr>
<td>CBL</td>
<td>1–2%</td>
</tr>
<tr>
<td>NPM1</td>
<td>1–2%</td>
</tr>
<tr>
<td>JAK2</td>
<td>1–2%</td>
</tr>
<tr>
<td>SETBP1</td>
<td>1–2%</td>
</tr>
<tr>
<td>SF3A1</td>
<td>1–2%</td>
</tr>
<tr>
<td>SF1</td>
<td>1–2%</td>
</tr>
<tr>
<td>U2AF65</td>
<td>1–2%</td>
</tr>
<tr>
<td>PRPF40B</td>
<td>1–2%</td>
</tr>
</tbody>
</table>

At least 52% of patients with a normal karyotype harbour at least one mutation and 74% have at least a copy number variation or molecular mutation, thus these tests can help confirm the diagnosis. These tests are not yet routinely available and are not essential for the diagnosis of MDS, nor do they form part of the classification or risk stratification in current standard practice.

**Bone marrow trephine**

This test will assess marrow cellularity, topography, presence of reticulin fibrosis and blasts, and exclude other metastatic disease or infections. The trephine biopsy should be stained with haematoxylin and eosin (H&E) or equivalent, Giemsa, myeloperoxidase, glycophorin A and C or equivalent, CD34, CD117, CD61 or CD42b for megakaryocytes, CD68 or CD68R for monocytes, CD20, CD3 and Gomori silver stain for reticulin.

Bone marrow cellularity in MDS is usually hyper- or normo-cellular, but is hypocellular in 10% of patients (hypocellular MDS) and needs to be differentiated from aplastic anaemia (AA). The presence of dysplasia, reticulin fibrosis, ring sideroblasts, CD34+ cells and micro-megakaryocytes favours a diagnosis of MDS.

In 10–20% of cases, a moderate to severe bone marrow fibrosis (grade 2–3) by European consensus may be seen. Fibrotic MDS classically occurs in the absence of splenomegaly, but shows concomitant dysplasia and transfusion dependence. It needs to be differentiated from primary myelofibrosis (PMF), chronic myelomonocytic leukaemia (CMML) and acute megakaryoblastic leukaemia.
### Table 3.1: WHO classification of MDS (2008) – diagnostic criteria

<table>
<thead>
<tr>
<th>Disease</th>
<th>Blood findings</th>
<th>BM findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractory cytopenia with unilineage dysplasia (RCUD):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractory anaemia [RA]</td>
<td>Unicytopenia or bicytopenia¹</td>
<td>Unilineage dysplasia: ≥10% of the cells in one myeloid lineage</td>
</tr>
<tr>
<td>Refractory neutropenia [RN]</td>
<td>No or rare blasts (&lt;1%)²</td>
<td>&lt;5% blasts</td>
</tr>
<tr>
<td>Refractory thrombocytopoena [RT]</td>
<td></td>
<td>&lt;15% of erythroid precursors are ring sideroblasts</td>
</tr>
<tr>
<td>Refractory anaemia with ring sideroblasts (RARS)</td>
<td>Anaemia</td>
<td>≥15% of erythroid precursors are ring sideroblasts</td>
</tr>
<tr>
<td></td>
<td>No blasts</td>
<td>Erythroid dysplasia only</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;5% blasts</td>
</tr>
<tr>
<td>Refractory cytopenia with multilineage dysplasia (RCMD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cytopenia(s)</td>
<td>Dysplasia in ≥10% of the cells in ≥2 myeloid lineages (neutrophil and/or</td>
</tr>
<tr>
<td></td>
<td>No or rare blasts (&lt;1%)²</td>
<td>erythroid precursors and/or megakaryocytes</td>
</tr>
<tr>
<td></td>
<td>No Auer rods</td>
<td>&lt;5% blasts in marrow</td>
</tr>
<tr>
<td></td>
<td>&lt;1 × 10⁹/L monocytes</td>
<td>No Auer rods</td>
</tr>
<tr>
<td></td>
<td></td>
<td>±15% ring sideroblasts</td>
</tr>
<tr>
<td>Refractory anaemia with excess blasts-1 (RAEB-1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cytopenia(s)</td>
<td>Unilineage or multilineage dysplasia</td>
</tr>
<tr>
<td></td>
<td>&lt;5% blasts²</td>
<td>5%–9% blasts³</td>
</tr>
<tr>
<td></td>
<td>No Auer rods</td>
<td>No Auer rods</td>
</tr>
<tr>
<td></td>
<td>&lt;1 × 10⁹/L monocytes</td>
<td></td>
</tr>
<tr>
<td>Refractory anaemia with excess blasts-2 (RAEB-2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cytopenia(s)</td>
<td>Unilineage or multilineage dysplasia</td>
</tr>
<tr>
<td></td>
<td>5%–19% blasts</td>
<td>10–19% blasts³</td>
</tr>
<tr>
<td></td>
<td>Auer rods ±3</td>
<td>Auer rods ±3</td>
</tr>
<tr>
<td></td>
<td>&lt;1 × 10⁹/L monocytes</td>
<td></td>
</tr>
<tr>
<td>Myelodysplastic syndrome – unclassified (MDS-U)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cytopenias</td>
<td>Unequivocal dysplasia in &lt;10% of the cells in one or more myeloid</td>
</tr>
<tr>
<td></td>
<td>&lt; 1% blasts²</td>
<td>lineages when accompanied by a cyogenetic abnormality considered as</td>
</tr>
<tr>
<td></td>
<td></td>
<td>presumptive evidence for a diagnosis of MDS (see Table 4.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;5% blasts</td>
</tr>
<tr>
<td>MDS associated with isolated del(5q)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anaemia</td>
<td>Normal to increased megakaryocytes with hypolobated nuclei</td>
</tr>
<tr>
<td></td>
<td>Usually normal or increased platelet count</td>
<td>&lt;5% blasts</td>
</tr>
<tr>
<td></td>
<td>No or rare blasts (&lt;1%)</td>
<td>Isolated del(5q) cytogenetic abnormality</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No Auer rods</td>
</tr>
</tbody>
</table>

¹ Bicytopenia may occasionally be observed. Cases with pancytopenia should be classified as MDS-U.

