ECN Protocol Book

ECN Erythropoietin Replacement Guideline for MDS and Haematological Malignancy

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Reason for document development: Network required guidelines
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- Cancer pharmacy staff within ECN
- Chemotherapy Nursing staff within ECN
Approved by: ECN MM Board
Date approved: 20th July 2012
Next Review date: 20th July 2014
Version No: 1
Responsibility for review: Lead Pharmacist, Essex Cancer Network
Reference: ECN_Protocol_Book_Epo_1
Scope of these Guidelines

These guidelines apply to adult haematology patients being considered for Erythropoietin replacement therapy only.

Patients with a diagnosis of MDS, Myelofibrosis, Myeloma and Lymphoproliferative disorders.

Patients requiring Erythropoietin for other indications, such as renal disorders and solid tumours; pre or post-operatively are excluded.

Introduction

The majority of 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.

- There is no single Hb threshold where transfusion/erythropoietin is indicated, but a threshold can usually be set for individual patients, depending on symptoms, the presence of co-morbidities and the patient’s level of activity

- In general, the majority of MDS patients are elderly and become symptomatic when the Hb is < 10 g/Lt. The majority of patients eligible for a trial of EPO have a baseline Hb between 8 and 10 g/dl.

- Patients with a baseline haemoglobin of between 10-12g/dl are not normally considered for erythropoietin except in special circumstances.

- Some patients with a baseline Hb 8 to 10 g/dl are relatively asymptomatic. This group of patients should be carefully observed and a trial of EPO (followed by transfusion if necessary) deferred until they become symptomatic.

- Patients with a low anticipated transfusion requirement, EPO < 400 iu/ml, and non-sideroblastic subtype have a >50% chance of responding to a trial of EPO

- Other haematological indications for a trial of EPO include transfusion dependent patients with:
  - Myelofibrosis
  - Multiple Myeloma
  - Lymphoproliferative disorders on chemotherapy – such as Lymphoma or CLL.

- Patients with heavy solid tumour infiltration of the bone marrow and transfusion dependent (non-haematological malignancy) are not eligible for a trial of EPO, as there is evidence that this shortens survival in this group of patients. They should be offered standard transfusion support instead.
Patient Selection

MDS - Inclusion Criteria – response rate > 70%
1) Symptomatic Anaemia – potentially requiring transfusion support
2) IPSS low or Int-1
3) Serum EPO of < 400 iu/ml
4) Anticipated or actual transfusion requirement < 4 units/month

MDS - Relative Exclusion Criteria – response rate <50%
1) Patients with ringed sideroblastic MDS have only a 10% chance of responding to EPO
2) Transfusion requirement > 4 units per month
3) Baseline Hb < 7g/lt
4) Serum EPO > 400 iu/ml

Myeloma and Lymphoma
1) Symptomatic anaemia – where transfusion support is being considered.
2) Serum EPO of < 400 iu/ml

Investigations prior to starting EPO

- FBC*
- Creatinine (or estimated GFR)*
- Serum EPO* level measured at the Hb nadir prior to transfusion
- Ferritin/B12/Folate*
- Fe/TIBC/transferrin saturation or equivalent (if ferritin < 500)
- Bone marrow* karyotype, blast percentage, ring sideroblast percentage,
- Record BP*

* essential

Erythropoietins available

Either short or long acting EPO may be used depending on acquisition costs

Short acting: Epoietin alpha (Eprex)  Epoietin beta (NeoRecormon)
Long acting: Darbepoietin alpha (Aranesp)
Starting and monitoring EPO therapy

- Once a decision to start a trial of EPO is made, the objective is to ascertain that EPO therapy alone can replace the need for transfusion, and the trial of EPO should last for no longer than 12 weeks.

- Ensure B12 and Folate deficiency has been excluded.

- Maintain good iron stores – typically ensure serum ferritin is > 200 mg/L

- Check serum ferritin at least 3 monthly and replenish PO or IV as necessary.

- Ensure hypertension, if present is well controlled, and that BP is checked prior to each injection. As a guide BP systolic should be < 160 mm Hg.

- Starting dose for short acting erythropoietin (Eprex) 20,000 to 40,000 units sc weekly.

- Target is to achieve transfusion independence with a stable Hb level 10-12g/dl

- Assess at four weekly intervals. If Hb increase is greater than or equal to 1.0g/dl continue at same dose. If Hb increase is less than 1.0g/dl increase dose by 10-20,000 per week and assess again after four weeks to a maximum dose of 80,000 units every week.

- There is evidence that some patients who have failed to respond to EPO 80,000 will respond with an Hb increment to the further addition of G-CSF – but this is not routinely practiced (see below).

- If there is no response to 80,000 i.u per week (Hb increment less than 1.0g/dl) no further EPO should be administered and transfusion program should be started as an alternative.

- During the trial of Erythropoietin, additional transfusional support should be avoided if possible.

- If the target is achieved (Hb 10-12 g/dl) and EPO well tolerated, then continue EPO at the minimal effective dose until response is lost. The average response duration is about 2 years. Responding patients are usually monitored in clinic three monthly.

- EPO dose should be titrated downwards once the haemoglobin concentration reaches 12.0g/dL or above as there is little evidence to support maintaining Hb > 12 g/dl.

- Reduce dose by 25-50% once Hb of > 12.0g/dL is attained.

- EPO should be discontinued if Hb > 14.0g/dL and restarted as appropriate when Hb <10g/dl - at a lower dose.

- Erythropoietin is normally continued for one month after completion of chemotherapy.

- Exclude iron deficiency as a cause of loss of response – before stopping EPO.

- Darbepoetin (long acting alternative): 150mcg once a week initially. If no response after 6 weeks increase to 300mcg once a week and consider adding G-CSF according to schedule below.

- G-CSF (optional): In patients not responding to Eprex 80,000, consider adding G-CSF at 75mcg daily and increase weekly to 150mcg daily and then to 300mcg daily (multiple sampling from single vials kept at 4°C). Aim to keep WBC between 6 and 10x10^9/l. Once maximal Hb response achieved reduce G-CSF to thrice weekly.

- Side-effects of EPO therapy are relatively few. The most common are exacerbation of hypertension. Possible increased risk of thrombosis, although thromboprophylaxis not routinely prescribed. Rare cases of Pure Red Cell Aplasia but no cases seen with sub-cutaneously administered Epoetin alpha.
### International prognostic scoring system (IPSS) for MDS

<table>
<thead>
<tr>
<th>Prognostic Variable</th>
<th>Score Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.5</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>

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


8. Murphy M et al. The clinical use of red cell transfusions BJH 2001; 113, 24-31


11. NICE guidance TA142 Anaemia (cancer-treatment induced) - erythropoietin (alpha and beta) and darbepoetin: May 2008