

## Management of Iron Deficiency Anemia in Cancer and Chemotherapy

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### Summary

- Anemia of cancer and treatment is very common.
  - Anemia of cancer leads to poor quality of life, unnecessary exposure to transfusion risk and may cause delay in treatment.
  - IV iron and ESA are infrequently used due to the safety concerns.
  - IV iron alone or given before ESA may help correct the anemia of malignancy and treatment.
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### Anemia Prevalence and Impact

The prevalence of anemia in cancer is 40% and can exceed 90% for those on treatment.<sup>1,2</sup> Anemia impacts quality of life by contributing to fatigue which is the leading patient reported symptom, can lead to treatment delays and expose patients to unnecessary transfusion risks. Anemia is often untreated or suboptimally treated due to concerns about the safety of both ESA and IV iron.

### Causes of Anemia in Cancer

Cancer associated anemia can be caused by nutritional deficiencies, hemolysis, blood loss, and chemotherapy or radiation induced myelosuppression. The underlying pathophysiology directly related to the malignancy includes:

- Impaired proliferation and differentiation in erythroid precursors
- Blunted erythropoietin response
- Cytokine release
- Impaired iron regulation

This functional iron deficiency results in part from an increased expression of hepcidin with downregulation of iron absorption and impaired recycling of iron from macrophages.<sup>3-4</sup>

### Treatment

The anemia of cancer is very often treated with transfusions without first assessing iron status or considering the use of either IV iron or ESA. Iron deficiency can be absolute (usually related to bleeding) with low iron stores, or functional iron deficiency. Iron-restricted erythropoiesis can occur

when ESA therapy stimulates erythropoiesis without adequate iron delivery from storage sites.<sup>5</sup>

The ESA are effective in increasing hemoglobin levels and decreasing transfusion requirements in chemotherapy – induced anemia but data has linked their use to inferior survival and worse cancer outcomes so are not recommended to be used in anemic cancer patients not on treatment or in whom treatment is given with the intent to cure.<sup>6-7</sup>

### Testing

The most frequently used tests to assess iron status are ferritin and TSAT percentage. When the ferritin is low absolute iron deficiency is present. Because it is an inflammatory biomarker and can be elevated in malignancy a TSAT under 20% suggests functional iron deficiency both of which can be treated with IV iron.<sup>8</sup>

### Oral Versus IV Iron

Although oral iron is more convenient and less expensive it may not be tolerated due to gastrointestinal side effects, may not be absorbed in functional iron deficiency and may be incapable of rapidly repleting iron stores.

There have been multiple clinical trials that have been published using IV iron monotherapy to treat chemotherapy induced anemia (CIA).<sup>9-11</sup> IV iron alone either improved hemoglobin levels, reduced transfusion or both. Any of the current IV iron preparations can be used with relative safety. Minor infusion reactions occur about 1 in 200 infusions with major infusion reactions 1 in 200,000.<sup>12</sup>

# IRON CORNER

## Guidelines

Several organizations have developed recommendations on iron monitoring and replacement in cancer patients.<sup>13</sup> **The National Comprehensive Cancer Network**, (NCCN) recommends monotherapy with iron (preferably IV) for absolute iron deficiency (ferritin <30 ng/mL and transferrin saturation (TS) <20%) and in patients using ESAs with ferritin between 30 and 800 ng/mL and TS between 20 and 50%. IV iron can reduce the number of transfusions in patients with functional iron deficiency.

The **European Society for Medical Oncology** (ESMO) recommends iron profile monitoring. IV iron replacement is recommended in patients with iron deficiency to produce an increment in hemoglobin and reduce the need for transfusion.

The **European Organization for Research and Treatment of Cancer** (EORTC) recommends iron replacement to be restricted to patients with absolute or functional iron deficiency.

## Recommended References

Three review articles that provide summaries to better understand the anemia of cancer and chemotherapy induced anemia are the following:

Gilreath JA and Rodgers GM. How I treat cancer-associated anemia. *Blood* 2020;136 (7):801-813.

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## Additional References

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13. Naoum FA. Iron Deficiency in Cancer Patients. *Rec Bras Hematol Hemoter*. 2106;38(4):325-330

Additional information from [SABM Literature Review and Recommendations: Cancer and Chemotherapy Induced Anemia](#)

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