Clinical Guidelines for Leukaemia and other Myeloid Disorders – Myeloproliferative Neoplasms

<table>
<thead>
<tr>
<th>Reference Number</th>
<th>Version</th>
<th>Status</th>
<th>Executive Lead(s) Name and Job Title</th>
<th>Author(s) Name and Job Title</th>
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<td>13-2H-106</td>
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<td></td>
<td>Dr Helen Barker MDT Lead Clinician</td>
<td>Dr Sebastian Francis</td>
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<tr>
<td>Approval Body</td>
<td>SY Region Haematology MDT</td>
<td>Date Approved</td>
<td>05/05/17</td>
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<td>Ratified by</td>
<td>The Sheffield Teaching Hospitals NHS Foundation Trust (STHFT), Barnsley Hospital NHS Foundation Trust (BHNFT), Chesterfield Royal Hospital NHS Foundation Trust (CRHFT), Doncaster and Bassetlaw Hospitals NHS Foundation Trust (DBHNFT) and The Rotherham NHS Foundation Trust (TRFT)</td>
<td>Date Ratified</td>
<td>05/05/17</td>
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<tr>
<td>Date Issued</td>
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<tr>
<td>Review Date</td>
<td>May 2018</td>
<td></td>
<td></td>
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<tr>
<td>Contact for Review Name and Job Title: Alison Collier, MDT Coordinator</td>
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</table>
For more information on this document please contact:-

Insert names of authors of the section: Dr Sebastian Francis

Version History

<table>
<thead>
<tr>
<th>Version</th>
<th>Date Issued</th>
<th>Brief Summary of amendments</th>
<th>Owner’s Name:</th>
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<tr>
<td>1</td>
<td></td>
<td></td>
<td>Dr</td>
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<tr>
<td>2</td>
<td></td>
<td>Chronic Myeloid Leukaemia updated Polycythemia Vera wording updated</td>
<td>Dr Sebastian Francis</td>
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</tbody>
</table>

(Please note that if there is insufficient space on this page to show all versions, it is only necessary to show the previous 2 versions)

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OUTLINE MANAGEMENT FOR PH+VE CHRONIC MYELOID LEUKAEMIA

Definitions of disease:

WHO Criteria for Chronic Phase
- Blasts <10% in bone marrow and peripheral blood
- Peripheral basophils <20%
- Not meeting criteria for AP/BC

WHO criteria for Accelerated Phase:
- Blasts in blood or bone marrow 10-19%
- Basophils of more than 20%
- Thrombocytopenia: persistent and unrelated to therapy (<100)
- Thrombocytosis >1000 and unresponsive to therapy
- Cytogenetic evidence of clonal evolution (i.e. abnormalities not present at diagnosis).

Criteria for Blast Crisis
- WHO criteria blast cells in peripheral blood or bone marrow >20%
- Extramedullary blast proliferation, or large foci or clusters of blasts in the bone marrow biopsy.

Investigations at Diagnosis

All diagnostic samples should be sent to the HODS lab for appropriate investigation.

Diagnostic samples:

Morphology
Peripheral blood film
Diagnostic Bone Marrow (if blood film morphology equivocal)
  Aspirate (assess blast %)
  Trephine

Cytogenetics
Peripheral blood sample (Lithium Heparin) or bone marrow aspirate sample for G-Banding cytogenetics and FISH for bcr-abl

Molecular genetics
EDTA peripheral blood sample x2
  a. Characterization of bcr-abl fusion breakpoint
  b. Q-PCR for baseline level of bcr-abl/abl ratio
Tissue typing

Consider tissue typing patients with clonal chromosomal aberrations (trisomy 8, double Philadelphia positive, isochromosome 17, trisomy 19, ider (22)(q10)t(9,22)(q34;q11) if less than 65 years.

Prognostic scoring systems

Sokal score (low/intermediate/high)
EUTOS score

Treatment (1st line)

NICE guidance

Imatinib

Imatinib 400mg daily is recommended as an option for untreated, chronic-phase Philadelphia-chromosome-positive chronic myeloid leukaemia in adults. Imatinib is recommended as an option for the treatment of people with Philadelphia-chromosome-positive CML who initially present in the accelerated phase or with blast crisis.

Nilotinib

Nilotinib 300mg bd is recommended, within its marketing authorisation, as an option for untreated chronic-phase Philadelphia-chromosome-positive chronic myeloid leukaemia in adults.

