Rappel des thérapies de l´anémia
Recommendations EORTC

Dr. Pere Gascon
Barcelona
European guidelines

EORTC guidelines for the use of erythropoietic proteins in anaemic patients with cancer: 2006 update and September 2007 update

EORTC = European Organisation for Research and Treatment of Cancer
EORTC Guidelines for Erythropoietic Proteins in Anaemic Patients with Cancer revisited

Bokemeyer et al. Eur J Cancer. 2007;43:258–270
Chemotherapy-induced anaemia: European guidelines

• **EORTC 2007 guidelines recommend:**
  – Initiation of ESA therapy at Hb concentration of 9–11 g/dL
  – Target Hb: ~12 g/dL

• **Major goals of ESA therapy:**
  – To prevent RBC transfusions
  – To improve QoL

• In patients with chemotherapy-induced anaemia (CIA), QoL can be significantly improved with ESA therapy

EORTC, European Organisation for Research and Treatment of Cancer
ESA, erythropoiesis-stimulating agent
RBC, red blood cell

## Summary of evidence-based EORTC guidelines for treating CIA

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>ASCO/ASH$^1$</th>
<th>NCCN$^2$</th>
<th>EORTC$^3$</th>
<th>ESMO$^4$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiate ESA therapy</td>
<td>Hb ≤10 g/dL (clinical decision if Hb 10–12 g/dL)</td>
<td>Hb ≤11 g/dL</td>
<td>Hb 9–11 g/dL (clinical decision if Hb ≤11.9 g/dL)</td>
<td>Hb ≤10 g/dL</td>
</tr>
<tr>
<td>Goal of treatment</td>
<td>The lowest Hb concentration needed to avoid transfusions</td>
<td>Maintain Hb between 10–12 g/dL</td>
<td>Symptomatic patients Target Hb should be around 12 g/dL</td>
<td>Hb should not exceed 12 g/dL</td>
</tr>
</tbody>
</table>

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## “International” guidelines

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>ASH/ASCO&lt;sup&gt;1&lt;/sup&gt;</th>
<th>EORTC&lt;sup&gt;2,3&lt;/sup&gt;</th>
<th>ESMO&lt;sup&gt;4&lt;/sup&gt;</th>
<th>NCCN&lt;sup&gt;5&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiate ESA therapy</td>
<td>Discuss harms/benefit if Hb &lt; 10 g/dL</td>
<td>Symptomatic Hb 9–11 g/dL</td>
<td>&lt;10 g/dL</td>
<td>Consider if Hb &lt; 11 g/dL</td>
</tr>
<tr>
<td>Iron supplementation</td>
<td>Consider IV iron to reduce ESA needs, but is not standard of care</td>
<td>If iron deficiency also present</td>
<td>iv iron To increase ESA efficacy Or if FID*</td>
<td>If iron deficiency and with ESAs</td>
</tr>
<tr>
<td>Transfusions</td>
<td>Considered for very severe anemia or individual clinical needs</td>
<td>Minimal use</td>
<td>Not discussed</td>
<td>Avoid use where possible</td>
</tr>
<tr>
<td>Iron level monitoring</td>
<td>Iron, TIBC, TSAT, ferritin</td>
<td>---</td>
<td>Iron, CRP, TSAT, ferritin</td>
<td>Monitor TSAT and ferritin</td>
</tr>
<tr>
<td>Target Hb</td>
<td>Lowest Hb needed to avoid Tx</td>
<td>≈12 g/dL</td>
<td>12 g/dL</td>
<td>&lt;12 g/dL (?)</td>
</tr>
</tbody>
</table>

TSAT: transferrin saturation

*FID*: ferritin >100 and TSAT <20%

• Erythropoiesis-Stimulating Agents-ESAs: The 2011 Position of the EORTC Working Party
EORTC Guidelines for Erythropoietic Proteins in Anaemic Patients with Cancer

“We confirm that QoL can be significantly improved in anaemic cancer patients following erythropoietic protein therapy”

The two major goals of erythropoietic protein therapy are prevention of transfusions and improvement of QoL (grade A).

Reference Cochrane review 2011
EORTC Guidelines for Erythropoietic Proteins in Anaemic Patients with Cancer

“We confirm that QoL can be significantly improved in anaemic cancer patients following erythropoietic protein therapy”

The two major goals of erythropoietic protein therapy are prevention of transfusions and improvement of QoL (grade A).

