Poster
EE148

Cost-effectiveness Analysis of Deferiprone Compared to Deferoxamine and Deferasirox for the Treatment of Iron Overload in Patients With Sickle Cell Disease and Other Anemias in Canada

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Introduction

- Sickle cell disease (SCD) is a group of inherited autosomal recessive hemoglobinopathies [1,2]. Red blood cell (RBC) transfusion improves microcirculation and oxygen carrying capacity of the blood by decreasing the number of circulating sickled RBCs [1,3].
- However, frequent RBC transfusion in patients with SCD is associated with the risk of iron overload [3,4], which can cause organ dysfunction and death.
- Iron chelation therapy (ICT) is the standard of care practice for removal of excess iron and management of iron overload in patients with SCD [5]. ICT agents have varying routes of administration and safety/toxicity profiles.
- Deferoxamine (DFO), deferasirox (DFX), and deferiprone (DFP) are ICTs approved to treat iron overload in the US and Canada [4,6,7].
- SCD is associated with considerable healthcare costs and utilization [8].

Objective

- **A cost utility analysis (CUA) was conducted to evaluate whether oral DFP is a cost-effective treatment option in Canada for iron overload in SCD and other anemias compared to oral DFX and parenteral DFO.**

Methods

- The base-case analysis was conducted from the perspective of a Canadian publicly funded healthcare payer and utilized a lifetime horizon with monthly cycles.
- The model base-case population is comprised of patients with transfusion-dependent SCD and other anemias (as included in the LA38-0411 FIRST trial) who are at risk of transfusional iron overload (ie, congenital dyserythropoietic anemia, pyruvate kinase deficiency, hereditary spherocytosis, Hb s-beta thalassemia, dyserythropoietic anemia, autoimmune hemolytic anemia, other rare hemoglobinopathies, and chronic non-spherocytic hemolytic anemia).
- The CUA utilized a semi-Markov structure with three health states (On ICT; Not On ICT; and Dead). All people in the model begin in the 'On ICT' state. The transition from 'On ICT' to 'Not on ICT' represents ICT discontinuation. In the model, ICT discontinuation could occur from renal impairment or from other causes. People could not transition from 'Not on ICT' back to 'On ICT'. Mortality could occur from both the 'On ICT' and 'Not on ICT' state. This was based on general population mortality with an assumed standardized mortality ratio of 1.25 for people with SCD applied. A constant probability of death post-end stage renal disease (ESRD) of 2.21% per cycle was applied when estimated glomerular filtration rate (eGFR) fell to ≤15 mL/min/1.73m^2 based on calculating the mortality rate from estimating median survival from a digitized Kaplan Meier curve from McClellan et al [9].
- An annual discount rate of 1.5% was applied to costs and benefits, and inflated costs were calculated using a 2.83% rate derived from the literature [10].
- Included costs were the costs of: treatment (drug costs), routine care (monitoring and healthcare resource utilization), adverse events, iron overload complications, wastage, mortality, and indirect costs **(Figure 1)**.
- The model assumed equivalent efficacy for DFP, DFX, and DFO based on the findings of the LA38-0411 FIRST trial, which established the safety and efficacy of DFP versus DFO in patients with SCD or other anemias, and an indirect treatment comparison comparing the relative efficacy of DFP, DFO, and DFX for the outcomes liver iron concentration, serum ferritin, and cardiac iron.
- The model was structured to track decline in renal function (eGFR) over time using a mixed model for repeated measures analysis of TriNetX US electronic medical record data.
- The conceptual framework and model state utility values are provided in **Figure 1 and Table 1,** respectively. **Table 2** reports the eGFR thresholds of discontinuation associated with each ICT being evaluated. If eGFR fell below the ICT eGFR threshold, then patients discontinued the associated ICT.
- **Table 3 and Figure 2** report discounted life year (LY) gains in the base case. **Table 4 and Figure 3** report discounted quality-adjusted life year (QALY) in the base case**.**
- Five thousand Monte Carlo iterations of the model were run, and mean model results over the 5,000 iterations were recorded to evaluate the economic endpoints.

