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Iron-Chelating Therapies in a Transfusion-Dependent Thalassaemia Population in Thailand

A Cost-Effectiveness Study

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Abstract

Background and Objective: β-Thalassaemia is a major public health problem in Thailand. Use of appropriate iron-chelating agents could prevent thalassaemia-related complications, which are costly to the healthcare system. This study aimed to evaluate the cost effectiveness of deferoxamine (DFO), deferiprone (DFP) and deferasirox (DFX) in Thai transfusion-dependent β-thalassaemia patients from the societal perspective.

Methods: A Markov model was used to project the life-time costs and outcomes represented as quality-adjusted life-years (QALYs). Data on the clinical efficacy and safety of all therapeutic options were obtained from a systematic review and clinical trials. Transition probabilities were derived from published studies. Costs were obtained from the Thai Drug and Medical Supply Information Center, Thai national reimbursement rate information and other Thai literature sources. A discount rate of 3% was used. Incremental cost-effectiveness ratios (ICERs) were presented as year 2009 values. A base-case analysis was performed for thalassaemia patients requiring regular blood transfusion therapy, while a separate analysis was performed for patients requiring low (i.e. symptom-dependent, less frequent) blood transfusion therapy. A series of sensitivity analysis and cost-effectiveness acceptability curves were constructed.

Results: Compared with DFO, using DFP was dominant with lifetime cost savings of $US91 117. Comparing DFX with DFO, the incremental cost was

$US522 863 and incremental QALY was 5.77 with an ICER of $US90 648 per QALY. When compared with DFP, the ICER of DFX was $US106 445 per QALY. A cost-effectiveness analysis curve showed the probability of DFX being cost effective was 0% when compared with either DFO or DFP, based on the cost-effectiveness cut-off value of $US2902 per QALY. When compared with DFP, DFX was cost effective only if the DFX cost was as low as $US1.68 per 250 mg tablet. The results of the analysis in patients requiring low blood transfusion therapy were not different from those of the base-case analysis.

Conclusions: Our findings suggest that using DFP is cost saving when compared with conventional therapy, while using DFX is not cost effective compared with either DFO or DFP in Thai patients with transfusion-dependent β-thalassaemia. Policy-makers and clinicians may consider using such information in their decision-making process in Thailand.

Introduction

β-Thalassaemia, a genetically inherited disease involving malfunction of haemoglobin synthesis, is one of the most serious public health problems in many countries including Thailand.[1,2] While the estimated worldwide prevalence of the globin gene variant is 4–7%,[3,4] the prevalence of thalassaemia traits in Bangkok and Northern Thailand is 20–30%.[5] Over 10 million Thai people carry the thalassaemia gene and approximately 600 000 people have thalassaemia disease.[6] Patients with β-thalassaemia produce abnormal haemoglobin, resulting in anaemia. Severe cases require regular blood transfusions and iron chelation therapy to prevent iron overload, which could cause increased iron deposition and consequent dysfunction in major organs including the heart, liver and endocrine organs.[7,8] The main cause of death in these patients is iron overload-induced heart failure.[9-11] Current evidence shows that reducing iron overload is associated with an increased survival rate and a reduced risk of cardiac death.[12,13]

The most commonly used iron-chelating agent in Thailand is deferoxamine. Due to its short plasma half-life and lack of oral activity, deferoxamine has to be administered subcutaneously over 8–12 hours, 5–6 times a week. The arduousness of this regimen and its high cost can lead to poor compliance and difficulties in patients' lives, with subsequent impacts on the effectiveness of the treatment. Recently, other therapeutic options have become available, including deferasirox and deferiprone. These agents are administered orally and are likely to enhance patient compliance and possibly quality of life. A recent meta-analysis and other clinical evidence have demonstrated that these oral treatments can reduce serum, liver and cardiac iron levels.[14-16] In Thailand, the cost of deferiprone is relatively low compared with the costs of deferasirox and deferoxamine. However, deferiprone has been reported to be associated with serious adverse effects including agranulocytosis, neutropenia and arthropathy.[17-19] From a policy-maker's perspective, information on value for money for these therapeutic options would facilitate informed decision making. However, little is known about the cost effectiveness of these products. This study aimed to determine the cost effectiveness of deferiprone and deferasirox compared with deferoxamine, the most commonly used iron-chelating therapy in Thailand. The expected costs and consequences of all options were compared using a life-time time horizon.

Methods

Overall Description

We employed a Markov model to determine the cost effectiveness of deferoxamine, deferiprone and deferasirox therapies in β-thalassaemia patients. The Markov model is designed to mimic the

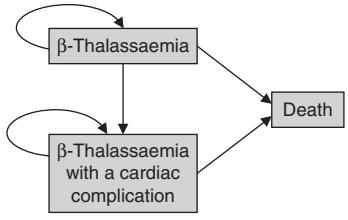

Fig. 1. Markov model with three health states.

natural history of thalassaemia patients by projecting the life-time outcomes including costs and quality-adjusted life-years (QALYs). Since cardiac disease is the major cause of death, we constructed the model with three health states: β-thalassaemia, β-thalassaemia with a cardiac complication, and death (figure 1). The cardiac complication was defined as chronic heart failure and/or cardiac arrhythmia.

