Intravenous iron for the treatment of iron deficiency anemia in China: a patient-level simulation model and cost-utility analysis comparing ferric derisomaltose with iron sucrose

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ABSTRACT

Objectives: Two intravenous (IV) iron formulations, ferric derisomaltose (FDI) and iron sucrose (IS), are currently available for the treatment of iron deficiency anemia (IDA) in China. Clinical studies have demonstrated that FDI has an improved efficacy and safety profile versus IS, while requiring fewer infusions to correct iron deficits. Based on these findings, the present study evaluated the costs and benefits of FDI and IS for the treatment of IDA, from a healthcare system and societal perspective in China.

Methods: A patient-level model was developed to project time to hematological response and incidence of cardiovascular adverse events and hypersensitivity reactions (HSRs) associated with FDI and IS over 5 years. Costs included iron acquisition, administration, and adverse event/HSR treatment costs, based on published studies, fee schedules, and a physician survey. Health state utilities associated with adverse events, HSRs, and the number of infusions were obtained from the literature and a time trade-off survey.

Results: From a healthcare system perspective, FDI was associated with incremental costs of RMB 1,934 (purchasing power parity USD 462) and incremental quality-adjusted life expectancy of 0.078 quality-adjusted life-years (QALYs) versus IS, yielding an incremental cost-utility ratio of RMB 24,901 (USD 5,949) in the base case scenario. From a societal perspective, FDI was associated with reduced total costs and therefore dominant versus IS.

Limitations: Limitations included the absence of clinical data specific to China and insufficient data to model persistence with treatment.

Conclusions: This was the first cost-utility analysis comparing FDI and IS for the treatment of IDA in China. Based on a patient-level model, FDI was found to improve quality of life and reduce administration and adverse events costs relative to IS. Using the 2020 Chinese gross domestic product per capita of RMB 72,447 (USD 17,307) as a cost-effectiveness threshold, FDI would be considered cost-effective in China.

PLAIN LANGUAGE SUMMARY

Ferric derisomaltose (FDI) was approved in February 2021 for the treatment of iron deficiency anemia (IDA) in China and allows for fast iron correction in one visit with a good safety profile. The current standard of care in China is iron sucrose (IS). Clinical and economic decision-making can benefit from having longer-term projections on the benefits and costs of new medications relative to the current standard of care, which is why we conducted the first cost-utility analysis of FDI and IS for China. We developed a patient-level model that captured the effects of the iron formulations on IDA, in addition to incidences of adverse events and hypersensitivity reactions (HSRs) associated with either formulation. Costs of the iron formulations, their administration, and of treatments for adverse events and HSR were modeled alongside the quality of life effects of IDA, adverse events, HSRs, and iron infusions. We used published clinical data and Chinese cost data to inform our model. Our results show that FDI was associated with higher quality-adjusted life expectancy than IS, regardless of the perspective of the analysis, and higher total costs from the healthcare system perspective. From a societal perspective, FDI was associated with lower costs due to reduced travel and waiting time and smaller productivity losses given there were fewer appointments. These results imply that FDI is likely good value for money for the healthcare system and indeed cost-saving for society relative to IS, which has so far been the most widely used IV iron treatment in China.
**Introduction**

Despite substantial improvements in recent decades, anemia and iron deficiency anemia (IDA) remains prevalent in China, with an estimated 282 million anemia cases, of which approximately 176 million are due to IDA. Chinese women of reproductive age are particularly at risk. A nationwide study of pregnant women in 2016 estimated the prevalence of anemia and IDA to be 19.8% and 13.9%, respectively. In a longitudinal study in southwest China, the overall anemia prevalence in women of reproductive age who had been or intended to become pregnant was 16.4% in 2018 (23.0% in 2014). In women of reproductive age living in Shanghai, the prevalence of IDA was 14.8%.

The burden of anemia and IDA in China is increasingly studied among elderly and chronically ill people. Chronic kidney disease (CKD) and its association with anemia have become a particular concern, given a CKD prevalence of nearly two-thirds of patients with Hb levels <10 g/dL and that patients’ quality of life (QoL) was reduced as levels of hemoglobin decreased. More severe anemia has also been suggested to impair work productivity in Chinese patients with CKD.