Figure 1. Conceptual framework

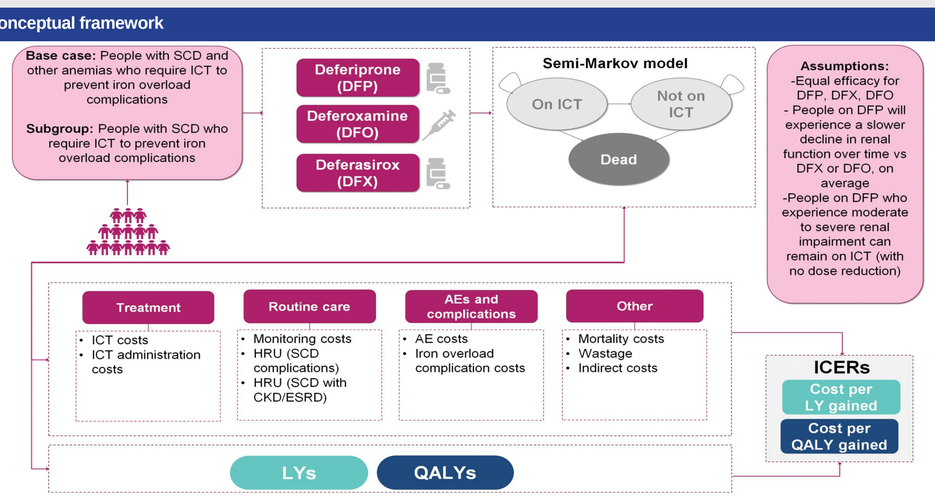


Table 1. Model state utility values

State	Utility value	SE	Source
On oral ICT	0.84	0.016	Karnon et al., 2008 [11]; Tolley et al., 2007[12]
On SC ICT	0.66	0.020	Karnon et al., 2008 [11]; Tolley et al., 2007[12]
Not on ICT	0.84	NA	Assumed equal to SCD on ICT (Oral)

Table 2. eGFR thresholds of discontinuation

ICT	eGFR threshold	Source
DFP	0 mL/min/1.73m^2	Chiesi
DFX	40 mL/min/1.73m^2	Novartis[13]
DFO	30 mL/min/1.73m^2	Pfizer[14]

Abbreviations: CKD, chronic kidney disease; DFO, Deferoxamine; DFP, Deferiprone; DFX, Deferasirox; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; ICER, incremental cost-effectiveness ratio; ICT, iron chelation therapy; LY, life year; QALY, quality-adjusted life year; SC, subcutaneous; SCD, sickle cell disease; SE, standard error

Limitations

- Data was sourced from real-world US electronic medical records data from TriNetX, which is not as robust a basis for comparing outcomes as randomized controlled trials and must be assumed to be generalizable to the Canadian context. TriNetX data was used because it was considered more representative of the target population based on it being more heterogeneous with respect to age and more likely to have kidney-related events or complications than the population in the FIRST trial. It also had a longer follow-up duration (2 years vs 1 year), which collectively provided a means to capture the impact of DFP, DFO, and DFX on renal function within the model.
- Probabilities of iron overload complications were elicited from expert key opinion leaders.
- Rates of complications of SCD and SCD with CKD or ESRD were sourced from publications of analyses conducted on a US population as no Canadian publications were identified.
- Costs used in the model are not country-wide costs but were sourced from provincial formularies and the Ontario ministry of health.
- When data was not available, assumptions had to be made regarding the level of uncertainty around an input. Inputs for which the standard error was estimated were the probabilities of experiencing iron overload complications and the standardized mortality ratio for people with SCD.

Abbreviations

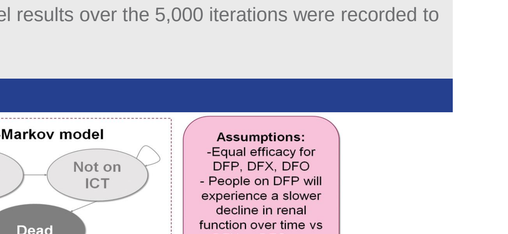
AE, Adverse events; CAD, Canadian dollar; CKD, chronic kidney disease; CUA, cost utility analysis; DFO, Deferoxamine; DFP, Deferiprone; DFX, Deferasirox; Endo Dysf, endothelial dysfunction; ESRD, end-stage renal disease; HC, Health care; HRU, Health resource use; ICER, incremental cost-effectiveness ratio; ICT, iron chelating therapy; LY, life year; QALY, quality-adjusted life year; RBC, red blood cell; SCD, sickle cell disease; WTP, willingness to pay

Table 3. Total discounted LYs

Treatment	DFP	DFO	DFX
On ICT	9.80	7.29	7.30
Not on ICT	11.69	8.32	8.03
Total	21.49	15.61	15.34

DFO, Deferoxamine; DFP, Deferiprone; DFX, Deferasirox; ICT, iron chelation therapy; LY, life year

