Lancashire and South Cumbria Haematology CRG
GUIDELINES FOR INVESTIGATION AND MANAGEMENT OF PRIMARY MYELOFIBROSIS (PMF)

Diagnostic criteria for primary myelofibrosis (PMF) - BCSH 2012

Diagnosis requires A1+A2 and any two B criteria	
A1	Bone marrow fibrosis ≥3 (on 0-4 scale)
A2	Pathogenetic mutation (eg Jak2, CALR or MPL), or absence of both BCR-abl and reactive causes of bone marrow fibrosis
B1	Palpable splenomegaly
B2	Unexplained Anaemia
B3	Leuco -erythroblastosis
B4	Tear – drop poikilocytes
B5	Constitutional symptoms*
B6	Extramedullary haematopoiesis (histology)
*Drenching night sweats, weight loss >10% over 6 months, unexplained fever > 37.5C or diifuse bone pain.	

Diagnostic criteria for post PV and post ET myelofibrosis - BCSH 2012

Diagnosis requires A1+A2 and any two B criteria	
A1	Bone marrow fibrosis ≥3 (on 0-4 scale)
A2	Previous diagnosis of PV or ET
B1	New palpable splenomegaly or increase of spleen size ≥ 5cm
B2	Unexplained Anaemia with 20g/l drop from baseline
B3	Leuco erythroblastic blood film
B4	Tear – drop poikilocytes
B5	Constitutional symptoms*
B6	Extramedullary haematopoiesis (histology)
*Drenching night sweats, weight loss >10% over 6 months, unexplained fever > 37.5C or diifuse bone pain.	

Prognostic Criteria*

Variable	IPSS	DIPSS	DIPSS+
Age >65	●	●	●
Constitutional Sy	●	●	●
HB < 100 g/l	●	●●	●
WCC >25 X 10^9/l	●	●	●
Circulating blasts ≥ 1%	●	●	●
Transfusion Dep			●
Plts < 100 X 10^9/l			●
Karyotype (unfavourable)			●

- Unfavourable Karyotype: +8; -7/7q-; i(17q);inv (3);-5/5g-; 12p-;11q23 rearrangement

- IPSS: low risk, 0 points; intermediate-1 risk, 1 point; intermediate-2 risk, 2 points; high risk, 3 to 5 points;
- DIPPS: low risk, 0 points; intermediate-1 risk, 1 to 2 points; intermediate-2 risk, 3 to 4 points; high risk, 5 to 6 points;
- DIPPS-plus: low risk, 0 points; intermediate-1 risk, 1 point; intermediate-2 risk, 2 to 3 points; high risk, 4 to 6 points.

- IPSS is only validated at diagnosis, whilst the DIPSS/DIPSS+ is dynamic

- There are newer scoring systems which include molecular information - MIPSS70/MIPSS70+/GIPSS/MIPSS70+ V 2 at http://www.mipss70score.it/

Risk Group	IPSS MS(years)	DIPSS MS(years)	DIPPS+ MS(years)
Low	11.3	NR	15.7
INT1	7.9	14.2	6.5
INT 2	4	4	2.9
HIGH	2.3	1.5	1.3

MS – Median Survival, NR – Not reached

Management of myelofibrosis:

General points

1. All patients should be risk stratified using the IPSS at diagnosis or DIPSS+ at any other time to assess prognosis and guide treatment strategies.

2. Patients with an IPSS risk of intermediate 2 or high should be assessed for their suitability to undergo an allogeneic stem cell transplant. If deemed unsuitable for a transplant option then they should be considered for a trial or treatment targeted to their symptoms.

3. Patients with IPSS low risk/Intermediate 1 without symptoms can be observed.

4. Patients with IPSS low risk/intermediate 1 with symptoms should be considered for a trial or treatment targeted to their symptoms.

5. There are newer scoring systems incorporating molecular mutations eg MIPP70+ V2, which may help in transplant related decisions for those under the age of 70 at http://www.mipss70score.it/

6. All patients should be discussed at MDT with appropriate histology/molecular studies reviewed at HMDS Leeds.

7. All patients should have holistic support with clinical nurse specialist input and written information about their disease.

Treatment:

Symptomatic splenomegaly

Medical Management:

- 1st line – Hydroxycarbamide, Ruxolitinib (Nice approved for Intermediate 2/high risk Primary myelofibrosis, Post ET/PV Myelofibrosis who are deemed unsuitable for a stem cell transplant)
- 2nd line – Immunomodulatory agents – Thalidomide and prednisolone. (consider lenalidomide if anaemia and platelets > 100)

Surgical management:

Routine splenectomy is inappropriate due to its high risk of morbidity and mortality. It should be restricted to carefully selected patients with extensive pre-operative assessment. The laparascopic route is not suitable due to high risk of bleeding. Typical indications would include:

- Drug refractory symptomatic splenomegaly
- Drug-refractory anaemia
- Symptomatic portal hypertension
- Severe catabolic symptoms.

Radiotherapy:

Radiotherapy can be considered for patients who are deemed unsuitable for surgery and have an adequate platelet count (>50 X 10^9/l)

Anaemia

Options include:

- Red cell transfusion programme (iron chelation not routinely recommended).
- Erythropoietin trial in patients with inappropriately low erythropoietin levels (< 125 u/l)
- Androgens – Danazol first line for a minimum of 6 months before assessing response
- Immunomodulators – Thalidomide and prednisolone, Lenalidomide

Constitutional Symptoms

- Consider myelosuppression or Ruxolitinib for symptoms that are impinging on quality of life. (Nice approved for intermediate 2 /high risk Primary myelofibrosis, Post ET/PV Myelofibrosis who are deemed unsuitable for a stem cell transplant)

Myelosuppression

- Indications for myelosuppressive treatment include :
  1. Control of hyperproliferative symptoms
  2. Splenomegaly and hepatomegaly
  3. Leucocytosis and or thrombocytosis

- Hydoxycarbamide is the first line choice. Interferon alfa and anagrelide are alternative options in selected cases.

Author	Dr S Kolade
Ratified by LSCCN Haematology CRG	
Review date:	Feburary 2024