Anemia and IDA also are frequently encountered challenges in managing patients with cancer and those undergoing surgery. Huang et al. showed that, in Chinese patients undergoing treatment for non-small cell lung cancer, pre-treatment anemia was associated with a reduction of 6.9 months in median overall survival and an increase in the risk of death by 60% relative to no pre-treatment anemia. Anemia is also a frequent complication following major surgery, for cancer and other diseases. Lin et al. reported that 28% of patients had preoperative anemia and that preoperative hemoglobin levels of less than 130 g/L were associated with increased length of hospital stay and hospital costs.

Iron administration is an important therapeutic option to meet the outlined burden imposed by anemia and IDA. Oral iron is widely used for iron supplementation, including in China, but its frequent association with gastrointestinal side effects and relatively low effectiveness make it a suboptimal choice if patients have chronic inflammatory diseases, if an iron deficit is substantial, or if an iron deficit requires rapid correction, including in perioperative settings.

In these scenarios, intravenous (IV) iron is likely preferable as IV iron can correct iron deficits safely and rapidly, and the benefits of IV iron are documented across conditions and settings. IV iron is more effective in resolving pre-treatment anemia and iron deficiency than oral iron, and there is evidence to suggest that IV iron increases hemoglobin levels relative to placebo and oral iron before major surgery and in the treatment of chemotherapy-induced anemia. Despite the availability of effective IV iron treatment, anemia and IDA are often not managed appropriately. In China, only an estimated 20% of patients with mild and 50% of patients with severe anemia receive treatment. In C-STRIDE, nearly two-thirds of patients with Hb levels <10 g/dL did not receive anemia treatment, while only 1.4% and 2.0% of patients with non-dialysis-dependent and dialysis-dependent CKD, respectively, received intravenous (IV) iron for anemia attributed to iron deficiency (ID). Non-dialysis-dependent patients with CKD in Shanghai mostly (73%) received no iron supplementation at all, and only 8.2% achieved the treatment target of 11–12 g/dL. Similar data were reported by Zhou et al., for dialysis-dependent patients with CKD from nine major dialysis facilities across China, of whom 60% failed to reach a target hemoglobin level of 11 g/dL, despite 85% of patients receiving treatment with erythropoietin and 40% receiving oral iron (only 20% received IV iron). This is mirrored in a recent patient survey by Hao et al., in which only 26% of patients with CKD and anemia reported receiving injections (either erythropoietin-stimulating agents or intravenous infusions), while 69% reported receiving dietary advice, 64% reported iron supplements, and 53% reported oral iron treatment for their anemia. Overall, 41% of patients with CKD and anemia reported receiving no treatment for anemia.

The treatment of ID and anemia in China could likely be improved by moving from oral to IV iron in a range of clinical contexts. However, as pointed out by Li and Zhang, the use of traditional IV iron formulations in China is unsatisfactory as multiple infusions are required to correct iron deficits, thereby increasing the risk of patient non-adherence to treatment, and given concerns around the safety of IV iron, including fear of hypersensitivity reactions (HSR).

For IV iron sucrose (IS) – the current standard IV iron formulation used in China – safety concerns limit the administration of IS to 200 mg per infusion and at most three infusions per week, so iron deficit correction requires several visits to a healthcare provider. In contrast, ferric derisomaltose (FDI), which was recently approved in China, is associated with a more rapid and more marked hematological response than iron sucrose, and FDI allows for a single-dose correction of iron deficits as it can be dosed at up to 20 mg per kilogram of body weight. FDI, therefore, reduces the need for repeat visits and the risk of non-adherence associated with longer-term treatment. Relative to iron sucrose, FDI is also associated with a lower incidence of HSRs.

Differences such as these between FDI and IS, when combined with cost and quality of life data, should be modeled in cost-utility analyses (CUA) to inform clinical and reimbursement decision-making; however, no such analyses have yet been conducted in China. The present study, therefore, aimed to evaluate, in the Chinese setting, the cost-utility of FDI relative to IS, for the treatment of patients with IDA.