Figure 2. Total discounted LYs



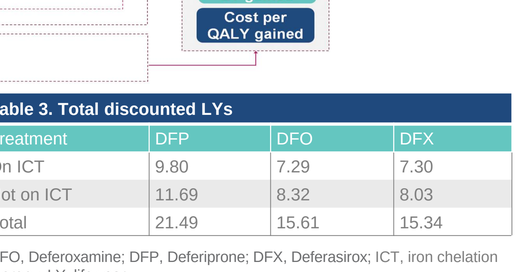
DFO, Deferoxamine; DFP, Deferiprone; DFX, Deferasirox; ICT, iron chelation therapy; LY, life year

Table 4. Total discounted QALYs

Treatment	DFP	DFO	DFX
On ICT	8.23	4.81	6.13
Not on ICT	9.51	6.65	6.41
Total	17.74	11.46	12.54

DFO, Deferoxamine; DFP, Deferiprone; DFX, Deferasirox; ICT, iron chelation therapy; QALY, quality-adjusted life year

Figure 3. Total discounted QALYs



DFO, Deferoxamine; DFP, Deferiprone; DFX, Deferasirox; ICT, iron chelation therapy; QALY, quality-adjusted life year

Disclosures

L.R. and G.T. are employees of Cytel. E.C. was an employee of Chiesi USA at the time of writing, and K.A. is an employee of Chiesi Canada Corporation, the sponsor of the study.

Results – base case, SCD and other anemias

- The pair-wise incremental cost-effectiveness ratio (ICER) results for DFP were compared to DFO and DFX.
- In the probabilistic base-case analysis, the overall average discounted costs for DFP, DFO, and DFX in 2022 Canadian dollars were $3,373,441, $2,669,889, and $2,575,271 **(Table 5)**.
- Overall average discounted QALYs were 17.74, 11.46, and 12.54, respectively, over a lifetime horizon (**Table 5)**.
- All ICERs showed a positive incremental cost benefit for DFP **(Table 6)**.

Table 5. Base case - total costs and outcomes (discounted)

Outcome	DFP	DFO	DFX
Total costs (CAD)	3,373,441	2,669,889	2,575,271
Total LYs	21.49	15.61	15.34
Total QALYs	17.74	11.46	12.54

CAD, Canadian dollar; DFO, Deferoxamine; DFP, Deferiprone; DFX, Deferasirox; LY, life year; QALY, quality-adjusted life year.

Table 6. Base case - ICERs

Treatment	QALYs	Costs (CAD)	Pairwise ICERs (DFP vs ICT to left)	Sequential ICERs (Reference)
DFO	11.46	2,669,889	112,132	Dominated
DFX	12.54	2,575,271	153,481	Referent
DFP	17.74	3,373,441		DFP vs. DFX: 153,481

CAD, Canadian dollar; DFP, Deferiprone; DFO, Deferoxamine; DFX, Deferasirox; SCD, sickle cell disease; ICER, Incremental cost-effectiveness ratio; ICT, iron chelation therapy

- **When considering a 10- and 20-year time horizon, DFP provided more benefits and fewer costs compared to DFX and DFO.**

- Scenario analyses generally showed consistency with the base case findings with some exceptions. Results were most sensitive to the time horizon used, treatment discontinuation assumed post 12 months, and the rate of eGFR decline over time.
- The cost effectiveness plane for probabilistic ICERs for the SCD and other anemias population is displayed in **Figure 4**. ICER values presented in the CE plane equal cost in CAD per QALY gained.
- These results indicate that 100% of probabilistic ICERs for the base-case fell in quadrant 1.
- **Figure 5** presents the net-benefit approach depicting the probability of each treatment being the optimal intervention at different willingness-to-pay (WTP) thresholds.
- DFP becomes the most cost-effective ICT between the thresholds of $150,000 and $200,000.

Figure 4. Cost-effectiveness plane of probabilistic ICER results
Base case - SCD and other anemias

