Effectiveness and tolerability of ferric carboxymaltose in the correction of cancer- and chemotherapy-associated anaemia – a multicenter observational study

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BACKGROUND

- Iron deficiency (ID) and cancer-related or chemotherapy-induced anaemia are frequent comorbidities in patients with cancer [1-3].
- Iron supplementation, erythropoiesis-stimulating agents (ESAs), blood transfusions and combinations of these are current therapeutic options for the treatment of anaemia [4-6].
- Functional iron deficiency (FID; i.e. transferrin saturation [TSAT] <20% and normal or elevated serum ferritin) can result in low response to ESAs [7].
- Based on clinical evidence [8-13], current anaemia treatment guidelines recommend iron therapy combined with an ESA in patients with FID. In doing so, guidelines acknowledge that oral iron is less effective than intravenous (I.V.) iron [5].
- Furthermore, guidelines aim to minimise blood transfusions and ESA usage [4-6].
- There is growing evidence that I.V. iron treatment even without an ESA can improve Hb levels and reduce blood transfusion requirements [14-16].
- This 12-week observational study evaluated the effectiveness and tolerability of ferric carboxymaltose (FCM, Vifor Pharma, Switzerland) in routine treatment of unselected anaemic cancer patients with absolute or functional ID.

PATIENTS AND METHODS

- Adult cancer patients assigned to FCM treatment for anaemia were enrolled from December 2008 to July 2010 at 68 haematology/oncology practices in Germany.
- Patients were observed weekly until the end of the study (EOS) at 12-14 weeks.
- FCM was administered without restriction on timing, dosing, use of ESAs or transfusions.
- Patients receiving at least one FCM dose were evaluated for safety. Patients with available baseline Hb and at least one follow-up visit were analysed for effectiveness.
- Data collected within four weeks from a transfusion were censored from analysis.
- Primary effectiveness parameter was the Hb increase from baseline to the last visit.
- Secondary effectiveness parameters included Hb levels at each weekly visit and the proportion of patients receiving blood transfusions after the first treatment with FCM.
- Data are shown as median (Q1, Q3) unless otherwise stated.

RESULTS

Baseline patient and disease characteristics

- Of 639 registered patients, 619 received at least one FCM dose (safety population) and 420 patients with baseline Hb taken within 7 days prior or 3 days after the first FCM dose were analysed for effectiveness.
- Median age was 67 years [58, 73], 54.8% were female and 61.0% had metastatic disease.
- Median haematological parameters at baseline were Hb 10.0 g/dL (9.1, 10.6), transferrin saturation (TSAT) 12.1% (7.7, 18.7) and serum ferritin 188 ng/mL (32, 509).
- 37.5% of tested patients in the effectiveness population had ferritin levels below 100 ng/mL and 75.6% a TSAT less than 20% at baseline.
- Most patients (91.2%) in the efficacy population presented with solid tumours (Fig 1).
- 74.3% were receiving cytotoxic chemotherapy; 17.1% did not receive any cancer therapy (Fig 2). 22.1% were on neoadjuvant therapy, 30.2% on 1st-line therapy and 30.5% on 2nd-5th-line therapy.

Fig 1: Tumour types

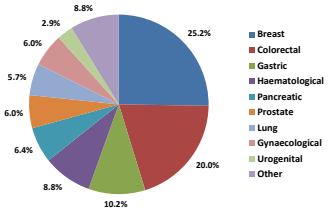
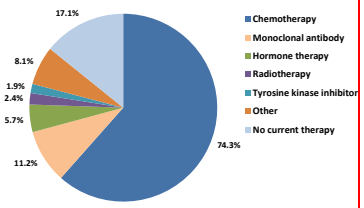


Fig 2: Anti-tumour treatments



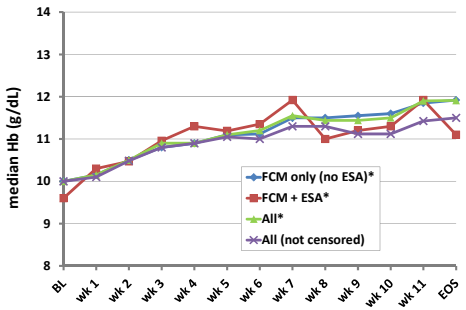
Anti-anaemia treatments

- 24.3% had received prior anti-anaemia therapy (13.1% transfusions, 8.3% ESA, 4.0% iron)
- During the study, 82.6% (n=347) received FCM alone and 17.4% (n=73) received additional ESA-treatment.
- Median total iron dose per patient was 1000 mg (600, 1500 mg).