Dasatinib

Dasatinib 100mg daily is recommended, within its marketing authorisation, as an option for untreated chronic-phase Philadelphia-chromosome-positive chronic myeloid leukaemia in adults.

Consider Nilotinib in newly diagnosed females of childbearing age (nilotinib achieves deeper responses faster).

Therapeutic leucopheresis can be considered if there is priapism or deteriorating Glasgow Coma Scale at initial presentation.

*Test patients for infection with hepatitis B virus (HBV) before starting treatment with BCR-ABL tyrosine kinase inhibitors. Consult experts in liver disease and in the treatment of HBV before starting treatment with BCR-ABL tyrosine kinase inhibitors in patients with positive HBV serology (including those with active disease) and for patients who test positive for HBV during treatment. Patients who are carriers of HBV who require treatment with BCR-ABL tyrosine kinase inhibitors should be closely monitored for signs and symptoms of active HBV infection throughout treatment and for several months after stopping*
Definitions of response to therapy

Complete Haematological Response
- Platelets <450
- WCC <10
- Differential showing no immature granulocytes and <5% basophils
- Non palpable spleen

Cytogenetic response (FISH on PB cells can be used instead of BM)
- *Complete 0% Ph+ve cells (>20 marrow metaphases)
- Partial 1-35%
- Minor 36-65%
- Minimal 66-95%
- None >95%
*Patients who achieve complete cytogenetic response should have their ongoing response to therapy monitored by serial bcr-abl/abl ratio testing.

Molecular Response
- Complete - Bcr-abl not-detectable
- Major <0.1% (i.e. >3 log reduction in bcr-abl/abl ratio).

Loss of response
- Loss of CCR
- Rising BCRABL of 0.5 log on 2 occasions

Monitoring Therapy

At diagnosis:
- Chromosome banding analysis (CBA) of metaphases in at least 20 metaphases analysed.
- FISH in case of Ph-(for cryptic or variant translocation)
- qualitative PCR(transcript type)

During treatment:
- RQ-PCR every 3 months until MMR has been achieved and then every 3-6 months

Failure, Progression:
- RQ-PCR, Kinase domain mutational analysis, and CBA.

Mutation analysis:
- failure to achieve milestones, rising BCRABL or loss of CCR
Response definitions for any TKI first line, and 2nd line in case of intolerance (as per ELN criteria)

<table>
<thead>
<tr>
<th>Time</th>
<th>Optimal response</th>
<th>Warning</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td>High risk Major route CCA/Ph+</td>
<td></td>
</tr>
<tr>
<td>3 mos.</td>
<td>BCR-ABL&lt;10%*</td>
<td>BCR-ABL &gt;10%* Ph+ 36-95%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ph+ ≤35% (CCyR)</td>
<td>Ph+ &gt;95%</td>
<td></td>
</tr>
<tr>
<td>6 mos.</td>
<td>BCR-ABL&lt;1%*</td>
<td>BCR-ABL 1-10%* Ph+ 1-35%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ph+ 0% (CCyR)</td>
<td>BCR-ABL &gt;10%* Ph+ &gt;35%</td>
<td></td>
</tr>
<tr>
<td>12 mos.</td>
<td>BCR-ABL&lt;0.1%*</td>
<td>BCR-ABL 0.1-1%* Ph+ 0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(MMR)</td>
<td>BCR-ABL &gt;1%* Ph+ &gt;0%</td>
<td></td>
</tr>
<tr>
<td>Then, and at any time</td>
<td>MMR or better</td>
<td>CCA/Ph- (-7, or 7q-)</td>
<td>Loss of CHR Loss of CCyR Loss of MMR, confirmed** Mutations CCA/Ph+</td>
</tr>
</tbody>
</table>

Optimal response
- Best long-term outcome
- No indication for a change of treatment.

Failure
- Patient should receive a different treatment to limit the risk of progression and death

Warning
- Characteristics of disease and response to treatment require more frequent monitoring to permit timely changes in therapy, in case of treatment failure.

**Key Points**

Failure to achieve milestones at particular time points requires MDM review for advice on alternative TKI

Try to maintain imatinib dose >300mg/day, gcsf may be required

**Response at 12 months**

<table>
<thead>
<tr>
<th>Response at 12 months</th>
<th>% of progression free survival at 42 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CCyR</td>
<td>75%</td>
</tr>
<tr>
<td>&lt;3 log reduction (CCyR)</td>
<td>90%</td>
</tr>
<tr>
<td>&gt;3 log reduction (MMR)</td>
<td>98%</td>
</tr>
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</table>

IRIS Study – the achievement of >3 log reduction (MMR) months predicts progression free survival and duration of CCyR.

