GUIDELINE ON THE USE OF ERYTHROPOIETIN IN MDS

INDICATION

Many patients with MDS require supportive care. The aim of supportive care is to maintain the blood count at a point where quality of life is maintained.

The objective of this guideline is to help clinicians identify groups of MDS patients who might respond to erythropoietin (Epo) and to offer guidance on the management of MDS patients requiring Epo and/or G-CSF.

Investigations prior to starting Epo

- FBC
- Creatinine (for estimated GFR)
- Serum epo level measured at the Hb nadir prior to transfusion
- Ferritin
- Fe/TIBC ratio or equivalent (if ferritin<500)
- Bone marrow karyotype, blast percentage, ring sideroblast percentage
- Record BP

Erythropoietins Products- Either short or long acting Epo may be used.

Short acting
Epoetin alpha (Eprex)
Epoetin beta (NeoRecormon)
Epoetin delta (Dynepo)

Long acting
Darbepoetin alpha (Aranesp)

1. Erythropoietin in non-sideroblastic MDS subtypes

Eligibility

- IPSS low or int-1 risk disease

In addition patients should have one or both of the following criteria:
- Serum Epo <500 iu/ml
- Transfusion requirement < 2 units/month
Approximately 50% of this group of MDS patients will have a meaningful response to Epo. Patients outside this group are much less likely to respond.

Patients with MDS and excess sideroblasts should be considered for upfront Epo/GCSF combination (see below)

**Dosing**

- **Epoetin** (alpha, beta, delta): 10,000 units weekly initially and uptitrated every 4 weeks to a maximum of 30,000 units. If no response is seen after 8 weeks, consider increasing to 60,000 units once per week and/or adding G-CSF according to schedule below.

  OR

- **Darbepoetin**: 500 mcg every three weeks initially and if no response after 8 weeks increase to 300mcg once every week and consider adding G-CSF according to schedule below.

  - **G-CSF (for patient with inadequate response)**: Start Filgrastim 300mcg or Lenograstim 263mcg, two to three times per week. Monitor blood count weekly and titrate dose to keep WBC between 6 and 10x10^9/l.

**Response Assessment**

An assessment of erythroid response should be made after 8 weeks. If there is a less than 10g/L increase in Hb, the dose of Epo should be increased and G-CSF considered. If there is no response after a further 8 weeks, stop the drugs.

Check BP at each clinic visit

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2. **Upfront Epo-GCSF (EpoG) combined therapy in sideroblastic subtypes of MDS**

**Eligibility**

Patients with MDS and ring sideroblasts who are IPSS low or int-1 risk with serum epo<500iu/ml and/or transfusion requirement <2 units/month

**Dosing**

Start with epoietin (alpha, beta, delta) 10,000 units weekly uptitrated 4 weekly to maximum of 30 000units or darbepoetin 500mcg every three weeks with G-CSF added incrementally as described above.

**Response Assessment**

Check response after 8 weeks, if increment in Hb <10g/L, increase epoietin to 60,000 units weekly or darbepoetin to 300mcg weekly. Re-assess response after 8 weeks, if increment in Hb <10g/L, stop Epo-G.
Check BP at each clinic visit

3. **Follow-up monitoring**

- FBC (aim for Hb 100-120g/L, higher Hbs are associated with poorer overall survival). Reduce Epo dose by 25% if rise in Hb is too rapid.
- BP (if systolic >150 or diastolic >100, consider Epo dose reduction of 25%)
- If response to Epo suboptimal consider oral iron (Ferrous Sulphate) 200mg daily

4. **Loss of response to Epo**

Median duration response is about 24 months. Loss of response to Epo does not necessarily herald transformation but the status of the MDS should be re-evaluated. Stop Epo if response is lost.
International prognostic scoring system (IPSS) for MDS

<table>
<thead>
<tr>
<th>Prognostic Variable</th>
<th>Score Value</th>
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<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>BM blasts (%)</td>
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<tr>
<td>&lt;5</td>
<td>5-10</td>
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<tr>
<td>Karyotype*</td>
<td>Good</td>
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<tr>
<td>Cytopenias</td>
<td>0/1</td>
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Scores for risk groups are as follows: Low, 0; INT-1, 0.5-1.0; INT-2, 1.5-2.0; High, ≥ 2.5.

* Good, normal, -Y, del(5q), del(20q); Poor, complex (≥ 3 abnormalities) or chromosome 7 anomalies; Intermediate, other abnormalities.

References