**Methods**

A Consolidated Health Economic Evaluation Reporting Standards 2022 checklist for this study can be found in Supplementary Table 1.

**Supporting studies**

Prior to commencing the development of the cost-utility model, two supporting studies were conducted to inform
the model development and generate data not otherwise available. The first supporting study was an expert survey of nine senior physicians from disciplines reflecting key etiologies of chronic and acute IDA, including hematology, nephrology, gynecology, obstetrics, and orthopedics. All physicians were affiliated with tertiary (AAA) hospitals, and hospitals were chosen from across China (Supplementary Table 2). Physicians completed a questionnaire covering epidemiological data and the IDA treatment pathway, including patient characteristics, IDA recurrence, and treatment persistence, as well as resource use and costs, including time and cost per infusion, length and cost of inpatient stay, and outpatient procedures and tests.

The second supporting study was a time trade-off (TTO) study, implemented as an online questionnaire in a general Chinese population sample, designed to elicit preferences for and utilities associated with the number, duration, and risk of IV iron infusions. Briefly, participants were presented with health state vignettes that combined treatment process attributes (1, 2, 5, or 7 infusions per year; infusion duration of 15–30 min or 30–60 min) and risk (no versus 1/1,000 risk of long-term adverse events). Disutilities for infusion numbers not directly included in vignettes (e.g. four infusions) were derived using non-linear regression analysis.

**Model structure**

The model was structured as a patient-level, discrete-time, illness-death model, implemented in Microsoft Excel (Microsoft, Redmond, WA, USA). A patient-level framework for modeling IV iron was used previously in a CUA for the United Kingdom and is aligned with National Institute for Health and Care Excellence technical guidance, which recommends patient-level simulations for non-linear relationships between patient characteristics and model outcomes, as is the case for the relationship between baseline body weight, hemoglobin levels, and iron demand. The framework also facilitated probabilistic modeling to account for stochastic (or first-order) uncertainty, uncertainty around model parameters (second-order uncertainty), and heterogeneity in patient characteristics.

Modeled patients were assigned initial age, body weight, and Hb values sampled from baseline distributions. Based on these characteristics, a mean iron need was determined, and the required number of treatment courses was calculated for each patient in each cycle (Figure 1). Chronic IDA etiologies were distinguished from non-chronic etiologies, with the latter requiring a single treatment course. From the infusions administered per cycle, the hematologic response (change in Hb levels), anemia-related QoL, and infusion-related costs were modeled. In addition, the model accounted for the incidence of post-infusion events, namely cardiovascular (CV) events and HSRs, as well as the costs and QoL impact of these events. Patient trajectories were evaluated using Monte Carlo methods, with costs and QoL outcomes aggregated per cycle.

Survival and quality-adjusted life expectancy (QALE; expressed as quality-adjusted life-years, QALYs), as well as cost outcomes, were summarized across modeled patients for each formulation and combined to yield an incremental cost-utility ratio (ICUR).

**Patient characteristics**

Baseline patient age, body weight, and pre-treatment hemoglobin levels were sourced from publicly available data from a randomized controlled trial (RCT; NCT03591406) comparing ferric carboxymaltose (FCM) with IS for the treatment of IDA in China (Table 1). These data had been validated in the above-described physician survey to reflect the target

![Figure 1. Schematic for a cost-utility model.](image-url)
population, including broad eligibility criteria covering a range of etiologies. The proportion of patients with chronic (as opposed to non-chronic) etiology of IDA was estimated to be 63.95% based on an analysis of prescription data covering 146 hospitals in nine locations, including Guangzhou and Shanghai\(^{31}\). The proportion of patients receiving IV iron as outpatients (as opposed to inpatients) was taken to be 15.3% based on the same data source. Median times to symptom recurrence and retreatment in patients with chronic IDA were assumed to be 10 and 16 months, respectively (a repeat IV iron course was assumed to start if retreatment became necessary)\(^{32}\). Background mortality was modeled using data from 2019 Chinese life tables\(^{33}\).

