# The CIROCO study: evaluating the correlation between fatigue and quality of life (QoL) in cancer patients treated with biosimilar epoetin alfa for chemotherapy-induced anemia (CIA)

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## Introduction

- Anemia is frequently observed in cancer patients who are receiving chemotherapy treatment, due to the cytotoxic effects on erythroid precursors in the bone marrow.[1]
- Chemotherapy-induced anemia (CIA) can have a negative impact on patient quality of life (QoL) due to fatigue, cognitive dysfunction, and reduced physical capacity. The most commonly reported symptom of anemia is fatigue, which can occur in >70% of patients.[2]
- The primary aims of anemia management are to reduce or resolve anemia symptoms, in particular fatigue, and to improve QoL, with the minimum invasive therapy.[3]
- Erythropoiesis-stimulating agents (ESAs) have been shown to increase hemoglobin (Hb) levels, reduce the need for blood transfusions, and improve QoL in cancer patients with CIA.[4]
- The most recent European Society for Medical Oncology (ESMO) guidelines recommend ESA therapy in patients with symptomatic anemia who receive chemotherapy or combined radiotherapy-chemotherapy and present with a Hb level of <10 g/dL, as well as in patients with asymptomatic anemia who receive chemotherapy and present with a Hb level <8 g/dL.[3]
- Here we report results from the CIROCO study, which aimed to determine the correlation between fatigue and QoL in cancer patients who were treated with biosimilar epoetin alfa (Sandoz) for CIA.

## Study Design

- CIROCO was a prospective, non-interventional, multicenter study, which included patients from 85 centers in France.
- The key entry criteria included: male and female patients aged >18 years with solid tumors, malignant lymphoma, or multiple myeloma, who were undergoing chemotherapy; with ≥2 cycles of chemotherapy planned after inclusion in the study; presenting with CIA for which biosimilar epoetin alfa (Sandoz) was indicated, and was prescribed to the patient before the decision was made to include them in the study.
- Data were collected on the first day of the chemotherapy cycle (at inclusion; T0), after 2–3 chemotherapy cycles (during follow-up; T1), and following 4–6 chemotherapy cycles (at end of follow-up; T2).
- The primary endpoint was evaluation of the correlation between fatigue (reported by both patient and treating physician) and QoL (patient-reported outcome only) at T0, T1, and T2. Fatigue was measured using a visual analog scale (VAS, range 0–10) and QoL was evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30).
- Secondary endpoints included the concordance between the treating physician's perception of the patient's fatigue and the fatigue felt by the patient.
- The full-analysis set (FAS) population included all patients who met inclusion/exclusion criteria for the study, received ≥1 dose of biosimilar epoetin alfa, completed ≥1 full collection time point (T0, T1, or T2) as defined by the completed electronic case report form, and had analyzable QoL questionnaire and fatigue VAS data, all of which had been validated by the investigator.
- The completers population was a subset of the FAS, which included patients for whom changes in fatigue and QoL (between T0 and T1 or T0 and T2) were collected and analyzable.