² If the marrow myeloblast percentage is <5% but there are 2–4% myeloblasts in the blood, the diagnostic classification is RAEB-1. Cases of RCUD and RCMD with 1% myeloblasts in the blood should be classified as MDS-U.

³ Cases with Auer rods and <5% myeloblasts in the blood and <10% in the marrow should be classified as RAEB-2. Although the finding of 5–19% blasts in the blood is, in itself, diagnostic of RAEB-2, cases of RAEB-2 may have <5% blasts in the blood if they have Auer rods or 10–19% blasts in the marrow or both. Similarly, cases of RAEB-2 may have <10% blasts in the marrow but may be diagnosed by the other two findings, Auer rod+ and/or 5–19% blasts in the blood.
Chronic myelomonocytic leukaemia (CMML) – diagnostic criteria

Persistent PB monocytosis >1 x 10⁹/L

No Ph chromosome or BCR-ABL1 fusion gene

No rearrangement of PDGFRα or PDGFRβ

<20% blasts in PB or BM

Dysplasia in ≥1 myeloid lines. If myelodysplasia is absent or minimal, the diagnosis of CMML may still be made if the other requirements are met, and:

- an acquired, clonal cytogenetic or molecular abnormality is present in haematopoietic cells, or
- the monocytosis has persisted for at least 3 months and all other causes of monocytosis have been excluded.

CMML-1 = blasts <5% in PB & <10% in BM.

CMML-2 = blasts 5–19% in PB & 10–19% in BM, or the presence of Auer rods

3.1. Pathology

Careful attention must be paid to the labelling of forms and samples before sending to the Specialist Integrated Haematological Malignancy Diagnostic Service (SIHMDS). Samples are unlikely to be processed unless clearly and correctly labelled.

For details of SIHMDS see Annex 4.

BMAT (see Annex 1)

- Slides for morphology to SIHMDS lab
- 2–5ml in EDTA for immunophenotyping with a slide
- 2–5ml in EDTA for molecular genetics
- 2–5ml in heparin (PFH or lithium heparin) for cytogenetics/FISH
- trephine for histopathology.
4. Risk Stratification

The risk stratification of MDS is as per the International Prognostic Scoring System (IPSS) that has recently been revised (IPSS-R) to reflect the increased recognition that cytogenetic abnormalities are independent predictors of outcome and have as much importance as the blast percentage. Both scores are validated at diagnosis and during the course of the disease. It is recommended that the IPSS and the IPSS-R are both applied at diagnosis.

The revised IPSS is a dynamic scoring system that applies to patients with primary MDS with <30% blasts in the marrow, <19% blasts in peripheral blood, WBC count <12x10^9/L and stable disease over two months. Five cytogenetic subgroups and importance to the depth of cytopenia have been incorporated (see Table 4.2).

Table 4.1: International Prognostic Scoring System (IPSS)

Sum-up variables to arrive at risk:

<table>
<thead>
<tr>
<th>Prognostic variable</th>
<th>Score value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>BM blasts (%)</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Karyotype*</td>
<td>Good</td>
</tr>
<tr>
<td>Cytopenias**</td>
<td>0/1</td>
</tr>
</tbody>
</table>

* Karyotype: Good = normal, -Y, del(5q), del(20q); Poor = complex (>3 abnormalities) or chrom. 7 anomalies; Intermediate = other abnormalities.
** Cytopenias: Hb <10g/dL; ANC <1.8 x 10^9/L; plt<100 x 10^9/L.

<table>
<thead>
<tr>
<th>Risk (Score)</th>
<th>Median survival (years)</th>
<th>25% AML progression (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW (0)</td>
<td>5.7</td>
<td>9.4</td>
</tr>
<tr>
<td>INT-1 (0.5–1.0)</td>
<td>3.2</td>
<td>3.3</td>
</tr>
<tr>
<td>INT-2 (1.5–2.0)</td>
<td>1.2</td>
<td>1.1</td>
</tr>
<tr>
<td>HIGH (&gt;2.5)</td>
<td>0.4 years</td>
<td>0.2</td>
</tr>
</tbody>
</table>

An online calculator can be found at: [www.qxmd.com/calculate-online/hematology/myelodysplastic-syndrome-prognosis-ipss](http://www.qxmd.com/calculate-online/hematology/myelodysplastic-syndrome-prognosis-ipss)

Table 4.2: MDS IPSS-Revised (IPSS-R)

IPSS-R score values

<table>
<thead>
<tr>
<th>Score</th>
<th>CGN</th>
<th>BM Blast %</th>
<th>Hb</th>
<th>Plts</th>
<th>ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>–</td>
<td>&lt;2</td>
<td>≥100</td>
<td>≥100</td>
<td>≥0.8</td>
</tr>
<tr>
<td>0.5</td>
<td>–</td>
<td>2.1–4.9%</td>
<td>≤100</td>
<td>50–99</td>
<td>&lt;50</td>
</tr>
<tr>
<td>1</td>
<td>Good</td>
<td>80–99</td>
<td>≤80</td>
<td>&lt;50</td>
<td>&lt;50</td>
</tr>
<tr>
<td>1.5</td>
<td>Int.</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>Poor</td>
<td>&gt;10</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>Very poor</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

IPSS-R cytogenetic prognostic subgroups

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Risk score</th>
<th>Survival (median years)</th>
<th>AML 25% evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>≤1.5</td>
<td>8.8</td>
<td>–</td>
</tr>
<tr>
<td>Low</td>
<td>&gt;1.5–3</td>
<td>5.3</td>
<td>10.8</td>
</tr>
<tr>
<td>Intermediate</td>
<td>&gt;3–4.5</td>
<td>3.0</td>
<td>3.2</td>
</tr>
<tr>
<td>High</td>
<td>&gt;4.5–6</td>
<td>1.6</td>
<td>1.4</td>
</tr>
<tr>
<td>Very high</td>
<td>&gt;6</td>
<td>0.8</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Table 4.3: CMML-Specific Prognostic Scoring System (CPSS)

<table>
<thead>
<tr>
<th>Variable</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO subtype</td>
<td>CMML-1</td>
<td>CMML-2</td>
<td>–</td>
</tr>
<tr>
<td>FAB subtype</td>
<td>CMML-MD (WBC &lt;13)</td>
<td>CMML-MP (WBC &gt;13)</td>
<td>–</td>
</tr>
<tr>
<td>CGN*</td>
<td>Low</td>
<td>Intermediate</td>
<td>High</td>
</tr>
<tr>
<td>RBC dependent</td>
<td>No</td>
<td>Yes</td>
<td>–</td>
</tr>
</tbody>
</table>

*Low = normal, -Y; Intermediate = other abnormalities; High = +8, complex (≥3 anomalies), chrom. 7 anomalies.