**Clinical data**

Data informing the clinical effectiveness and safety estimates used in the model were sourced preferentially from RCTs. Trials were identified from a 2019 systematic literature review that conducted an indirect treatment comparison of FDI and ferric carboxymaltose via iron sucrose\(^{34}\) and a 2020 network meta-analysis on the risk of hypophosphatemia following IV iron\(^{15}\) with incremental literature search updates performed in PubMed (including MEDLINE) in October 2021 to identify any newly published RCTs.

The effectiveness of FDI versus IS was modeled as the time to hematological response (Hb increase $\geq 2$ g/dL from baseline), based on the PROVIDE RCT (NCT02130063), which was the only available RCT in patients with IDA of different etiologies. The proportion with a hematological response at different time points was assumed to achieve a fixed target hemoglobin level after a set period, as different target levels are used in the literature and in clinical practice in China for different patient population with IDA\(^{7,20,21}\) and because response proportions over time are naturally suited to modeling efficacy as time in the model progresses. Data from PROVIDE showed a faster response with FDI than IS over the first 5 weeks (Supplementary Table 3). Beyond 5 weeks, response proportions were assumed to remain at their 5-week value for FDI and IS, respectively.

The incidence of CV events was sourced from two safety-focused RCTs comparing FDI and IS, namely the FERWON-IDA\(^{23}\) and FERWON-NFHPRO\(^{36}\) studies (Supplementary Table 4), as the PROVIDE trial did not report detailed CV events. The HSR incidence was taken from an indirect comparison study including FDI and IS\(^{26}\) (Supplementary Table 4).

**Resource use**

The number of infusions per treatment course was calculated from baseline body weight and hemoglobin values as per the respective label insert. A simplified table approach could therefore be used for FDI (see Supplementary Table 5), while the more complex Ganzoni formula had to be used to determine the iron need for IS\(^{24}\).

Assumptions around in- and outpatient resource utilization and laboratory tests were informed by the supporting physician survey. As most IV iron administrations are performed in inpatient settings, the mean number of days in the hospital per administration was elicited from the survey (Supplementary Table 6). The mean number of hospital days was calculated from physicians’ estimates as 1.27 for FDI and 1.36 for IS due to FDI’s improved safety profile and smaller risk of adverse events. Similarly, fewer outpatient visits and laboratory tests (routine blood, ferritin, and serum iron) were required per treatment course with FDI.

Productivity losses resulting from hospitalization, consultation, and travel were calculated for the patient and one caregiver accompanying the patient. An 8-hour working day was assumed. Surveyed physicians estimated that, on average, traveling to the treatment location was associated with a 1-hour one-way trip, while an outpatient visit was estimated to last 4 h. An inpatient stay was assumed to take up all working hours in a day for the patient, with no caregiver time required. Productivity losses were weighted by the proportion of patients and caregivers in employment in each age group, using labor force participation rates published by the National Bureau of Statistics (NBS).

**Costs**

Costs were expressed in 2021 Renminbi (RMB), with cost-related model results also presented as US dollars (USD) following conversion using the 2020 purchasing power parity for RMB relative to USD by the Organisation for Economic Co-operation and Development\(^{37}\).

The cost of FDI was obtained from the national insurance tariff (1 mL containing 100 mg of FDI at a cost of RMB 192.5), for a unit cost of RMB 1.93 per mg. The cost of IS was obtained from public drug procurement platforms for the originator IS (5 mL containing 100 mg of IS at a cost of RMB 84.95). An alternative cost for use in a scenario analysis was calculated as the market share-weighted average cost of the originator and generic IS products, at RMB 42.1, with market shares obtained from the IQVIA Drug Sales database.

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**Table 1. Baseline population characteristics and disease parameters.**

| Item                                              | Baseline value | Source                                                                 |
|---------------------------------------------------|----------------|------------------------------------------------------------------------|
| Baseline mean (SD) age, years                      | 39.40 (9.31)   | Randomized controlled trial comparing ferric carboxymaltose and iron sucrose for treatment of IDA in China (NCT03591406) and validated in physician survey |
| Baseline mean (SD) body weight, kg                 | 60.07 (12.0)   | Analysis of prescription database covering 146 hospitals in nine locations |
| Pre-treatment mean (SD) hemoglobin level, g/dL     | 7.90 (1.48)    | Kulnigg et al.\(^{32}\)                                                |
| Patients with chronic IDA etiology, %             | 63.95          | Analysis of prescription database covering 146 hospitals in nine locations |
| IV iron received during outpatient procedure, %   | 15.30          | Analysis of prescription database covering 146 hospitals in nine locations |
| Median time to IDA recurrence, months              | 10             | Kulnigg et al.\(^{32}\)                                                |
| Median (SD) time to iron retreatment in chronic IDA, months | 16.00 (4.34) | Analysis of prescription database covering 146 hospitals in nine locations |

