Ferumoxytol (Rienso): new intravenous iron preparation

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Ferumoxytol (Rienso) is a new intravenous iron formulation for the treatment of iron-deficiency anaemia in chronic kidney disease. In our New products review, Steve Chaplin presents the clinical data relating to its efficacy and adverse events and Dr Matthew Brookes discusses its place in the treatment of iron-deficiency anaemia.

The National Institute for Health and Care Excellence (NICE) recommends correction of anaemia and maintenance iron therapy in patients with anaemia due to chronic kidney disease. Parenteral iron is recommended for patients with functional iron deficiency and when oral iron is ineffective, and will be required by patients on haemodialysis.

The introduction of ferumoxytol (Rienso) brings to five the number of iron formulations for intravenous administration in the UK; the others are ferric carboxymaltose (Ferinject), iron dextran (CosmoFer), iron isomaltoside (Monofer) and iron sucrose (Venofer).

The technology

Ferumoxytol is a colloidal iron-carbohydrate complex that releases iron following uptake by the reticuloendothelial system. Iron then either enters the intracellular iron pool or is transported to erythroid precursor cells for incorporation into haemoglobin.

Ferumoxytol is licensed for the intravenous treatment of iron-deficiency anaemia in adults with chronic kidney disease. The dose is administered as an undiluted intravenous injection over a minimum of 17 seconds. Patients should be monitored for signs and symptoms of hypotension and/or hypersensitivity for at least 30 minutes.

A course of treatment comprises either 510mg or 1020mg according to the patient’s pretreatment haemoglobin and body weight (see SPC for further details). For patients receiving two doses, the second injection is to be administered two to eight days later.

Ferumoxytol should not be administered when haemoglobin is >12g per dl, serum transferrin saturation is >50 per cent or ferritin is >800ng per ml. Haematological and blood iron parameters should be reassessed at least one month after the completion of treatment.

There is little experience of long-term use or treatment in patients with hepatic impairment, for whom the risks and benefits should be considered individually. Treatment is contraindicated in patients with hypersensitivity to any iron preparation, iron overload and anaemia not due to iron deficiency.

KEY POINTS

- Ferumoxytol is a colloidal iron-carbohydrate complex for the treatment of iron-deficiency anaemia in adults with chronic kidney disease
- It is administered by bolus intravenous injection; a course of treatment comprises one 510mg injection or two injections given 2–8 days apart; NHS cost £65 per 510mg injection
- In clinical trials, ferumoxytol increased haemoglobin by more than a short (21 days) course of oral iron in haemodialysis and nondialysis patients
- It has not been compared with another parenteral iron preparation in a published clinical trial
- Ferumoxytol is associated with fewer adverse gastrointestinal effects than oral iron and fewer adverse reactions leading to treatment discontinuation
- Ferumoxytol increases the choice of safe and effective intravenous iron treatments in patients with chronic kidney disease
Table 1. Primary end-point and proportion of responders in phase 3 trials of ferumoxytol

<table>
<thead>
<tr>
<th>End-point</th>
<th>Nondialysis</th>
<th>Haemodialysis</th>
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<tr>
<td></td>
<td>F (n=228)</td>
<td>oral iron (n=76)</td>
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<tr>
<td>Baseline Hgb (mean ± SD, g/dl)</td>
<td>10.0 ± 0.7</td>
<td>9.9 ± 0.8</td>
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<tr>
<td>Hgb change from baseline at day 35 (mean ± SD, g/dl)</td>
<td>0.8* ± 1.2</td>
<td>0.2 ± 1.0</td>
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<tr>
<td>Proportion of Hgb responders (%)</td>
<td>39</td>
<td>18</td>
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F = ferumoxytol  
Hgb = haemoglobin  
Responder = proportion of subjects with an increase in Hgb of ≥1.0 g/dl  
*p<0.001

Clinical trials
Three nonblinded trials of similar design, including one in patients undergoing haemodialysis, have compared ferumoxytol with oral iron. The total of 944 participants (mean age 60–70) with anaemia (Hgb <11 or <11.5 g per dl; transferrin saturation ≤30 per cent and ferritin ≤600 ng per ml) were randomised to treatment with ferrous fumarate (equivalent to 200 mg elemental iron per day) for 21 days or ferumoxytol (two 510 mg doses two to eight days apart). Between 36 and 44 per cent of patients not undergoing dialysis and all patients on dialysis were taking a stable dose of an erythropoiesis-stimulating agent (ESA). The primary end-point was the change in haemoglobin at day 35.