5. Patient Information/Support

If the diagnosis of MDS is certain, patients should be informed that MDS is a clonal disorder and that it is considered malignant/neoplastic. Their prognosis based on the IPSS/IPSS-R should be discussed, along with possible treatment options.

All patients must have access to a key worker. This is usually (but not always) the clinical nurse specialist. The LCA has produced a key worker policy (please see Appendix 4: LCA Key Worker Policy) which sets out the definition of a key worker and provides an overview of their role and responsibilities.

The clinical nurse specialist/key worker should be present at diagnosis and at any significant discussion where treatment changes and outcomes are discussed. In the absence of the clinical nurse specialist, a senior nurse may deputise and must ensure that all conversations are documented in the patient’s notes and on the electronic patient record. Where it is not possible for the clinical nurse specialist or a deputy to be present, patients should be given the clinical nurse specialist’s contact numbers. The clinician leading the consultation should advise the clinical nurse specialist who should then arrange to make contact with the patient.

The clinical nurse specialist should ensure that all patients are offered a holistic needs assessment (HNA) (please see Appendix 5: LCA Holistic Needs Assessment Tool) at key pathway points, including within 31 days of diagnosis; at the end of each treatment regime; and whenever a person requests one. Following each HNA, every patient should be offered a written care plan. This plan should be developed with the patient and communicated to all appropriate healthcare and allied healthcare professionals.

Written and verbal information are essential and the key worker/clinical nurse specialist plays a key role in ensuring that patients have access to appropriate and relevant written information about their condition.

The Leukaemia & Lymphoma Research and the Macmillan Cancer Support MDS information booklets, the NHS Information Prescription and MDS Foundation websites are good sources of patient information at diagnosis and are available for download on the following websites:

https://leukaemialymphomaresearch.org.uk/information/other-blood-cancers/myelodysplastic-syndromes-mds
www.macmillan.org.uk/Cancerinformation/Cancerinformation.aspx
http://mdspatientsupport.org.uk/what-is-mds/information-material
www.beatbloodcancers.org/sites/default/files/MDS%20leaflet_1.pdf
www.nhs.uk/ipg/pages/ipstart.aspx
6. Treatment

The management of MDS may vary from monitoring blood counts for evidence of disease progression in early MDS and supportive care, to intensive chemotherapy followed by stem cell transplantation in those with advanced disease. Patients with ICUS (Intermediate low to Int1) should be followed up in the same way as for low risk MDS until the diagnosis is clear. Responses to treatment should be recorded using the Chesson 2006 criteria.

The goals of treating MDS are to prolong survival, improve quality of life and improve the blood counts. In order to achieve these goals, treatment options vary from best supportive care, replacement therapy, low intensity therapy and high intensity therapy. In early MDS, the predominant goal is haematological improvement with best supportive care. The imminent threat to life in high risk MDS makes disease-modification the primary goal.

As patients with MDS are usually older and likely to have co-morbidities, the use of the Cumulative Illness Rating Scale (CIRS) to assess the impact that co-morbidities may have on treatment is recommended when planning treatment for MDS.

When discussing oral treatments with patients for the first time, ensure that the Oral Chemotherapy Patient Education Checklist (Annex 2) is used and signed-off. Some centres may also have hand-held chemotherapy booklets.

Formal written consent should be obtained for all patients before commencing any cytoreductive or epigenetic therapy including HU.

6.1. Low or intermediate-risk MDS

Also see section 7: Management of Disease and Treatment-related Complications.

Patients with IPSS-low or IPSS-INT1 may be eligible for a clinical trial – see section 12: Research/Clinical Trials. The LCA website has an up-to-date list of trials actively recruiting at present.

6.1.1. Growth factor support (EPO +/- G-CSF)

For those patients with low risk disease and primarily anaemia and an EPO predictive score that is low (serum erythropoietin <500IU and less than 2U blood transfusion), treatment with recombinant human erythropoietin (EPO) 30,000 to 60,000 IU SC weekly for at least 8 weeks, followed by a higher dose for 8 weeks, is recommended. The addition of G-CSF 300µg once a week (to maintain neutrophils between 5–10 x 10^9/L) should be considered in all patients with refractory anaemia with ring sideroblasts (RARS) and other patients where the response to EPO alone is suboptimal. The target Hb is 10-12g/dl but dose adjustments need to be made prior to this to prevent overshooting. The ferritin should be maintained >100µg/ml for those on erythropoietin replacement with IV iron infusions.

6.1.2. Anti-thymocyte globulin (ATG)/ciclosporin

Hypocellular/normocellular patients who have a normal karyotype or trisomy 8 may respond to immunosuppressive therapy with ATG/ciclosporin. The HLA-DR15 haplotype is a good predictor of response to immunosuppressive therapy, especially ATG.
6.1.3. Lenalidomide

Patients with anaemia and del(5q) are eligible for treatment with lenalidomide 10mg per day for 21 of 28 days. Where blast percentage is >5% or there is an additional cytogenetic abnormality, response rates may be lower and advice from a haematologist with sub-specialist expertise is advisable. Responses occur rapidly at a median of 4 weeks from starting therapy, and therapy should be continued until loss of response or disease progression. Failure to achieve a complete cytogenetic response, the presence of TP53 mutation, two or more additional chromosomal abnormalities and blasts >20% are predictors of poor response to lenalidomide.