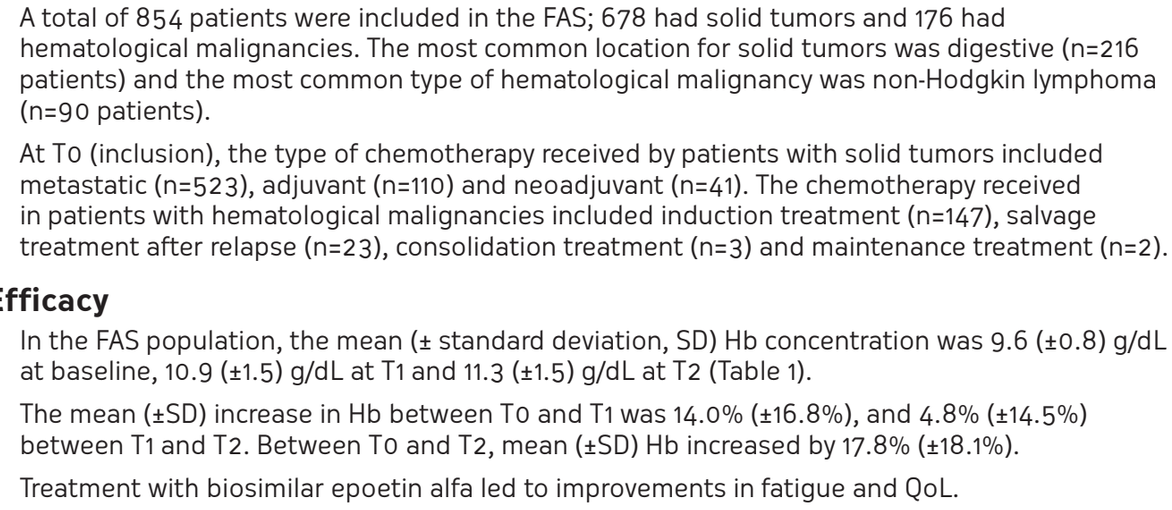
## Results

- A total of 854 patients were included in the FAS; 678 had solid tumors and 176 had hematological malignancies. The most common location for solid tumors was digestive (n=216 patients) and the most common type of hematological malignancy was non-Hodgkin lymphoma (n=90 patients).
- At T0 (inclusion), the type of chemotherapy received by patients with solid tumors included metastatic (n=523), adjuvant (n=110) and neoadjuvant (n=41). The chemotherapy received in patients with hematological malignancies included induction treatment (n=147), salvage treatment after relapse (n=23), consolidation treatment (n=3) and maintenance treatment (n=2).

### Efficacy

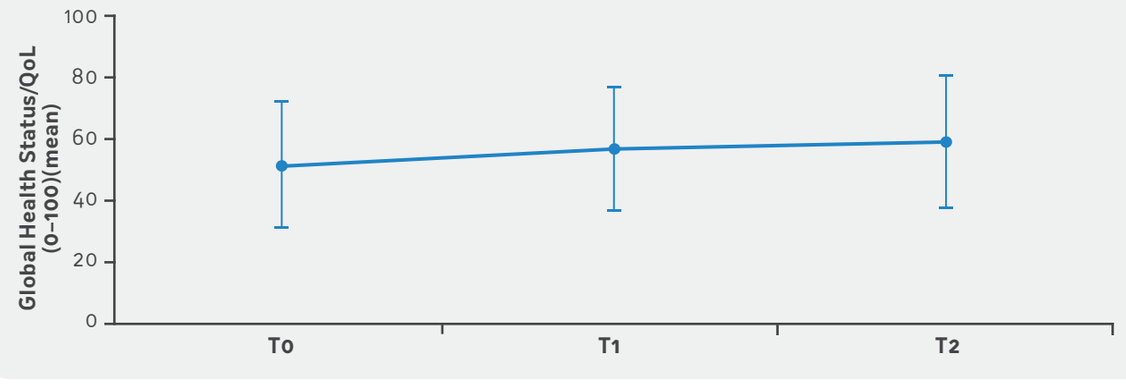
- In the FAS population, the mean (± standard deviation, SD) Hb concentration was 9.6 (±0.8) g/dL at baseline, 10.9 (±1.5) g/dL at T1 and 11.3 (±1.5) g/dL at T2 (Table 1).
- The mean (±SD) increase in Hb between T0 and T1 was 14.0% (±16.8%), and 4.8% (±14.5%) between T1 and T2. Between T0 and T2, mean (±SD) Hb increased by 17.8% (±18.1%).
- Treatment with biosimilar epoetin alfa led to improvements in fatigue and QoL.
  - Between T0 and T2, mean (±SD) relative percentage change in patient-reported and physician-reported fatigue VAS score was -4.4% (±85.9%) and -6.8% (±81.9%), respectively (Figure 1).
  - The mean (± SD) relative improvement in patient-reported QoL between T0 and T2 was 31.3% (±88.7%) (Figure 2).
- The reported improvements in fatigue and QoL can be considered as clinically meaningful, based on previously reported data for the minimal clinically important differences in fatigue VAS score and EORTC QLQ C30.[5–7]

