Management of Iron Status in Oncology Patients

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Guidelines for Advanced Medical Therapies (AMT) and Sanoviv Hospital
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Iron Status in Oncology Patients

**Note: “ESA” = Erythropoetin Stimulating Agent**

The next three slides are from this paper:

<table>
<thead>
<tr>
<th>ESA Use: Organization</th>
<th>Anemia related to chemotherapy</th>
<th>Untreated patients</th>
<th>Patients treated with curative intent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASH/ASCO</strong></td>
<td>ESAs indicated for Hb ≤10 g/dl. Hb target is lowest value to avoid BT. BT is an option if Hb is between 10 and 12 g/dl, consider ESAs according to clinical condition. BT is an option</td>
<td>ESAs are not recommended</td>
<td>There is no specific recommendation</td>
</tr>
<tr>
<td><strong>NCCN</strong></td>
<td>BT if immediate correction is necessary. Consider treatment with ESAs by US FDA indications/dosing/dosing adjustments, under REMS</td>
<td>BT according to symptoms ESAs are not recommended</td>
<td>ESAs are not recommended</td>
</tr>
<tr>
<td><strong>US FDA</strong></td>
<td>Therapy should not be initiated at Hb levels ≥10 g/dl. Use the lowest dose of ESAs able to raise the levels of Hb values to avoid BT</td>
<td>ESAs are not recommended</td>
<td>ESAs are not recommended</td>
</tr>
<tr>
<td><strong>EORTC</strong></td>
<td>ESAs should be initiated at an Hb level of 9–11 g/dl based on anemia-related symptoms. ESAs may be considered in selected asymptomatic patients with a Hb level of 11–11.9 g/dl if this would prevent a further decline in Hb - iv. iron use should be reserved for patients with absolute or functional iron deficiency</td>
<td>ESAs may be given in selected patients with a Hb level of 9–11 g/dl</td>
<td>There is no specific recommendation</td>
</tr>
</tbody>
</table>
Use of Iron in Oncology Patients

Therefore, in all cancer patients with any degree of anemia, it is important to investigate whether there is iron deficiency. If the parameters indicate:

- Low levels of ferritin
- Transferrin Saturation
- or Reticulocyte Hemoglobin Content

iron supplementation is indicated, preferably through parenteral administration. Such treatment could also be considered in patients who will start treatment with an ESA, due to the improved responses in terms of hemoglobin levels resulting from the combined treatment.

At present, there appears to be enough scientific support for the use of intravenous iron supplementation to improve hemoglobin responses in anemic patients with cancer, and this has been included in various guidelines.

Conclusions:

- Chemotherapy is associated with abnormal iron metabolism.
- Another mechanism contributing to iron deficiency in cancer patients is the low bioavailability of orally administered iron.
- The use of intravenous iron (and not oral iron) during treatment with ESAs may improve hemoglobin levels even in the absence of depleted iron stores (or absolute iron deficiency).
- Recommendations for the optimal formulations, doses and treatment schemes of iron supplementation concurrently with ESA treatment in cancer-related anemia need to be established.
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Parenteral Iron – AMT Guidelines

General:

• As parenteral iron can have anaphylactic type reactions patients must be screened for history of intolerance to injectable iron products. Any patient having a suspicious history should be counselled regarding the increased risks and offered premedication with 25-50 mg IV Benadryl.

• Another complicating factor is that parenteral iron compounds have greatly different safety profiles. This is generally less due to the iron component and more due to the solubilizing agent compounded with the iron. Statistically dextran is the most reactive and sucrose and gluconate are the least reactive. (The only major exception being dextran form rapidly infused causing cardiac arrhythmia and arrest). Regardless of form used appropriate emergency medications and equipment to respond to cardiac and other Type-1 reactions must be on hand.
Follow up testing:

- While **Hemoglobin and Hematocrit** will improve more quickly and can be measured 72 hours following an infusion assessment of **Ferritin** must be made after a 3-4 week wash out (following termination of parenteral iron therapy) for the ferritin to be stable. The ultimate goal initially is ferritin over 100 as the ferritin will drop over time as the iron redistributes to the tissues. The exceptions are the patients who begin to tolerate and absorb oral iron after the ferritin reaches 40-50.