Abbreviations: IDA, Iron Deficiency Anemia; SD, Standard Deviation.
IV infusion administration costs consisted of service and equipment charges. The former was RMB 11.66 per administration, based on the median of public medical service fees in Beijing, Guangzhou, Shanghai, Shenzhen, and Xiamen; the latter was RMB 22.00 from a public hospital procurement platform, for a total per-administration fee of RMB 33.66 (Table 2). The daily cost of an inpatient stay, the cost per outpatient visit and laboratory test costs were obtained as the respective median public list price from the same five cities as above. Treatment costs of adverse events were obtained from the physician survey, the NBS, and the literature.

These costs were used to model cost-utility outcomes from both a healthcare system perspective, which excluded transportation costs and productivity losses, and a societal perspective, which included all costs and productivity losses listed above.

### Health state utilities

The baseline health state utility (HSU) value for patients with IDA was the general Chinese population mean of 0.9854, to which an IDA-specific utility decrement of 0.1547 was applied in line with a previous pharmacoeconomic evaluation of FDI conducted for the Canadian Agency for Drugs and Technologies in Health. The annual per-infusion disutility was derived from a non-linear regression applied to the supporting TTO survey (see subsection on Supporting studies) and calculated to be 0.0161. Utility decrements associated with CV events and HSR were derived from the literature (Supplementary Table 4). The treatment costs for adverse events were obtained from the physician survey, the NBS, and the literature.

### Model parameters

The base case analysis was performed over a 5-year time horizon, which was considered sufficient to account for potential IDA relapse. The model was run with a monthly cycle length, which facilitated accurate modeling of multiple treatment courses and adverse events over the course of a year with a reasonable computational burden. Both benefits and costs were discounted at 5% per annum. As there is no formal willingness-to-pay (WTP) threshold in China, cost-utility results were assessed against the gross domestic product (GDP) per capita, which was RMB 72,447 in 2020.

### Scenario and sensitivity analyses

The base case scenario was conducted from a healthcare system perspective, using the originator IS unit cost. A second scenario took the same perspective but used an IS unit cost calculated as the market share-weighted average of the originator and generic IS unit costs. A third scenario took a societal perspective while using the originator IS unit costs. One-way sensitivity analyses were performed to assess the robustness of the model results in changes in input values, including patient baseline characteristics, costs, and utilities. In these analyses, baseline values were varied by ±20%. An additional analysis was conducted in which the difference in
Results

**Base case analyses**

**Survival and QoL**

FDI was associated with an incremental gain in QALE relative to IS (Table 3). The difference of 0.078 QALYs in favor of FDI resulted from reduced anaemia-related QALY loss (−0.572 QALYs with FDI versus −0.614 QALYs with IS) and lower incidence of adverse events and HSRs (−0.002 QALYs with FDI versus −0.003 QALYs with IS). In addition, treatment with FDI was associated with fewer iron infusions per patient (5.7 versus 19.6 infusions over five years), despite delivering more iron per treatment course (1,552.4 versus 1,235.4 mg) relative to IS; infusion-related reductions in QALE were also, therefore, smaller with FDI than IS (−0.057 QALYs versus −0.092 QALYs).

**Cost and cost-utility**

In the base case scenario, FDI was associated with incremental costs of RMB 1,934 (USD 462) relative to IS (Table 3). This difference was due to higher acquisitions costs of FDI (RMB 8,176 [USD 1,953] versus RMB 2,871 [USD 686]), which were partially offset by reduced costs for IV iron administration and treatment of adverse events and HSR (Supplementary Table 7). The increased QALE at increased costs for FDI relative to IS yielded an ICUR of RMB 24,901 (USD 5,949) per QALY gained in the base scenario.