**Figure 1. Mean (SD) patient- and physician-reported VAS scores for fatigue over time (FAS population)**




FAS, full-analysis set; SD, standard deviation; T0, at inclusion; T1, during follow-up; T2, at end of follow-up; VAS, visual analogue scale

**Figure 2. Mean (SD) patient-reported Global Health Status/QoL score over time, assessed using the EORTC QLQ C30 (FAS population)**




EORTC QLQ C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; FAS, full-analysis set; QoL, quality of life; SD, standard deviation; T0, at inclusion; T1, during follow-up; T2, at end of follow-up

- The Pearson correlation co-efficient for fatigue (VAS, range 0–10) and QoL was -0.3876 at T0 (p=0.0152), -0.5399 at T1 (p<0.0001), and -0.6369 at T2 (p<0.0001) (Table 2).
- Assessment of fatigue (mean fatigue VAS score ± SD) by treating physicians was consistent with their patients' perceptions of fatigue at T0 (5.0±2.0 vs 5.3±2.2), T1 (4.3±2.2 vs 4.7±2.3) and T2 (4.0±2.3 vs 4.3±2.4) (Figure 1).
  - The overall concordance of fatigue VAS scores evaluated by patient and by physician was moderate and increased over time: the intra-class correlation coefficient was 0.52 [0.47;0.57] at T0, 0.56 [0.50;0.61] at T1 and 0.66 [0.61;0.71] at T2.

### Safety

- Of the 921 patients in the safety population, 312 (33.9%) reported adverse events (AEs; 748 events) and 23 (2.5%) patients had AEs that were considered related to the study treatment (35 events) (Table 3).
- In total, 347 AEs in 152 (16.5%) patients were considered serious (SAE) (Table 3). The most frequently reported SAEs were disease progression (42 events) and general physical health deterioration (15 events). Treatment-related SAEs were reported in 7 (0.8%) patients (14 events).

**Table 1. Hemoglobin concentration over time (FAS population; n=854)**

| | | Hemoglobin concentration, g/dL | | |
|---|---|---|---|---|
| **Time point** | **n** | **Mean** | **SD** | **Min, Max** |
| **T0 (at inclusion)** | 854 | 9.6 | 0.8 | 6.3, 12.7 |
| **T1 (during follow-up)** | 844 | 10.9 | 1.5 | 5.8, 16.2 |
| **T2 (at the end of follow-up)** | 602 | 11.3 | 1.5 | 6.6, 17.4 |

FAS, full-analysis set; SD, standard deviation.

**Table 2. Pearson correlation coefficient at each timepoint (completers population; n=602)**

| Time point | Pearson correlation coefficient | *p* value |
|---|---|---|
| **T0 (at inclusion)** | -0.3876 | 0.0152 |
| **T1 (during follow-up)** | -0.5399 | <0.0001 |
| **T2 (end of follow-up)** | -0.6369 | <0.0001 |

**Table 3. Summary of adverse events (safety population; n=921)**

| **Total number of patients, n=921** | **Patients** | | **Events** |
|---|---|---|---|
| | **n** | **%** | **n** |
| **Any AE** | 312 | 33.9 | 748 |
| Treatment-related AE | 23 | 2.5 | 35 |
| Serious AE | 152 | 16.5 | 347 |
| Treatment-related SAE | 7 | 0.8 | 14 |
| Treatment-related AE leading to temporary or definitive premature treatment discontinuation | 10 | 1.1 | 13 |
| Death | 55 | 6.0 | |
| Treatment-related death | 0 | 0 | |

AE, adverse event

## Conclusions

- **Treatment of CIA with biosimilar epoetin alfa (Sandoz) in patients with solid tumors and hematological malignancies was well tolerated and effective, leading to improvements in Hb levels, fatigue and QoL.**
- **In these patients, a significant correlation was observed between fatigue and QoL across the observation period.**
- **These results may be useful in clinical practice, as fatigue VAS is simpler and quicker to administer than the EORTC QLQ C30.**

## References

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