6.2. High risk MDS

Patients should be assessed for eligibility to undergo an allogeneic stem cell transplant: assess fitness and co-morbidities using the HC-TCI, and carry out tissue typing for potential donors, including siblings where familial MDS is not suspected.

6.2.1. Allogeneic stem cell transplant

If patients are transplant-eligible, a donor should be identified at the earliest possible opportunity. Patients may be treated either directly with a myeloablative transplant (if fit, young and blasts <10%) or following induction chemotherapy with daunorubicin/cytarabine (DA 3+10) or a similar regimen to remission (blasts<5% and no MRD by normal karyotype). For older patients, or for those with co-morbidities, a RIC transplant is preferred, although the risk of relapse is higher. Results from an allele-matched 10/10 VUD donor approximate those of a matched sibling transplant and is a viable option.

For those who have tolerated chemotherapy and regenerated within 4–5 weeks, one cycle of treatment to consolidate the remission is preferably to be administered prior to an allogeneic stem cell transplant. It is recognised that a proportion of patients with MDS may develop chemotherapy-induced aplasia and experience a prolonged time to recover counts, in which case a rescue allograft may be necessary.

For patients with a complex karyotype or monosomal karyotype, there is some evidence to suggest that treatment with hypomethylating agents such as 5’-azacitidine may be a good option.

In cases that are refractory to chemotherapy, the use of sequential chemotherapy and transplantation is experimental; if it is being considered, it should be undertaken early in the course of treatment.

6.2.2. Hypomethylating agents: 5’-azacitidine (5’-Aza)

Where a patient declines, or is not a suitable candidate for, allogeneic stem cell transplantation, the standard of care is treatment with 5’-aza based on a Phase III open label randomised controlled trial that demonstrated disease-modifying activity in IPSS-INT2 high risk patients, non-proliferative CMML and in AML with less than 30% blasts. The licensed regimen consists of 5’-aza 75mg/m$$^2$$ SC daily for 7 days every 28 days, for at least 4–6 cycles to assess response, and continued until loss of response or disease progression. The trial demonstrated improved overall survival at 2 years of approximately 50%, compared with 24% for low dose cytarabine, but there was no difference compared with chemotherapy. Treatment with 5’-aza may result in a complete remission in 16% of cases. Given that the median time of response to 5’-aza is 18–24 months, in suitable cases an allogeneic stem cell transplant in CR may be considered.
6.2.3. Hypomethylating agents: decitabine

Decitabine 20mg/m² IV for five days every 28 days and, more recently, an extended 10-day schedule may be useful in high risk MDS as an alternative to 5’-aza. However, the drug is not licensed for MDS in Europe, and so IFR funding or treatment on a clinical trial should be sought.

6.2.4. Patients refractory to induction chemotherapy or hypomethylating agents

- Best supportive care
- Treatment on a clinical trial
- Referral to palliative care teams may be considered.

6.3. Chronic myelomonocytic leukaemia (CMML)

CMML was part of the original FAB classification. However, in WHO (2008) it has been included in the MDS/MPN overlap category. Patients with CMML may have varying prognosis and the Dusseldorf scoring system or the CMML-specific prognostic score is recommended in order to determine prognosis.

6.3.1. Active monitoring

For some patients (CMML-1 and some stable CMML-2 patients), active monitoring may be sufficient.

6.3.2. Supportive care

Treatment with supportive care and hydroxycarbamide to control counts is recommended in the absence of excess blasts.

6.3.3. 5’-azacitidine

The National Institute for Health and Care Excellence (NICE) has approved the use of 5’-aza for patients requiring treatment for CMML-2 only. For non-proliferative (WBC <13,000) CMML, 5’-zza at conventional dosing may be used, but a funding application would be required.

6.3.4. Intensive chemotherapy

For patients with disease progression to CMML-2, AML induction chemotherapy followed by an allogeneic stem cell transplant may be considered, based on patient characteristics and donor availability.

6.4. Fertility

For young patients with MDS due to undergo AML induction-type chemotherapy and or a stem cell transplant, the options for fertility preservation should be discussed and the patient referred to an onco-fertility specialist for preservation of sperm, ovarian tissue or fertilised embryos.

Consideration of fertility preservation should be made for those of reproductive age (men below the age of 55 and women below the age of 40). Please see the LCA guidance and recommendations for referral to fertility services for more information.
7. Management of Disease and Treatment-related Complications

7.1. Anaemia

The onset of symptomatic anaemia is an independent prognostic factor in MDS. It is important to record the number of transfusions a patient has had, with transfusion-dependence defined as the need for >2 units per month for 4 months.

Assessment of anaemia should include haematinics, screening for haemolysis and infection. Identification of 5q- syndrome, a PNH clone or hypocellularity may alter therapies. Serum erythropoietin levels may be low in elderly patients and should be measured in all patients with MDS.

For those with an EPO predictive score that is low (serum erythropoietin <500IU and less than 2U blood transfusion), treatment with recombinant human erythropoietin (EPO) 30,000 to 60,000IU SC weekly for at least 8 weeks, followed by a higher dose for 8 weeks, is recommended. The addition of G-CSF 300µg once a week (to maintain neutrophils between 5–10 x 10⁹/L) should be considered in all patients with RARS and in other patients where the response to EPO alone is suboptimal. The target Hb is 10–12g/dl, but dose adjustments need to be made prior to this to prevent overshooting.

The ferritin should be maintained at >100µg/ml for those on erythropoietin replacement with IV iron infusions.

Blood transfusions may be the mainstay for those predicted to have a low response to EPO (serum erythropoietin >500IU and >2U blood transfused).

It is important to identify patients who may need iron chelation.

7.2. Severe neutropenia

There is no evidence to suggest routine use of G-CSF in neutropenic patients.

There is also no evidence to suggest routine prophylaxis with antimicrobials or antifungal drugs.