**Criteria for consideration BMT opinion.**

- Patients failing imatinib and another TKI (resistance)
- Patients intolerant of at least 2 TKI
**Indications for second generation TK inhibitors**

- Patients intolerant to Imatinib
- Patients who fail/resistant to Imatinib therapy
- The European LeukaemiaNet definition of Imatinib failure in chronic phase CML

**Treatment (2nd line)**

**NICE guidance**

*Dasatinib* and *nilotinib* are recommended as options for treating only chronic- or accelerated-phase Philadelphia-chromosome-positive chronic myeloid leukaemia in adults, if: they cannot have imatinib, or their disease is imatinib-resistant.

*Dasatinib* is administered orally. The recommended starting dosage is 100 mg once daily in the chronic phase or 140 mg once daily in the accelerated and blast-crisis phase and treatment should continue until disease progression or until no longer tolerated by the patient.

*Nilotinib* is administered orally. The recommended starting dosage is 400 mg twice daily for imatinib-resistant or intolerant CML in the chronic phase and 400 mg twice daily in the accelerated phase and treatment should be continued as long as the patient continues to benefit.

**Bosutinib**

*Bosutinib* is recommended as an option for chronic, accelerated and blast phase Philadelphia chromosome positive chronic myeloid leukaemia in adults, when:

- they have previously had 1 or more tyrosine kinase inhibitor and
- imatinib, nilotinib and dasatinib are not appropriate

All patients require a kinase domain mutation analysis prior to starting second generation TKI if resistant to imatinib. If patient <65 then consider referral for allograft discussion if haematological toxicity with imatinib/2nd generation TKI.

Patients failing imatinib have approximately 40-50% of achieving CCR on nilotinib. There is evidence that third line therapy using 2nd generation TKI can achieve a response in 30% of patients. However, if cytopenias are a significant problem, a state that probably reflects inadequate normal stem cells, then third line therapy is unlikely to be better tolerated (Abruzzese E et al, 2008; Quintas-Cardama A et al, 2007).
Management of CML after second line treatment failure

- Ponatinib
- Refer for BMT discussion

The Hammersmith group has produced a scoring system that helps to identify patients unlikely to respond to 2G-TKI before their initiation.

Low risk scores = reasonable to commence Nilotinib / Dasatinib irrespective of transplant risk

High risk scores (>2.5) = use EBMT pre transplant risk assessment score

Table
Pre-second-generation tyrosine kinase inhibitor (2G-TKI) score

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sokal risk group</td>
<td>Low</td>
<td>Intermediate or high</td>
</tr>
<tr>
<td>Neutropenia during Imatinib therapy</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Institution of 2G-TKI&gt;18 months after Imatinib failure</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Best cytogenetics response on Imatinib (% Ph-positive cells)</td>
<td>&lt;95%</td>
<td>&gt;95%</td>
</tr>
</tbody>
</table>

The three-year cumulative incidence of complete cytogenetics remission (p<0.0001)

<table>
<thead>
<tr>
<th>Score</th>
<th>0-1</th>
<th>2</th>
<th>3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete cytogenetic remission</td>
<td>95.6%</td>
<td>50%</td>
<td>18.7%</td>
</tr>
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</table>

Indications for 3rd generation TKI

Ponatinib

For the treatment of Chronic Myeloid Leukaemia (CML) in adult patients with chronic phase, accelerated phase, or blast phase CML who:
- Are resistant to dasatinib or nilotinib or,
- Who are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate or
- Who have the T315I mutation

Relevance of BCR-ABL kinase domain mutations

Advanced phase patients:-

Mutations should be sought in any patient presenting in advanced phase disease. The search could be repeated in such cases if they fail to achieve a response to a TK inhibitor or if having responded subsequently has a rise in the number of BCR-ABL transcripts.

If patient has T315I then requires ponatinib as per the CDF.
Management of intolerance to Imatinib
Supportive care and side effect management should be employed
If the patient is truly intolerant (grade 3/4), options that may be considered include:-
• Nilotinib, Dasatinib or Bosutinib.