Effektiveness

- Median Hb increase was comparable and significant vs. baseline (p≤0.0001) for patients that received FCM as sole anaemia therapy (1.4 g/dL [0.2, 2.3]) and those that received a combination of FCM and an ESA (1.6 g/dL [0.7, 2.4]. Median Hb increase was equal among patients who were censored for transfusions and those who were not (All *censored* 1.4 g/dL [0.3, 2.3]; All *not censored* 1.4 g/dL [0.2, 2.3]).

Fig 3: Similar increase in Hb levels of FCM-treated patients with or without concomitant ESA

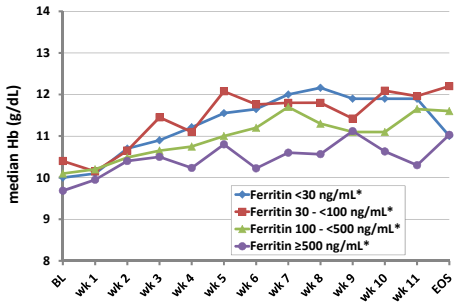


n at baseline:
277 FCM only , 51 FCM + ESA, 328 All, 420 All (not censored)

* Data series are censored for transfusions (see methods)

- Median Hb levels increased steadily after first FCM administration. From week 5 onwards, median Hb levels remained stable in the range of 11-12 g/dL.
- Comparable Hb levels were reached in patients treated with FCM only and FCM+ESA.
- Median increase in Hb levels was similar in the overall population (1.4 g/dL [0.2, 2.3]) and patients censored for transfusions during the study (1.4 g/dL [0.3, 2.3]).

Fig 4: Hb improvement in patients with low and elevated ferritin levels



n at baseline:
65 Ferritin <30, 29 Ferritin 30-100, 92 Ferritin 100-500, 60 Ferritin >500

* Data series are censored for transfusions (see methods)

- Patients with baseline ferritin levels <100 ng/mL achieved Hb levels >11 g/dL earlier (week 3-4) than those with higher (100 - <500 ng/mL) baseline ferritin levels (week 7).
- In patients with very high ferritin levels (≥ 500 ng/mL), Hb levels increased slowly suggesting that other factors (e.g. impaired erythropoietin production) in addition to low iron availability may have limited erythropoiesis in these patients.

Tab 1: Transfused patients (%)

	FCM (N=347)	FCM+ESA (N=73)
4 weeks prior FCM	42 (12%)	13 (18%)
Baseline Hb g/dL (Q1,Q3)	10.0 (9.4,10.7)	9.6 (8.9,10.4)
wk 1-4 post FCM	41 (12%)	17 (23%)
After wk 4 post FCM	25 (7%)	8 (11%)

- The proportion of patients requiring transfusions decreased from 14% during weeks 1-4 after the first FCM-dose to 9% during weeks 5 -12 (Tab 2)

Tolerability

- FCM was well tolerated. Possibly or probably drug-related adverse events (AEs), mainly nausea and diarrhoea, were reported for 2.3% (n=14) of patients.
- Three serious AEs comprised one fatal case after a possibly related respiratory insufficiency and two unlikely related events of tachycardia and dyspnoea.

CONCLUSIONS

- **FCM significantly increased and stabilised median Hb levels at 11-12 g/dL after week 5 in the routine treatment of anaemic cancer patients**
- **The study results suggest a role for I.V. iron alone in the correction of anaemia in cancer patients with absolute or functional iron deficiency**

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