The study population was β-thalassaemia and β-thalassaemia/haemoglobin E patients receiving regular blood transfusions requiring iron-chelating therapy. Using a life-time time horizon, the model simulated patients aged 6–70 years as deferiprone use is restricted to patients aged >6 years.[20] The cycle length was 1 year. All costs and consequences were discounted at a rate of 3% and adjusted to 2009 values.[21] The costs were converted at a rate of 34.46 baht per $US1 as the average rate for 2009.[22] The perspective undertaken was the societal perspective according to pharmacoeconomic guidelines in Thailand.[23] In addition, we performed a separate analysis for patients with low (i.e. symptom-dependent, less frequent) blood transfusion.

Efficacy and Safety Data Inputs

Current published evidence suggests there are no differences in terms of clinical efficacy between the three products. Based on a recent meta-analysis,[14] both deferoxamine and deferiprone have comparable clinical efficacy as demonstrated by serum ferritin levels and liver iron concentrations. In addition, recent studies that compared the clinical efficacy of deferoxamine and deferasirox have shown that deferasirox is non-inferior to deferoxamine as shown by liver iron concentrations and serum ferritin level reductions.[15,16]

It is important to note that there have been no studies directly comparing deferasirox and deferiprone, which means only indirect comparisons are possible. Based on an absence of any comparative effectiveness reviews of deferoxamine, deferiprone and deferasirox, we assumed comparable efficacy for all three products in this cost-effectiveness study. As a result, we assumed that the risks of having a cardiac complication and non-cardiac death resulting from iron overload were comparable with all three therapeutic options.

Increased risk of neutropenia is a major adverse event associated with deferiprone, although there is no evidence of agranulocytosis according to a systematic review.[14] We performed a meta-analysis of two studies[17,18] reporting neutropenia among those receiving either deferoxamine or deferiprone over a 1-year follow-up period. One study showed that patients using deferiprone have neutropenia at a rate of two events in every 71 patients[17] while another study showed one event in every 29 patients.[18] Thus, the pooled incidence of neutropenia was 3% (95% CI 0, 0.06) in the model. A mortality rate associated with neutropenia could not be incorporated into the model as there were no mortality reports in these studies.[14,17,18] Other adverse events resulting from use of the three iron chelators, such as local reactions, nausea/vomiting, joint pain and abdominal pain, were not included in this analysis since most of these events were mild and transient.[14-16]

Probability Parameters

The probability of transitioning from β-thalassaemia to β-thalassaemia with a cardiac complication was derived from a cohort study of 1073 thalassaemia patients.[13] This study provided a heart failure-free probability, which was converted into an annual risk of having cardiac complications. For thalassaemia patients without cardiac disease, we estimated the risk of death by multiplying Thai age-specific mortality[24] by a relative risk of 3.9. This relative risk value was derived by Delea et al.[25] using the cohort data of 257 thalassaemia patients reported in a study by Gabutti and Piga.[26] For patients with cardiac complications, we estimated the risk of death by combining the

age-specific mortality rate for patients with thalassaemia without complications and the age-specific mortality rate related to cardiac diseases. The latter mortality rate was obtained from a cohort study of 648 thalassaemia patients who were followed up to determine the risk of cardiac-related death over a median of 27.8 years.[27]

Cost Data Inputs

As this study was undertaken from the societal perspective, cost data inputs included direct medical care, direct non-medical care and indirect costs. All costs were adjusted to Thai baht currency, 2009 values.[21] The rate of discounting was 3%. Direct medical care costs were estimated using a micro-costing approach.[28] Cost incurred among patients receiving deferoxamine therapy included drug cost, cost of medical visit, cost of infusion pump and cost of injection set, while cost in those receiving deferiprone included drug cost, cost of medical visit, cost of complete blood count (CBC) monitoring and cost of neutropenia treatment. Cost in patients receiving deferasirox included only drug cost and cost of medical visit. We assumed the prescribed dosages of these interventions were deferoxamine 50 mg/kg/day administered subcutaneously, 7–8 hours per day, 5 days a week, while deferasirox 30 mg/kg/day and deferiprone 75 mg/kg/day were given orally, once and three times daily, respectively. Patients' weights were estimated based on the average value for each age for the Thai general population.[29] Drugs and injection set costs were obtained from the Drug and Medical Supply Information Center (DMSIC).[30] The cost of deferoxamine (Desferal®) and the cost of deferasirox (Exjade®) were $US10.77 and $US58.56 per gram, respectively (table I). In Thailand, two brands of deferiprone are available (Kelfer® [an imported brand] and GPO-L-One® [a locally made brand]). The cost of deferiprone (Kelfer®), $US2.09 per gram, was used for the base-case analysis, while the cost of deferiprone (GPO-L-One®), $US0.20 per gram, was used in a sensitivity analysis. The cost of the injection kit was estimated as $US0.45 per infusion, while the cost of the infusion pump was $US362.79, a value obtained directly from the sole supplier in Thailand, UDOM Medical.[32] The life-time of the infusion pump was assumed to be 10 years. The costs of a medical visit and CBC were $US1.47 and $US2.65, respectively; these costs were derived from the reimbursement rate specified by the Ministry of Public Health (MOPH), Thailand.[31] The frequency of medical visits was assumed to be once per month (12 visits/year) for all treatment approaches except in the first year of using deferiprone, which required more frequent visits (18 visits/year) to monitor CBC levels according to the guidelines for use of deferiprone.[39] The cost of neutropenia management in patients receiving deferiprone was calculated as $US303.99 based on an analysis of 1519 patients with a primary diagnosis of neutropenia included in the National Public Hospital Service database.[33] A cost-to-charge ratio (i.e. the ratio of the actual cost of hospital care to what the hospital actually charges for care) of 0.8, adopted from a research report from the National Health Security Office (NHSO),[34] was applied to convert this charge to cost.