Pregnancy
Women of child bearing age who have not completed their family should consider
nilotinib treatment as first line treatment.
The rational for this is a fast and deep response can be achieved. Once achieved a
stable MMR for at least 2 years then stop TKI to allow for conception. Patients will
require regular fbc and bcrabl monitoring. If wcc rises then start interferon.
Breast feeding is contraindicated while on TKI therapy.

References
Abruzzese E et al. Nilotinib in chronic myelogenous leukemia patients who fail prior
imatinib and dasatinib therapy: updated results of an open-label phase II study. J Clin
Oncol. 2008;26, 385

Quintas-Cardama A et al. Dasatinib (BMS-354825) is active in Philadelphia
cromosome-positive chronic myelogenous leukemia after imatinib and nilotinib
GUIDELINES ON THE DIAGNOSIS AND MANAGEMENT OF POLYCYthaEMIA VERA

Modified diagnostic criteria for polycythaemia vera (2007 BCSH Amendment to the guideline for diagnosis and investigation of polycythaemia/erythrocytosis)

JAK2-positive polycythaemia vera

A1  High haematocrit (>0.52 in men; >0.48 in women) OR raised red cell mass (>25% above predicted)
A2  Mutation in JAK2/Jak2 exon 12

Diagnosis requires both criteria to be present.

JAK2-negative polycythaemia vera

Major
A1  Raised red cell mass (>25% above mean normal predicted value) or Hct > 0.60 males; > 0.56 females)
A2  Absence of mutation in JAK2
A3  No cause for secondary erythrocytosis (Normal arterial oxygen saturation and no elevation in EPO)
A4  Palpable splenomegaly
A5  Presence of acquired genetic abnormality (excluding BCR-ABL).

Minor
B1  Thrombocytosis (platelet count > 450 x 10^9/l).
B2  Neutrophil leucocytosis (neutrophil count > 10 x 10^9/l in non-smokers; >12.5 x 10^9/l in smokers).
B3  Splenomegaly (demonstrated on isotope/ultrasound scanning)
B4  Characteristic BFU-E growth or low serum erythropoietin.

Diagnosis requires A1 + A2 + A3 + either another A or two B criteria

Management

Primary care:
Address risk factors such as DM, Hypertension, peripheral vascular disease and Hyperlipidaemia

Venesection:
The Hct should be maintained at less than 0.45 by venesection. The volume removed should be commensurate with the patient’s size and comorbidities.

Aspirin:
75mg/day unless it is contraindicated
**Cytoreduction** (should be considered if):
- Poor tolerance of venesection
- Symptomatic or progressive splenomegaly
- Other evidence of disease progression e.g. weight loss, night sweats, fevers
- Thrombocytosis

**Choice of therapy:**

< 40 years:  
1\(^{st}\) line Interferon  
2\(^{nd}\) line hydroxycarbamide or anagrelide

40-75 years  
1\(^{st}\) line Hydroxycarbamide  
2\(^{nd}\) line interferon or anagrelide

>70 years  
1\(^{st}\) line Hydroxycarbamide  
2\(^{nd}\) line 32P or i/m low dose busulphan
DIAGNOSIS AND MANAGEMENT OF ESSENTIAL THROMBOCYTHAEMIA

Diagnostic Criteria
(based on BCSH, 2015) Diagnosis requires A1-A3 OR A1 + A3-A5

JAK2-positive thrombocythaemia

A1 Platelet count >450
A2 Presence of an acquired pathogenetic mutation (eg in the JAK2 or CALR genes + CMPL)
A3 No other myeloid malignancy, especially PV\(^1\), PMF\(^2\), CML\(^3\), MDS\(^4\)
A4 No reactive cause for thrombocytosis and normal iron stores
A5 Bone marrow aspirate and trephine biopsy showing increased megakaryocyte numbers displaying a spectrum of morphology with predominant large megakaryocytes with hyperlobated nuclei and abundant cytoplasm. Reticulin is generally not increased

1-Excluded by a normal haematocrit in an iron replete patient
2-Indicated by significant marrow bone marrow fibrosis and palpable splenomegaly, blood film abnormalities or unexplained anaemia
3-Excluded by absence of BCRABL1 from marrow or PB
4-Excluded by absence of dysplasia on examination of blood film and bone marrow aspirate

Risk Stratification
Once the diagnosis is established then the patient risk group should be determined as follows:-

Low-risk:
(Patients having all of the following features)
- Age < 40 years
- Platelet count less than 1500\(^9\)/l
- No history of ischaemia, thrombosis or embolic features or erythromelagia
- Absence of haemorrhage considered related to ET
- Absence of diabetes
- Absence of hypertension