In patients with hypoplastic MDS, the use of immunosuppression with anti-thymocyte globulin (ATG) and ciclosporin (CYA) or single agent ciclosporin may be helpful with responses, depending on the patient’s age and the severity of neutropenia. HLA-DR15 haplotype may be a good predictor of response.

It is important to examine a peripheral film to exclude T-LGL, as treatment with ciclosporin and methotrexate may be beneficial.

7.3. Neutropenic sepsis

Patients with neutropenic pyrexia or sepsis should be treated according to local protocols for neutropenic sepsis (and following National Institute for Health and Care Excellence/NICE guidance and the LCA Acute Oncology Clinical Guidelines).
In addition, for haematology-oncology patients the following are mandatory:

- urinalysis
- midstream specimen of urine
- chest X-ray
- swabs: throat (bacterial and viral), CVAD site if present and any other focal lesions as appropriate
- sputum and stool culture
- CMV, EBV, adeno PCR if indicated.

Such patients should ideally be cared for by specially trained nurses in a BCSH Level 2b–3 unit.

7.4. **Severe thrombocytopenia**

Platelet anisocytosis/clumping may give artefactually low platelet counts. An element of immune destruction may also cause thrombocytopenia in MDS.

Platelet transfusion may be used in MDS if there is bruising or bleeding. Steroids, IV immunoglobulin in doses used to treat ITP may be tried if an immune component is suspected. For non-bleeding patients and those not at high risk of spontaneous bleeding (i.e. not hypertensive), transfuse platelets only when clinically indicated. Consider tranexamic acid in order to maintain haemostasis. When a platelet transfusion programme is initiated, use single-donor apheresis platelet products only, in order to avoid platelet refractoriness, unless in an emergency.

In refractory cases, eltrombopag or romiplostim may be used (unlicensed and unfunded indication) or in a clinical trial as trilineage responses to these drugs have been reported.

Clinical trials may be available for such patients (please see section 12: Research/Clinical Trials).

7.5. **Haemostasis and thrombosis**

Although counts may be adequate, platelets (and neutrophils) may be dysfunctional in MDS. Such patients may need platelet transfusions regardless of count for surgical procedures and/or tranexamic acid in order to maintain haemostasis.

Platelet transfusion may be used in MDS if there is severe bruising or bleeding. For non-bleeding patients and those not at high risk of spontaneous bleeding (i.e. not hypertensive), transfuse platelets only when clinically indicated. Consider tranexamic acid in order to maintain haemostasis when platelets <20 x 10^9/L or in the bleeding/high risk patient.

Ensure that patients have good control of blood pressure (if they are known to be hypertensive) and do not suffer from constipation — if not appropriately managed, both conditions can increase the risk of severe life-threatening haemorrhage.

7.6. **Transfusional iron overload**

Blood transfusions contribute to iron overload and transfusion in excess of 100 units may result in evidence of end-organ damage (abnormal liver function, glucose intolerance or reduced left ventricular ejection fraction). Iron chelation therapy is recommended for patients with a serum ferritin >1000ng/ml or who
have received in excess of 20 blood transfusions and are expected to have a life expectancy in excess of 3 years. If a patient has a life expectancy of <3 years when the transfusion regimen commences, they are unlikely to become symptomatically iron-overloaded and chelation therapy should not normally be started.

The serum ferritin is the most convenient way to monitor iron accumulation. However, it is an acute phase reactant and may be elevated in liver disease as well. It is not clear in MDS at what levels of ferritin end-organ iron-overloading occurs. However, iron-overload may contribute to dyserythropoiesis. It is also an independent predictor of poor outcomes following stem cell transplantation.

It is recommended that a cumulative record of number of units transfused be kept in the notes and serum ferritin be checked after 20 units of blood have been transfused. Thereafter, ferritin levels should be measured after every further 10 units transfused until a decision is made to chelate. Consider a clinical trial for this patient group, if available.
8. Supportive Care

8.1. Anaemia

See section 7: Management of Disease and Treatment-related Complications. Transfusion triggers should be chosen in advance for patients, depending on their co-morbidities. For patients with no co-morbidities or bleeding risk, and in those who do not lead active lifestyles, it would be reasonable to aim for a target Hb<8.0g/dL.

8.2. Transfusions

See section 7: Management of Disease and Treatment-related Complications.

Transfusion triggers should be chosen in advance for patients, depending on co-morbidities. For patients with no co-morbidities or bleeding risk, and in those who do not lead active lifestyles, it would be reasonable to aim for a target of Hb>80g/L.

Administer CMV-negative blood products until the patient’s CMV status is known. Red cell transfusions should be avoided if there is any risk of leukostasis. All platelet products should be single donor collections in order to limit the risk of allo-sensitisation. HLA-typing should be done prior to starting treatment in order to address donor status if transplantation is appropriate for the patient, and in case HLA-matched platelets become necessary during treatment (as often occurs in women who have had children). Irradiated blood products should be requested for patients on protocols containing fludarabine, cladribine and clofarabine and for at least one month prior to a planned SCT.

8.3. Haemostasis and thrombosis

See section 7: Management of Disease and Treatment-related Complications

8.4. Infection prophylaxis

There is no evidence to suggest routine use of G-CSF in neutropenic patients. There is also limited evidence to suggest routine prophylaxis with antimicrobials or antifungal drugs (see section 7: Management of Disease and Treatment-related Complications).

Patients with high risk MDS should be managed as AML.

In neutropenic patients with recurrent infections, prophylactic antimicrobial and antifungal therapy should be administered according to local flora and sensitivities, and as per local protocols on neutropenic sepsis (and following National Institute for Health and Clinical Excellence/NICE guidance and the LCA Acute Oncology Clinical Guidelines).

In non-neutropenic patients, neutrophils may be dysfunctional and in this case patients will have recurrent infections. Such patients would benefit from prophylactic antimicrobial and antifungal therapy directed towards local flora and sensitivities according to local protocols. Such patients may also benefit from intermittent G-CSF.

