Synopsis

Name of Sponsor: GlobiFer International bvba **Name of Finished Product:** GlobiFer Forte **Name of Active Ingredient:** *Iron integrated haemolysed haemoglobin powderequal to 18 mg Fe++*	**Individual Study Table Referring to Part of the Dossier** **Volume:** **Page:**	**(For National Authority Use only)**

Title of Study:
The effectiveness and tolerability of Globifer Forte (haem iron) tablets compared to ferrous sulphate tablets in inflammatory bowel disease: a randomised controlled trial.

Investigators:

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Study centers:
2 study centers in the United Kingdom

Publication (reference):

Study period: **Date of first enrolment:** 19/05/2011 **Date of last completion:** 06/05/2015	**Phase of development:** II

Objectives:
To investigate if oral haem iron supplementation is more effective and better tolerated than non-haem iron in patients with inflammatory bowel disease over 12 weeks

Methodology:
multicenter, randomized, open

Number of patients (planned and analysed):
planned size: 80 patients (80 in each treatment group)
randomized: 22 patients (11 GlobiFer Forte treated vs. 11 ferrous sulphate treated)

In total only 21 patients were enrolled until termination of the entire study due to unscheduled slow recruitment.
Premature study termination occurred in 4/21 patients. One patient terminated the study before week 4, 2 patients terminated the study before week 12 and one patient between week 12 and 24.

Diagnosis and main criteria for inclusion:
Adults patients with established inactive or mild to moderately active IBD. This is defined for patients with Crohn's disease as CDAI≤220. For patients with ulcerative colitis a Simple Clinical Colitis Activity Index score of ≤8 defines inactive or mild-moderately active disease.
Patients with a haemoglobin level at least 1g/dl below the sex specific lowest normal value (i.e. 13g/dl for men and 12g/dl for women; and either mean cell volume (MCV) ≤ 80 fl or ferritin ≤100 µg/l or transferrin saturation <20% will be considered as having iron deficiency anaemia and offered iron intervention.

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Test product, dosage and mode of administration, batch-number:
GlobiFer Forte (active ingredient: Iron integrated haemolysed haemoglobin powderequal to 18 mg Fe++/tablet) was supplied as 900 mg tablets for oral intake twice daily with sufficient liquid.
Batch Nos.: 911183, 102029, 320030, 320030, 420010

Reference therapy, dose and mode of administration, batch number:
Ferrous sulphate was supplied as 200 mg tablets for oral intake twice daily with sufficient liquid. In addition.
Batch Nos.: FL2061, FM28, FM66, FT6, FT30, FT25

Duration of treatment:
12 weeks of therapy followed by 12 weeks observation period

Criteria for evaluation:

Efficacy
Primary criteria: Proportion of patients in each of the patient groups who achieve a 1g/dl increase in haemoglobin over baseline at 12 weeks.

Secondary criteria were the following:

- Proportion of patients in the GlobiFer Forte group sustaining the 1g/dl increase in haemoglobin (baseline to 12 weeks) at week 24
- Arithmetic meaning of the compliance to the trial medication
- Arithmetic meaning of the difference in the scores CAI (colitis ulcerosa patients) and CDAI (crohn's disease patients) over baseline at 12 weeks
- Average of the haemoglobin increase in each of the patient groups over baseline at 12 weeks in both groups
- Proportion of patients in each of the patient groups with an effect on the colonic microbiota

Safety :
The main safety variables were the incidence and the severity of possible or probable adverse events and evaluation of laboratory tests.

Statistical methods:
The study was stopped due to unscheduled low recruitment. Due to the inhomogeneity of the patient population and the very low number of patients no statistical analysis was performed.

SUMMARY

EFFICACY RESULTS:

Due to the inhomogeneity of the patient population and the very low number of patients no statistical analysis was performed.

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SAFETY RESULTS:

The analysis considered all events as documented in the CRFs.

Adverse events occurred in 11/11 (100%; GlobiFer Forte) and 8/10 patients (80%; Ferrous sulphate). The event most frequently concerned the gastrointestinal system affecting 7 patient (64%; GlobiFer Forte) and 8 patients (80%; Ferrous sulphate); mainly Diarrhoea, vomiting, colitis ulcerative and constipation.

Of 21 patients enrolled 11/11 (100%; GlobiFer Forte) and 8/10 patients (80%; Ferrous sulphate) had not related adverse events. Of 21 patients enrolled 3/11 (27.3%; GlobiFer Forte) and 0/10 patients (0%; ferrous sulphate) had possible related adverse events. Of 21 patients enrolled 0/11 (0%; GlobiFer Forte) and 3/10 patients (30%; ferrous sulphate) had probable related adverse events (diarrhoea, flatulence and abdominal discomfort). One patient of the Ferrous sulphate group had two probable related adverse events. All other patients with possible or probable related adverse events had in each case one event.

No patient died in the study and no serious events were detected. The laboratory results indicated no specific risks.

CONCLUSION:

The small number of patients and the inhomogeneous data situation does not allow a statement to compare the efficacy of the two drugs. Nevertheless GlobiFer Forte seems to be better tolerated than ferrous sulphate. In the GlobiFer Forte group, 27.3% of the patients had possible related adverse events. On the other hand, in the ferrous sulphate group 30% of the patients had probable related adverse events, although patients not tolerating ferrous sulphate were not in the trial due to the exclusion criteria.

Date of the report: March 1, 2016