Intermediate risk:
(Patients having all of the following features)
- Age 40-59 years
- Platelet count <1500\(^9\)/l
- No history of ischaemia, thrombosis or embolic features or erythromelagia
- Absence of haemorrhage considered related to ET
- Absence of diabetes
- Absence of hypertension
High risk:
(Patients having any of the following features)
- Age > 60 years
- Platelet count > 1500³/l
- History of ischaemia, thrombosis or embolic features or erythromelagia
- Haemorrhage considered related to ET
- Presence of diabetes
- Presence of hypertension

Treatment options
Assess and optimise other vascular risk factors such as smoking, DM, HTN.

Low/Intermediate risk disease:
- Aspirin only
- Manage vascular risk factors
- Cytoreductive therapy only if symptomatic (splenomegaly, erythromelagia), severe microvascular symptoms not improving with aspirin, uncontrolled bleeding associated with high platelets

High Risk Disease:
1st line Hydroxycarbamide (interferon in patients <40)
2nd line Anagrelide (Bone marrow trephine every 3 years while on anagrelide to monitor MF transformation). Other agents to consider are interferon, busulphan and P32 (busulphan/p32 only in patients>70). Consider relaxing platelet target to 400-600 in patients intolerant/resistant to Hydroxycarbamide.

Failure of hydroxycarbamide is defined as follows:-
(LeukaemiaNet definition of clinical resistance/intolerance to hydroxycarbamide in ET)

Platelet count > 600,000/ul after 3 months of at least 2g/day of hydroxycarbamide (2.5g/day in patients with body weight > 80kg).

Or

WBC <2500/ul and platelet count between 400,000/ul and 600,000/ul, or WBC <3000 and platelet count >600,000 ay any dose of hydroxycarbamide

Or

Hb <10g/dl and platelet count >400,000/ul at any dose of hydroxycarbamide

Or

Presence of leg ulcers or other unacceptable muco-cutaneous manifestation at any dose of hydroxycarbamide

Or

Hydroxycarbamide- related fever
Pregnancy and ET

- All patients should be managed by a multidisciplinary team
- Therapeutic strategies in pregnancy and ET are influenced by patients’ disease status and prior obstetric history
- Pregnancy is likely to be high risk if one or more factors listed below are present. High risk pregnancies in ET should be considered for LMWH and IFN-a from the outset or during pregnancy

- Previous venous or arterial thrombosis in mother (whether pregnant or not);
- Previous haemorrhage attributed to ET (whether pregnant or not);
- Previous pregnancy complication that may have been caused by ET; e.g.
  - Unexplained recurrent first trimester loss (three unexplained first trimester losses)
  - Intrauterine growth restriction (birthweight <5th centile for gestation)
  - Intrauterine death or still birth (with no obvious other cause, evidence of placental dysfunction and growth restricted fetus);
  - Severe pre-eclampsia (necessitating preterm delivery <34 weeks) or development of any such complication in the index pregnancy;
  - Placental abruption
  - Significant ante- or postpartum haemorrhage (requiring red cell transfusion);
  - Marked sustained rise in platelet count rising to above 1500 × 10^9/l.
Algorithm for pregnancy management in ET (as per BCSH 2010)

ALL Patients
ET specific therapy
Low dose aspirin

On-going assessment of thrombotic risk
Use GECS and LMWH if appropriate

Fetal monitoring
Uterine artery dopplers at 20 weeks
Repeat at 24 weeks if bilateral notches escalate to high risk

Labour
Avoid dehydration
Potential risk of haemorrhage

Puerperium
Continue ET therapy including aspirin
6 weeks LMWH – all patients

Preconception plan
Assess risk (Table VI)
Optimize and adjust therapy

ALL PATIENTS

HIGH RISK PATIENTS
in addition

HIGH RISK PATIENTS (Table VI) IN ADDITION
ET specific therapy
Interferon alpha
Consider LMWH if adverse previous
Pregnancy or thrombosis

Fetal monitoring
Regular fetal growth scans

Labour
Adhere to local protocols for timing of LMWH and interventions

Breastfeeding
Individual discussion if taking interferon
GUIDELINES ON THE DIAGNOSIS AND MANAGEMENT OF IDIOPATHIC MYELOFIBROSIS

Diagnostic Criteria (BCSH 2015)