Mouthwashes should be used as per local protocols in susceptible patients
9. Treatment Summary and Care Plan

The MDT outcome form and clinic letters will serve to communicate new lines of treatment with the patient’s GP.

Most therapies are administered until loss of response or disease progression. It is important to ensure that a treatment summary is completed when there are any significant changes in treatment or follow-up plans. Holistic needs assessments (HNAs) should be offered through follow-up, with a care plan completed to document the plans to address the issues raised by the patient. See Appendix 5 for the LCA Holistic Needs Assessment Tool.

9.1. Treatment summary and care plan

There are two related but distinct documents which patients should be given when there are changes in treatment.

- A **treatment summary** provides a summary of the cancer treatments received by the end of the first treatment, planned follow-ups (including mechanisms for these), and signs and symptoms of which to be aware. Their 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 (please see Appendix 6: NCSI Treatment Summary).

- A **care plan** is generated as a result of an HNA and 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 (e.g. through an information prescription), onward referral for specialist assessment and intervention (e.g. breathlessness management), or things which the patient themselves can do (e.g. contact their HR department about graduated return to work options).

**Recommendation:** An end of treatment consultation should be offered to every patient when there are any significant changes in treatment and follow-up arrangements. This should include an HNA and associated written care plan, and should also include the discussion and provision of a comprehensive treatment summary.
10. Follow-up Arrangements

Patients with low risk MDS not on treatment or supportive care may be followed up every 6–12 months. Patients on treatment will need more frequent monitoring, depending on the therapy and the degree of supportive care required. Patients with intermediate-2 or high risk disease on therapy may need weekly (or more) blood count monitoring and supportive therapies.

Patients may have shared care between a specialist site and the local treating hospital. These arrangements must be clearly outlined so that the patient is clear where to attend in an emergency, and understands the lines of communication between the sites.

11. Rehabilitation and Survivorship

Rehabilitation and survivorship needs should be monitored throughout the patient pathway and highlighted to the appropriate allied health professionals if required. Survivorship issues can relate to the effects of the disease process and/or management of long-term adverse effects of treatment.

Any patient experiencing or reporting reduced mobility and/or ability to perform activities of daily living should be referred for occupational therapy and physiotherapy assessment.

Patients should have access to supportive care information and rehabilitation throughout the cancer pathway. Consider referral to the appropriate services, including rehabilitation, when indicated. Please refer to the LCA Survivorship Guidelines for more information on the treatment and care that should be offered as a minimum.

People reporting ongoing consequences such as fatigue, anxiety and pain should be considered for non-pharmacological intervention, including but not limited to transcutaneous electrical nerve stimulation (TENS), complementary therapies and psychological interventions such as mindfulness.

11.1. Psychological impact

It is apparent that a diagnosis of MDS potentially has a great psychological impact on individuals. The unpredictability of the disease, the frequent hospital attendance and potentially frequent hospital admissions can have an enormous impact on an individual’s psychological needs. Consideration should be given to access and referral to professional counselling services.
12. Research/Clinical Trials

The LCA has produced a directory of clinical trials that are actively recruiting patients with MDS. Please refer to the LCA website (www.londoncanceralliance.nhs.uk/trials) for the most up-to-date list.

13. End-of-life Care

For older patients and in those with high risk diseases, discussions regarding prognosis and treatment options should also include discussions of end-of-life care. These discussions are to facilitate transitions between active disease-modifying therapy and clinical trials to supportive care only, at the time of disease progression/non-response. Care may be required from specialist palliative care teams which are available in all the cancer centres and units affiliated to the LCA.

To support consideration of referral to specialist palliative care, please refer to the LCA’s referral criteria for specialist palliative care (Appendix 8). The LCA form for referral to specialist palliative care can be found in Appendix 7: LCA Specialist Palliative Care Referral Form.

The named clinical nurse specialist (CNS)/key worker, patient, family members and palliative care teams, as well as members of the inpatient ward team, may be involved. Clear documentation of the discussion with guidance to the treating teams is helpful in communicating these discussions and outputs to the wider team that may care for the individual.

14. 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 multidisciplinary team with support from a data manager. Haematology services are required to submit data to nationally mandated datasets for all patients diagnosed with haematological cancer; further details on these datasets are available in Annex 6. In line with peer review requirements, the LCA Haematology Oncology Pathway Group and the LCA Clinical Board review this data on a regular basis to ensure all patients receive treatments intended to provide the best possible outcomes, consistent across all MDTs.
References


### Annex 1: LCA Acute Leukaemias and Myeloid Neoplasms BMAT Diagnostics Summary Chart

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>AT DIAGNOSIS</th>
<th>RESTAGING</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aspirate (NPH)</td>
<td>Immuno (RMH EDTA (purple)</td>
</tr>
<tr>
<td>AML/AUL/MPL</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APML</td>
<td>YES</td>
<td>YES (PML-RARA)</td>
</tr>
<tr>
<td>Ph+ AML or ALL</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>ALL/Burkitt lymphoma</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>MDS (if ?AML/blasts on film, follow AML guide)</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>MPN</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>CML (if ?AML/blasts on film, follow AML guide)</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Cytopenias/macrocytosis</td>
<td>YES</td>
<td>ONLY IF AML/LYMPHOMA SUSPECTED</td>
</tr>
</tbody>
</table>

KGC = Kennedy Galton Regional Centre for Cytogenetics (located at NPH site, St Mark’s Level 8; ext 3104)  
GST = Guy’s & St Thomas’ Hospital (call when sending; 020 7188 7188, ext 51060)  
ICHNT = Imperial College Healthcare NHS Trust (020 8383 2179/2167/2177)  
TDL = The Doctors Laboratory (Pathology Laboratory at NWLHT)  
RMH = The Royal Marsden Hospital (020 8722 4221)  

A = Aspirate I = Immunophenotyping C = Cytogenetics M = Molecular T = Trephine TS = Trial sample ? = Ask Trial Coordinators
## Annex 2: LCA Oral Chemotherapy Patient Education Checklist

### Oral anti-cancer patient and carer education checklist

#### Prior to first cycle:

*This checklist must be completed with the patient/carer at the point of handing the medication to the patient, either in conjunction with or following a pre-treatment consultation.*