The increase in haemoglobin was significantly greater in patients treated with ferumoxytol; this was matched by increases in serum ferritin and transferrin saturation (see Table 1). The proportion of patients with an increase in haemoglobin of at least 1 g per dl was 39–52 per cent with ferumoxytol and 18–25 per cent with oral iron.

The duration of oral iron treatment was too short to establish the maximum effect of oral iron therapy and patients on haemodialysis normally require parenteral administration. However, the increase in haemoglobin levels was consistent with the range reported in published studies.

Ferumoxytol was more effective than oral iron regardless of ESA use, though the increase in haemoglobin was greater in patients taking an ESA. In one study, the increase in haemoglobin was only slightly lower with oral iron + ESA (0.86 g per dl) than with ferumoxytol without ESA (0.91 g per dl).

Patients from either treatment arm who continued to meet the eligibility criteria after the first five weeks could enter an optional nonrandomised extension phase and receive two 510 mg doses of ferumoxytol. Ferumoxytol further increased haemoglobin by approximately one- to two-thirds compared with oral iron.

Observational data from 8666 patients followed up for up to 12 months, of whom half received more than one dose, suggest that ferumoxytol maintained haemoglobin within the target range 10–12 g per dl in 50–80 per cent of patients.

Adverse effects
In clinical trials, ferumoxytol was associated with significantly fewer adverse gastrointestinal effects than oral iron, including diarrhoea (4.0 vs 8.2 per cent), nausea (3.1 vs 7.5 per cent) and constipation (2.1 vs 5.7 per cent). It was associated with a higher frequency of back pain (1.0 per cent vs none) and hypotension (2.5 vs 0.4 per cent). There were fewer adverse events leading to treatment discontinuation in patients treated with ferumoxytol.

References

Declaration of interests
None to declare.

Steve Chaplin is a pharmacist who specialise in writing on therapeutics

Place in therapy
The use of parenteral iron products has found increasing favour in recent years for the management of iron-deficiency states where enteral iron supplementation is either ineffective or intolerable or where the anaemia is clinically significant. Intolerance to oral iron products is a particular problem due to gastrointestinal side-effects that can be reported in up to 43 per cent of patients.

Ferumoxytol is a new intravenous iron preparation containing a superparamagnetic iron oxide coated with a carbohydrate shell. Older intravenous iron products – iron dextran and iron sucrose – have been associated with variable levels of toxicity that can limit their use and, in particular, their rate of administration. These constraints have made the use of these preparations both inconvenient and time consuming in clinical practice.
In recent years a number of newer intravenous iron preparations have emerged with better safety profiles, enabling larger doses to be administered more rapidly. These include ferric carboxymaltose and iron isomaltoside 1000. There is now early clinical trial data to support the use of these newer agents in a number of iron deficiency-associated conditions including chronic kidney disease (CKD), inflammatory bowel disease and preoperative anaemia.

More recently three open-label, controlled clinical trials have shown ferumoxytol to be safe and efficacious compared to oral iron in adult patients with iron-deficiency anaemia and CKD.

To date it appears that the safety profile of ferumoxytol and the other newer intravenous iron preparations is good, but there is a need for long-term postmarketing data to evaluate the occurrence of rare or chronic adverse events. Head-to-head clinical trials are also needed to compare the efficacy of ferumoxytol with ferric carboxymaltose and iron isomaltoside 1000 in a number of different clinical states associated with iron-deficiency anaemia.

References

Declaration of interests
Dr Brookes has received honoraria and a research grant from Vifor International.

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