- Iron delivery to tissues over time – Considering Hemoglobin-Hematocrit / Ferritin / TIBC / etc:
  - Hb/Hct are the quickest to change.
  - Then RBC and TIBC / % Saturation.

Testing continued:

- Ferritin is quite labile initially.
- Picture the Ferritin rising as the temporary storage site, then ferritin giving iron to the transferrin dropping the TIBC. The highly saturated transferrin then delivers the iron to the mitochondrial receptors for use in electron transport, and the marrow for hematopoiesis. Over time if the initial loading dose was sufficient the labs will normalize and stay stable as mentioned below. If not sufficient then the ferritin will continually drop and eventually you will see a low Ferritin and generally a high TIBC with a low % saturation.
- Ferritin will rise as mentioned above and slowly redistribute the iron to the transferrin and eventually the tissues. So the initial finding desired is high ferritin, low TIBC and high % Sat. Generally 8-12 weeks later the ferritin should drop slightly, the TIBC should rise some and the % Sat should drop to normal. Ideal stable numbers are ferritin between 50-100, TIBC in the mid-range and % Sat normal. If the ferritin drops below 40 during the follow up process another series of iron infusion should be considered.
- Aside from waiting 3-4 weeks to run the first follow up labs, repeat labs including CBC, Ferritin, TIBC, % Sat should be run every 8-12 weeks.
Venofer (iron sucrose)

- “Venofer® (iron sucrose injection, USP) is administered as a total cumulative dose of 1000 mg as a 200 mg slow IV injection undiluted over 2 to 5 minutes on 5 different occasions within a 14 day period. There is limited experience with administration of an infusion of 500 mg of Venofer®, diluted in a maximum of 250 mL of 0.9% NaCl, over a period of 3.5-4 hours on day 1 and day 14; hypotension occurred in 2 of 30 patients treated.”

- Our general preferred infusion is 100 to 200 mg diluted in 100 mL NS via IV.

- In our facility we do not generally push Venofer, although some patients do tolerate it.

- [http://www.venofer.com/hcp/HCPAbout_Ind.aspx](http://www.venofer.com/hcp/HCPAbout_Ind.aspx)

Ferrlecit (sodium ferric gluconate)


- “Safe administration as an IV push (12.5 mg/min) or by IV infusion over 1 hour (diluted in 100 mL of 0.9% sodium chloride)” Cumulative dosing of 1000 mg prior to re-evaluation of labs.

- Our general preferred infusion is 62.5 to 125 mg diluted in 100 mL NS via IV.

- In our facility we do not generally push Ferrlecit, although some patients do tolerate it.

- [http://www.ferrlecit.com/confidence/Dosing_and_Administration.aspx](http://www.ferrlecit.com/confidence/Dosing_and_Administration.aspx)
Parenteral Iron – AMT Guidelines

Dexferrum, INFeD (Iron Dextran)
• ONLY USED DEEP IM – VIA Z-TRAK INJECTION PROCEDURE
• While IV protocols do exist for this product our policy is to use it via IM administration only due to anaphylactic and cardiac high grade adverse events.
• Our preferred injection is 50-100 mg deep IM / Z-Trak weekly for 12 weeks
• http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/040024s022lbl.pdf

Assess iron status per the above guidelines
• IV Iron is acceptable in series with IV Nutrient therapies on the same day
• IV Iron should not be given the same day as any oxidative therapy
Order IV iron if indicated
• Dose at:
  • 100 mg Venofer or 62.5 mg Ferrlecit IV once to twice weekly for 4-8 infusions (based on deficiency).
• Follow up labs:
  • As outlined above
  • Follow Hb/HCT weekly but consider the alterations in labs mentioned above