<table>
<thead>
<tr>
<th>Instructions for taking</th>
<th>Tick if discussed with the patient/carer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Explain how and when to take the medicine, including any treatment breaks.</td>
<td></td>
</tr>
<tr>
<td>If the patient is unable to swallow tablets or capsules or has a feeding tube, please refer to the oral systemic anti-cancer therapies (SACT) counselling handbook to dissolve or open capsules (if appropriate for the oral anti-cancer medicine).</td>
<td></td>
</tr>
<tr>
<td>Missed doses can be taken if near to the scheduled time. Otherwise, do not try and catch up or double the next dose. Wait until the next dose is due.</td>
<td></td>
</tr>
<tr>
<td>In case of vomiting after taking a dose, do not repeat the dose. Take the next dose at the normal time. If this occurs again, contact the chemotherapy team/24-hour advice line.</td>
<td></td>
</tr>
<tr>
<td>Check that the patient is aware of side effects and has received written information. Any side effects should be reported to your chemotherapy nurse or doctor.</td>
<td></td>
</tr>
<tr>
<td>If the patient is taking any prescribed/over-the-counter medicine/supplement – the patient should inform their medical team.</td>
<td></td>
</tr>
<tr>
<td>Return any unused oral anti-cancer medicine to the hospital pharmacy. Do not flush or throw them away (for high-cost drugs see the counselling handbook).</td>
<td></td>
</tr>
</tbody>
</table>

#### Storage and handling

The oral anti-cancer medicine should not be handled by anyone who is pregnant or planning a pregnancy (except on the advice of medical team).

If the carer is giving the anti-cancer medicine, they should not handle the medicine directly but wear gloves or push the medicine out of the blister pack (if applicable) directly into a medicine pot.

Store the tablets/capsules in the container provided.

Store the tablets/capsules in a secure place, away from and out of sight of children.

Wash hands thoroughly after taking/giving the oral anti-cancer medicine.

Check that the patient understands how to take the treatment, by asking them to repeat back their instructions.
### Written information provided

<table>
<thead>
<tr>
<th>Written information provided</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>‘Taking an oral anti-cancer medicine’ patient information sheet</td>
<td></td>
</tr>
<tr>
<td>Diary for taking your oral anti-cancer medicine (if applicable)</td>
<td></td>
</tr>
<tr>
<td>For swallowing difficulty only – give relevant factsheet if appropriate for the oral anti-cancer medicine and an oral anti-cancer pack with disposables (e.g. oral/enteral syringes)</td>
<td></td>
</tr>
<tr>
<td>Dissolving oral anti-cancer tablets safely</td>
<td></td>
</tr>
<tr>
<td>Opening oral anti-cancer capsules safely</td>
<td></td>
</tr>
<tr>
<td>Giving an oral anti-cancer medicine through a feeding tube</td>
<td></td>
</tr>
<tr>
<td>Giving an anti-cancer syringe by mouth</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient name</th>
<th>Counselling/education by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital number</td>
<td>Pharmacist/Pharmacy technician/Nurse/Interpreter</td>
</tr>
<tr>
<td>Signature and date</td>
<td>Signature and date</td>
</tr>
</tbody>
</table>

### Before all subsequent cycles:

Check that the patient has understood the checklist above and repeat if necessary.

Check that any side effects experienced with their previous cycle were discussed with their medical team.

If a dose adjustment has been made, check that the patient is aware why their dose has been changed and how many tablets/capsules they should now take.

Check that the patient had no problems taking their previous cycle.

Check that the patient understands how to take the treatment, by asking them to repeat back their instructions.

Please retain a copy and/or endorse the prescription/electronic patient record as evidence counselling took place at each cycle.
### Annex 3: Multidisciplinary Teams (MDTs) and Constituent Hospital Trusts

<table>
<thead>
<tr>
<th>South East London MDT 1</th>
<th>Guy’s &amp; St Thomas’ NHS Foundation Trust/Lewisham and Greenwich NHS Trust (Lewisham Hospital and Queen Elizabeth Hospital)</th>
</tr>
</thead>
<tbody>
<tr>
<td>South East London MDT 2</td>
<td>King’s College Hospital NHS Foundation Trust (including Princess Royal University Hospital)</td>
</tr>
<tr>
<td>South West London MDT 1</td>
<td>Kingston Hospital NHS Foundation Trust/St George’s Healthcare NHS Trust</td>
</tr>
<tr>
<td>South West London MDT 2</td>
<td>Epsom and St Helier University Hospitals NHS Trust/Croydon Health Services NHS Trust</td>
</tr>
<tr>
<td>South West London MDT 3</td>
<td>The Royal Marsden NHS Foundation Trust</td>
</tr>
<tr>
<td>North West London MDT 1</td>
<td>Imperial College Healthcare NHS Trust/The Hillingdon Hospitals NHS Foundation Trust/Chelsea and Westminster Hospital NHS Foundation Trust/West Middlesex University Hospital NHS Trust/Ealing Hospital</td>
</tr>
<tr>
<td>North West London MDT 2</td>
<td>The London North West Healthcare NHS Trust (Northwick Park Hospital and Central Middlesex Hospital)</td>
</tr>
</tbody>
</table>
Annex 4: SIHMDS or Current Diagnostic Services and Contacts

**Guy’s & St Thomas’ NHS Foundation Trust**
Cytogenetics/Flow Lab
ViaPath Pathology
4th Floor, Southwark Wing
Guy’s Hospital
Great Maze Street
London, SE1 9RT

**Imperial College Healthcare NHS Trust**
Imperial Molecular Pathology Laboratory
G Block, North Corridor
Hammersmith Hospital
Du Cane Road
London, W12 0HS

**London North West Healthcare NHS Trust**
Processed centrally in TDL laboratories on-site for SIHMDS (in progress), cytogenetics/molecular to:
North West Thames Regional Genetics Service, Haematology Section
Northwick Park Hospital
Watford Road
Harrow, HA1 3UJ