<table>
<thead>
<tr>
<th>Diagnosis requires A1 + A2 and any two B criteria</th>
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</thead>
<tbody>
<tr>
<td>A1 Bone marrow fibrosis ≥3 (on 0–4 scale)</td>
</tr>
<tr>
<td>A2 Pathogenetic mutation (e.g. in JAK2, CALR or MPL), or absence of both BCR-ABL1 and reactive causes of bone marrow fibrosis</td>
</tr>
<tr>
<td>B1 Splenomegaly</td>
</tr>
<tr>
<td>B2 Unexplained anaemia</td>
</tr>
<tr>
<td>B3 Leuco-euthroblastosis</td>
</tr>
<tr>
<td>B4 Tear-drop red cells</td>
</tr>
<tr>
<td>B5 Constitutional symptoms</td>
</tr>
<tr>
<td>B6 Histological evidence of extramedullary haematopoiesis</td>
</tr>
</tbody>
</table>

* Drenching night sweats, weight loss >10% over 6 months, unexplained fever (>37.5°C) or diffuse bone pains.

- If Jak2 negative check for CALR/MPL
- BCRABL should be checked in atypical trephines or if Jak2, c-mpl and CALR are negative
- PDGFRA/B should be excluded if significant eosinophilia present
Prognostic Factors

Therapeutic decisions on MF should be based on DIPSS Plus score. DIPSS and DIPSS plus score can be used in post-PRV and post-ET.

<table>
<thead>
<tr>
<th>Variable</th>
<th>IPSS</th>
<th>DIPSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 65 years</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin &lt;100 g/dl</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Leucocyte count &gt; 25 x 10^9/l</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Circulating blasts ≥ 1%</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

DIPSS Plus: add 1 point to the DIPSS RISK GROUP* (low = 0, intermediate 1 = 1, intermediate 2 = 2 and high risk = 3) in addition for:
- Platelet count <100 x 10^9/l
- RBC transfusion need
- Unfavourable karyotype: +8, -7/7q-, i(17q), inv(3), -5/5q-, 12p-, 11q23 rearrangement

<table>
<thead>
<tr>
<th>Risk group</th>
<th>IPSS</th>
<th>DIPSS</th>
<th>DIPSS-Plus</th>
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<tbody>
<tr>
<td></td>
<td>Predictors (n)</td>
<td>Median survival (years)</td>
<td>Predictors (n)</td>
</tr>
<tr>
<td>Low</td>
<td>0</td>
<td>11.3</td>
<td>0</td>
</tr>
<tr>
<td>Intermediate-1</td>
<td>1</td>
<td>7.9</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Intermediate-2</td>
<td>2</td>
<td>4.0</td>
<td>3 or 4</td>
</tr>
<tr>
<td>High</td>
<td>≥3</td>
<td>2.3</td>
<td>5 or 6</td>
</tr>
</tbody>
</table>

*Note that this is the risk group NOT the sum of points.

Treatment

Anaemia
- EPO Injections if inadequate EPO levels (<125mU/ml)
- If after 3 months no response following increased EPO dose then consider Danazol (In males check PSA and exclude prostate ca prior to starting danazol. Require annual u/s liver and regular LFT monitoring)
- Thalidomide/prednisolone

Low risk
- Watch and wait.
- Interferon if symptomatic
- Hydroxycarbamide for cytoreduction

Intermediate 2 /High risk DIPSS
- Patients with symptomatic splenomegaly or constitutional symptoms in primary myelofibrosis, post ET myelofibrosis or post essential thrombocythaemia myelofibrosis are eligible for **Ruxolitinib** (if platelets>50). Patients must have INT2/HIGH risk disease DIPSS score
- For objective monitoring of symptoms while on Ruxolitinib suggest using MPN-SAF
Allograft candidates (as per EBMT/ELN IWG)

- INT-2/High risk disease according to DIPSS or DIPSS plus and age<70 should be considered potential candidates
- INT-1 and age <65 should be considered candidates for allogeneic-SCT if they present either refractory, transfusion dependent anaemia or adverse cytogenetics (as defined by DIPSS+)

References


BCSH Guidelines 2012: Guideline for the diagnosis and management of myelofibrosis

BCSH Guidelines 2014: Modification of British Committee for Standards in Haematology diagnostic criteria for essential thrombocythaemia

BCSH guidelines 2007: Amendment to the diagnosis, investigation and management of polycythaemia/erythrocytosis