In the alternative scenario using weighted IS unit costs, the total costs of IS were reduced to RMB 6,998 (USD 1,672), yielding a total cost difference of RMB 3,382 (USD 808) relative to FDI. The resulting ICUR was RMB 43,549 (USD 10,403) per QALY gained. In contrast, in the scenario using a societal perspective, FDI was associated with lower total costs relative to IS (RMB 12,396 [USD 2,961] versus RMB 14,258 [USD 3,406]) as direct nonmedical and transportation costs and productivity losses were reduced with FDI (Supplementary Table 7). FDI was therefore dominant as it was associated with improved QALE at lower societal costs relative to IS.

**Sensitivity analyses**

**One-way sensitivity analyses**

In deterministic, one-way sensitivity analyses, FDI acquisition costs and patients’ baseline Hb levels were identified as key drivers of ICURs across all three scenarios (Figure 2). They were followed by IS acquisition costs and daily hospitalization costs in the base case scenario, hospitalization costs and patient’s baseline body weight in the alternative scenario using market share-weighted originator and generic IS costs, and by patients’ baseline body weight and IS acquisition costs in the scenario reporting a societal perspective. Additional drivers of ICURs included patient baseline body weight and age, the proportion of patients with chronic (as opposed to acute) IDA, the median time to retreatment for IDA, and costs of outpatient visits and infusion administrations.

When the hematological response was set to initial values (i.e. to zero) in both arms after 5 weeks, the ICURs were RMB 43,809 (USD 10,466) and RMB 76,618 (USD 18,303) per QALY gained for the base and first alternative scenario, while FDI was dominant over IS in the analysis from a societal perspective.

**Probabilistic sensitivity analysis**

In the PSA around the base case scenario, results from all model iterations fell in the northeast quadrant of the scatter-plot (Supplementary Figure 1), and there was a 100% likelihood that FDI would be cost-effective relative to IS at a WTP threshold.

| Table 3. Cost-utility outcomes, in RMB (and USD) per QALY, for different scenarios over a 5-year time horizon. |
|---|---|---|
| **FDI** | **IS** | **Difference** |
| Life expectancy (years) | 4.965 | 4.965 | 0 |
| Quality-adjusted life expectancy (QALYs) | 3.814 | 3.736 | +0.078 |
| Base scenario: Healthcare system perspective, originator IS unit cost | | | |
| Total costs (RMB) [USD] | 10,380 [2,480] | 8,446 [2,018] | +1,934 [+462] |
| ICUR (RMB [USD] per QALY) | 24,901 [5,949] | 3,406 [-445] |
| Alternative scenario: Healthcare system perspective, market-share weighted unit costs of originator and generic IS | | | |
| Total costs (RMB) [USD] | 10,380 [2,480] | 6,998 [1,672] | +3,382 [+808] |
| ICUR (RMB [USD] per QALY) | 43,549 [10,403] | 43,549 [10,403] |
| Alternative scenario: Societal perspective, originator IS unit cost | | | |
| Total costs (RMB) [USD] | 12,396 [2,961] | 14,258 [3,406] | −1,862 [-445] |
| ICUR (RMB per QALY) | FDI dominant | | |

Abbreviations: FDI, Ferric Derisomaltose; ICUR, Incremental Cost-Utility Ratio; IS, Iron Sucrose; QALY, Quality-Adjusted Life-Year; RMB, Renminbi; USD, United States dollar.

Notes: Survival and cost outcomes are all discounted.
threshold equal to GDP per capita, i.e. RMB 72,477 (USD 17,307) per QALY gained (Figure 3). In the alternative healthcare system scenario that used the market share-weighted originator and generic IS prices, there was also a 100% likelihood of FDI being cost-effective at a WTP threshold of RMB 72,477 (USD 17,307) per QALY gained in the alternative scenario relative to IS from a societal perspective, and that FDI dominated IS from a societal perspective. At the 2020 GDP per capita value of RMB 72,447 (USD 17,307) in China, FDI would therefore likely provide good value for money relative to IS. These findings were aligned with previous analyses for other settings and reflected the improved effectiveness and safety of FDI relative to IS, which resulted in reduced costs and smaller QoL losses due to earlier hematological response as well as due to fewer adverse events and HSR, thereby partially offsetting higher FDI acquisition costs.