CHANGE in 2010

EORTC Guidelines for Erythropoietic Proteins in Anaemic Patients with Cancer

• Patients **under chemotherapy** whose Hb level is below 8 g/dL should be evaluated for need of transfusions, in addition to erythropoietic proteins +/- iron (Grade C) (unchanged in 2007)
EORTC Guidelines for Erythropoietic Proteins in Anaemic Patients with Cancer

• In symptomatic cancer patients receiving chemotherapy, treatment with erythropoietic proteins should be initiated at a Hb level of 8–11 g/dL.

*In 2007 radiotherapy alone is deleted from this recommendation

EORTC Guidelines for Erythropoietic Proteins in Anaemic Patients with Cancer

• Erythropoietic proteins may be considered in selected asymptomatic, anaemic cancer patients under chemotherapy with a Hb level of <11.9 g/dL to prevent a further decline in Hb

• According to individual factors (eg, type/intensity of chemotherapy, baseline Hb) and the duration and type of further planned treatment (Grade B)

EARLY INTERVENTION actually minimises exposure

*words in orange added in 2007

EORTC Guidelines: Use of Erythropoietic Proteins in Anaemic Patients with Cancer

• We do not recommend the prophylactic use of erythropoietic proteins to prevent anaemia* in patients undergoing chemotherapy and/or radiotherapy who have normal Hb values at the start of treatment (Grade A)
EORTC Guidelines: Use of Erythropoietic Proteins in Anaemic Patients with Cancer

- In selected patients with cancer-related anaemia not undergoing chemotherapy or radio-chemotherapy

- Treatment with erythropoietic proteins *may be initiated at a Hb level of 9-11 g/dL based on anaemia-related symptoms (Grade B) and careful assessment of need.

* was in 2006 “should”

• The target Hb concentration (Grade B) is about 12 g/dl

– 2007: Wording modified from «should be 12 to 13 g/dL»

NO CHANGE...but point out some meta-analyses (darbo, epoetin beta) do not show an increased risk with an absolute higher level, but actually responding patients do better (darbo analysis). This limit is related to lack of data of symptom benefit and further transfusion avoidance above this Hb level.
EORTC guidelines for the use of erythropoietic proteins in anaemic patients with cancer

• We do not recommend dose-escalation as in patients not responding within 4–8 weeks (grade B)
EORTC guidelines for the use of erythropoietic proteins in anaemic patients with cancer

◆ Treatment should be continued until a level around 12* g/dL level is reached and patients show symptomatic improvement.

◆ For patients reaching the target Hb, individualised treatment with increased intervals of dosing and/or titration of lowest effective maintenance dose should be made repeatedly (grade C).

◆*deleted –13 in 2007

EORTC Guidelines: Use of Erythropoietic Proteins in Anaemic Patients with Cancer

- There is no evidence of increased response to erythropoietic proteins with the addition of oral iron supplementation (grade B).
- There is evidence of improved response to erythropoietic proteins with intravenous iron supplementation (grade A as 6/7 published STUDIES increased response and decreased use of ESA).
EORTC guidelines: Use of erythropoietic proteins in anaemic patients with cancer receiving chemotherapy

- Epoetin alpha and epoetin beta can be used on a fixed dose weekly basis (Grade A).
- Darbepoetin can be used on an every 3 week fixed dose basis or alternatively, once weekly dosing can be given at 2.25 µg/kg body weight (Grade A). An every 2-week regimen is also used in some countries (Grade C).
EORTC Guidelines for Erythropoietic Proteins in Anaemic Patients with Cancer Chemotherapy: 2011 Update

Correct causes of anaemia other than cancer

- Normal Hb levels
  - Prophylactic treatment not recommended

- Symptomatic Hb 8-11 g/dL*
  - Consider ESA/iron treatment

- Asymptomatic Hb ≤ 11.9 g/dL
  - Consider ESA/iron treatment according to individual factors
    - Including risk of rapid worsening of anaemia

- Hb < 8 g/dL
  - Evaluate for transfusion need and consider ESA/iron treatment according to individual factors

Treat to target about 12 g/dL

Individualise treatment to maintain target Hb with minimal amount of treatment

Normal Hb levels: Symptomatic Hb 8-11 g/dL* Asymptomatic Hb ≤ 11.9 g/dL Hb < 8 g/dL

* 8-10 in some cases Tx is needed

ESAs: The 2011 Position of the EORTC Working Party

- Clinical trials have established that
  - ESAs decrease transfusion needs
  - Hb levels are sustained on ESAs, not with intermittent transfusions
  - ESAs increase quality of life*
  - ESAs should be used within guidelines

No change in 2007
Thank you for your attention