**The Royal Marsden Hospital NHS Foundation Trust**
The Centre for Molecular Pathology
Downs Road
Sutton, SM2 5PT
Tel: 020 8915 6570
Immunophenotyping Tel: 020 8915 6517 or 020 8915 6518
Cytogenetics Tel: 020 8722 4232
Molecular Genetics Tel: 020 8915 6565

**For APML diagnostic and MRD**
Dr Yvonne Morgan
Molecular Oncology Diagnostics Unit
GSTT Pathology, 4th Floor, Southwark Wing
Guy’s Hospital
Great Maze Street
London, SE1 9RT

**King’s College Hospital NHS Foundation Trust**
KingsPath: Clinical Diagnostic Pathology Service
Haematological Medicine
King’s College Hospital
Denmark Hill
London, SE5 9RS
Annex 5: JACIE-accredited Transplant Centres in the LCA

**Imperial College Healthcare NHS Trust**
Dr Eduardo Olavarria  
Consultant Haematologist  
BMT Programme Director  
Haematology Department  
ICHNT  
Hammersmith Hospital  
Du Cane Road  
London, W12 0HS  
Tel: 020 8383 3237  
Fax: 020 8742 9335  
Email: eduardo.olavarria@imperial.nhs.uk

**The Royal Marsden NHS Foundation Trust**
Dr Mike Potter via 020 8661 3670  
katrina.sharpe@rmh.nhs.uk  
Dr Chloe Anthias, contact details as above.  
Dr Mark Ethell, via 020 8661 3794,  
PA: janet.bromell@rmh.nhs.uk  

**Department of Haemato-Oncology**  
**The Royal Marsden NHS Foundation Trust**  
RS11, 2nd Floor, Orchard House,  
Downs Road, Sutton,  
Surrey, SM2 5PT  
Tel: 020 8661 3670  
Fax: 020 8642 9634 (safe haven)  
Alternative email: katrina.sharpe@nhs.net

**St George’s University Hospitals NHS Foundation Trust**
Dr Mickey Koh  
Director: Stem Cell Transplantation  
Consultant Haematologist  
St George’s Hospital and Medical School  
Jenner Wing Corridor 6  
Blackshaw Road  
London, SW17 0QT  
Tel: 020 8725 3545  
Fax: 020 8725 2859  
Email: mickey.koh@stgeorges.nhs.uk

**King’s College Hospital NHS Foundation Trust**
Bone Marrow Transplant Team  
4th Floor, Hambleden Wing  
King’s College Hospital  
Denmark Hill  
London, SE5 9RS  
Tel: 020 3299 4694, 020 3299 5268
Annex 6: Data Requirements

Haematology oncology services within the LCA are required to submit data to the following nationally mandated datasets for all patients diagnosed with haematological cancers.

The Cancer Outcomes and Services Dataset (COSD)

The core dataset for all tumour types including haematological cancers is mandated from January 2013, and the site-specific dataset is mandated from July 2013. Details of the dataset can be found on the National Cancer Intelligence Network website:


The local cancer registry will be collating this dataset using Trust data feeds which should include all these items. The feeds are:

- Trust PAS
- Trust pathology
- Trust radiology
- Trust multidisciplinary team (MDT) feed.

In line with the requirements set out in Provider Trust contracts, this data should be submitted within 25 workings days of the end of the month in which the activity took place.

Three groups of haematological cancers are considered stageable by the Registry:

- Lymphomas, using Ann Arbor (or Murphy St Jude for children)
- Myelomas, using ISS
- CLLs, using Rai and Binet

For the purposes of COSD, any other haematological cancers are not counted as stageable.

For CLL both Rai (0-IV) and Binet (A-C) stages need to be recorded and submitted to COSD to be considered “fully staged”

MGUS does not need to be recorded and submitted as is not defined as an invasive tumour.

Systemic Anti-Cancer Therapy dataset (SACT)

Provider Trusts that provide chemotherapy to patients are required to submit data to the SACT dataset. Details of the audit and the dataset requirements are available on the dataset homepage:

www.chemodataset.nhs.uk/home.aspx
Radiotherapy Dataset (RTDS)

Provider Trusts that provide radiotherapy to patients are required to submit data to the RTDS dataset. Details of the audit and the dataset requirements are available on the dataset homepage: [http://www.canceruk.net/rtservices/rtds/](http://www.canceruk.net/rtservices/rtds/)

Cancer Waiting Times dataset

Trusts are required to submit data to the Cancer Waiting Times dataset, which includes details of all patients who are referred as a 2 week wait (2ww) referral, and all patients who are treated for cancer. Trusts are required to submit this data within 25 working days of the month of either when the patient was first seen for the 2ww target, or when the patient was treated. The cancer waiting times dataset can be found at: [www.datadictionary.nhs.uk/data_dictionary/messages/clinical_data_sets/data_sets/national_cancer_waiting_times_monitoring_data_set_fr.asp](http://www.datadictionary.nhs.uk/data_dictionary/messages/clinical_data_sets/data_sets/national_cancer_waiting_times_monitoring_data_set_fr.asp)

Local data requirements

The LCA Haematology Oncology Pathway group is working on developing a suite of metrics to inform the group and services within the LCA on areas of priority and potential service improvement. The LCA is currently collating information which is available through sources of data currently available, though the Haematology Oncology Pathway Group or LCA clinical board may require Trusts to submit additional MDT data to the LCA if additional priority areas are identified.
Appendices

Appendix 1: 2 Week Wait Referral Forms
   - North West London
   - South East London
   - South West London

Appendix 2: Treatment of Children

Appendix 3: Treatment of Teenagers and Young Adults
   - Teenagers and Young Adults PTC Referrals
   - Teenagers and Young Adults MDT Proforma

Appendix 4: LCA Key Worker Policy

Appendix 5: LCA Holistic Needs Assessment Tool

Appendix 6: NCSI Treatment Summary

Appendix 7: LCA Specialist Palliative Care Referral Form

Appendix 8: LCA Referral Criteria to Specialist Palliative Care