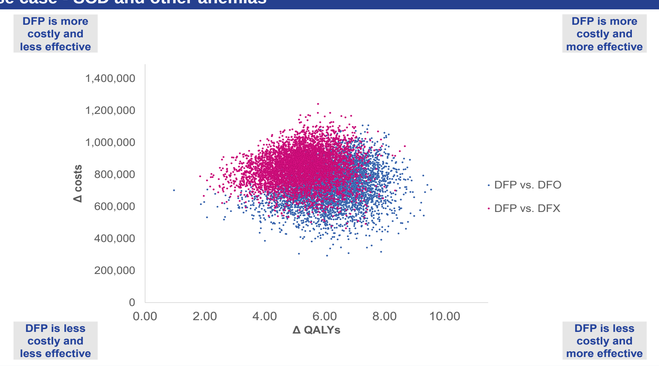
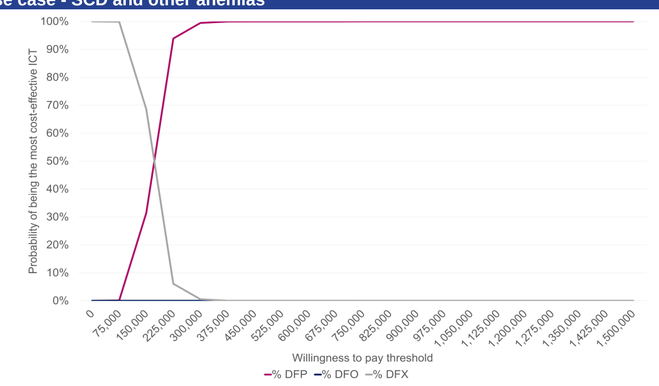


Figure 5. Net benefit approach
Base case - SCD and other anemias



Results – SCD-only subgroup

- In the probabilistic analysis for the subgroup population of people with SCD, the overall average discounted costs for DFP, DFO, and DFX were $3,354,397, $2,672,248, and $2,574,486 and overall average discounted QALYs were 18.04, 11.54, and 12.56, respectively **(Table 7)**.
- The sequential ICER results (reference ICER) and pairwise ICER results are presented in **Table 8**. The pairwise ICER results for DFP vs. DFO and DFP vs. DFX were $105,006, and $142,448 per QALY gained, respectively.
- All ICERs fell within the first quadrant of the cost-effectiveness plane.

Table 7. Total discounted costs and outcomes
SCD-only subgroup

Treatment	DFP	DFO	DFX
Total costs (CAD)	3,354,397	2,672,248	2,574,486
Total LYs	21.84	15.71	15.36
Total QALYs	18.04	11.54	12.56

CAD, Canadian dollar; DFO, Deferoxamine; DFP, Deferiprone; DFX, Deferasirox; LY, life year; QALY, quality-adjusted life year; SCD, sickle cell disease. Note: all costs were in CAD$.

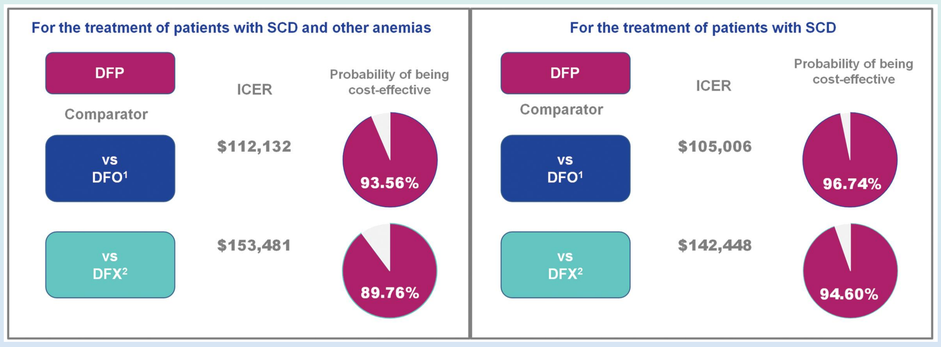
Table 8. ICERS
SCD-only subgroup

Treatment	QALYs	Costs (CAD)	Pairwise ICERs (DFP vs ICT to left)	Sequential ICERs (Reference)
DFO	11.54	2,672,248	105,006	Dominated
DFX	12.56	2,574,486	142,448	Referent
DFP	18.04	3,354,397		142,448

CAD, Canadian dollar; DFP, Deferiprone; DFO, Deferoxamine; DFX, Deferasirox; SCD, Sickle cell disease; QALY, Quality-adjusted life-year; ICER, Incremental cost-effectiveness ratio

Conclusions

- **DFP is a cost-effective treatment alternative for iron overload in SCD and other anemias versus DFO and DFX, as DFP contributed to higher LY gains as well as higher QALY gains than DFO and DFX.**
- **When considering a 10- and 20-year time horizon, DFP was dominant.**
- **Canadian clinicians should consider DFP as a cost-effective alternative to other ICTs for use in SCD or other anemias.**



[1]At a WTP threshold of $150,000 per QALY
[2]At a WTP threshold of $200,000 per QALY
DFP, Deferiprone; DFO, Deferoxamine; DFX, Deferasirox; ICER, incremental cost-effectiveness ratio; LY, life-year; QALY, quality-adjusted life-year; SCD, sickle cell disease; WTP, willingness to pay. All dollar values in Canadian dollars.

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