In addition, as a higher dose of iron can be delivered with FDI, iron deficits in the model could be corrected with fewer IV administrations than with IS, which further reduced administration costs and infusion-related reductions in QoL, while also saving patients and their caregivers’ time. Such economic benefits might be relatively limited in certain patient groups, such as those regularly undergoing dialysis; however, as current dialysis care in China is unable to meet IDA treatment needs, there are still likely to be economic benefits of using a more efficacious treatment that requires fewer administrations.

The physician survey and the TTO study conducted to inform model development confirmed the notion that an IV iron treatment option allowing for fewer consultations and infusions would be welcome in China, to increase patient compliance with treatment and reduce patient loss between infusions, while also meeting preferences for more convenient treatment. However, as no quantitative data on treatment compliance are currently available for China, treatment compliance could not be included in the cost-utility model, which represents a limitation of the present analysis.
A similar limitation resulted from basing differences in dosing in the model on those from an RCT (PROVIDE) which may overestimate iron doses delivered over a treatment course in clinical practice, where patient follow-up and management is less rigorous than in an RCT. No real-world data were available to correct for this limitation, so readers should bear in mind that iron doses might be lower in clinical reality than estimated here, particularly given the compliance concerns for formulations such as IS that require multiple administrations.

More broadly, the analysis was limited by a lack of country-specific data on IV iron infusions in general, similar to previous health economic analyses of anemia treatments in China. Data on FDI and IS efficacy and safety as well as on some health state utilities, therefore, had to be sourced from non-Chinese populations, including several US-based RCTs, or, in the case of missing variation around some non-Chinese populations, including several US-based RCTs, or, in the case of missing variation around some input values, had to be assumed. In contrast, patient baseline characteristics, costs and resource use could be sourced mostly from Chinese sources. While a more homogenous, China-specific set of input parameters would have been preferable, physicians’ and decision-makers’ need for timely information regarding the benefits and costs of a newly available IV iron formulation was considered to outweigh the limitations associated with the use of non-Chinese clinical data.

The analysis also had several strengths. The use of a patient-level simulation model, compared to a cohort-level approach, allowed to better account for the non-linearity in the relationship between Hb and body weight as well as patient-level infusion timing and heterogeneity in Hb, body weight, and age, thereby yielding a more nuanced representation of patient trajectories in IDA. The present model also expanded on previous analyses by including a range of cardiovascular adverse events and HSR, each associated with a specific disutility and cost. An additional strength of this study is its contribution to resource use and costing data as well as to utility data associated with anemia, iron deficiency, and IDA in China, through a dedicated physician survey and TTO study.

Conclusions

The present cost-utility analysis was the first comparison of the costs and benefits of FDI relative to IS for the treatment of IDA in China. Relative to IS, FDI was projected to reduce costs associated with IV infusions and treatment of adverse events (at higher acquisition costs) and was associated with improved infusion-related QoL outcomes. Model results suggested that FDI was good value for money in China relative to IS and would likely reduce societal costs associated with IDA.

Declaration of financial/other relationships

SH, LL, DW, and YZ have received honoraria from Pharmacosmos China for participation in advisory board meetings conducted by Pharmacosmos China. RFP is a director and shareholder in, and JP is a full-time employee of, Covalence Research Ltd, which received consultancy fees from Pharmacosmos A/S to develop the simulation model and analysis and prepare the manuscript.

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Author contributions

RFP was involved in the conception and design of the analysis. RFP developed the simulation model and conducted the statistical and health economic analyses. JP prepared the first draft of the manuscript, which was revised critically for intellectual content by all authors. All authors approved the final version to be published. All authors agree to be accountable for all aspects of the work.

Previous presentations

The supporting time trade-off study was previously presented at Virtual ISPOR Europe 2021 (November 30 to December 1, 2021) as poster POSA319.

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Transparency

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