Because of the limited data in the literature, an assumption was made that the cost of treating iron-overload cardiac complications in thalassaemia patients was the same as the cost of treating chronic heart failure complications in patients with diabetes mellitus. Accordingly, the cost of treatment of iron-overload cardiac disease per year was estimated at $US736.69 (table I). This was based on the results of a study evaluating chronic heart failure complications among a diabetic population receiving care at a 1000-bed tertiary care hospital located in the north of Thailand.[35]

Direct non-medical care costs included transportation costs, additional food costs during visits and caregiver costs. Based on a prospective study of 351 β-thalassaemia patients in Thailand,[36] the costs of transportation and additional food for each visit were $US4.42 and $US3.53, respectively (table I). These costs were applied to all patients aged 6–70 years. In addition, we assumed that a caregiver needs to spend half an hour per day preparing for the deferoxamine injection for 5 days/week for thalassaemia children aged 6–12 years. In order to conservatively estimate the cost of a caregiver, we based our calculation

Table I. Base-case values for the model parameters

Input parameters	Value	References
Costs ($US, year of costing 2009)		
Direct medical care costs		
drug costs		
DFO (Desferal®), per g	10.77	30
DFP (Kelfer®), per g	2.09	30
DFP (GPO-L-ONE®), per g	0.20	30
DFX (Exjade®), per g	58.56	30
cost of medical visit, per visit	1.47	31
administration cost: DFO		
infusion pump	362.79	32
injection kit, per infusion	0.45	30
adverse events management cost: DFP		
neutropenia, per event	303.99	33,34
CBC test: DFP, per test	2.65	31
treatment of iron-overload cardiac disease, per year	736.69	35
Non-direct medical care costs		
transportation cost, per visit	4.42	36
additional food cost, per visit	3.53	36
caregiver cost, per week	1.37	37
Indirect costs		
productivity cost, per day	4.38	37
Transition probabilities		
β-Thalassaemia → β-thalassaemia with a cardiac complication	0.0114	13
β-Thalassaemia → death	Varies	24-26
β-Thalassaemia with a cardiac complication → death	Varies	13,27
Utility values (QALYs)		
β-Thalassaemia with DFO	0.61	38
β-Thalassaemia with DFP	0.61	38
β-Thalassaemia with DFX	0.85	38
β-Thalassaemia with DFO and a cardiac complication	0.46	38
β-Thalassaemia with DFP and a cardiac complication	0.46	38
β-Thalassaemia with DFX and a cardiac complication	0.70	38

CBC = complete blood count; **DFO** = deferoxamine; **DFP** = deferiprone; **DFX** = deferasirox; **QALY** = quality-adjusted life-year.

on the minimal wage rate of $US4.38 per day, as reported by the Ministry of Labour, Thailand, in 2009.[37] The cost of a caregiver was calculated as $US1.37 per week. There was no need for caregiver time for those patients taking oral chelation therapy. Indirect costs were estimated from productivity costs. We assumed patients aged 15–60 years lose productivity when they visit doctors. The productivity cost was calculated from the number of visits multiplied by the minimum wage rate per day.[37]

Utility Data Inputs

We adopted the approach of Delea et al.[25] for deriving utility values from the literature. The utility values for patients taking deferoxamine or deferasirox were 0.61 (95% CI 0.56, 0.66) and 0.85 (95% CI 0.81, 0.89), respectively (table I). These values were taken from an Australian study[38] that used a time trade-off (TTO) method to elicit utility values from a sample of 120 individuals of various demographic characteristics.

In the absence of a utility value for patients taking deferiprone, a three-times-daily regimen, we assumed a conservative utility value for deferiprone that would be similar to that for deferoxamine, which is a subcutaneous infusion therapy. For health states with cardiac complications, we adopted the approach of Delea et al.[25] and deducted a utility of 0.15. This value was obtained from a cohort study estimating a disutility value of heart failure based on 1365 random samples of US adults in a community population.[40] For adverse effects associated with deferiprone, we assumed the utility of those with neutropenia to be similar to those without such an event because this adverse event was transient, reversible and unlikely to affect patients' long-term utility values.

Analyses

The Markov model was simulated to calculate the expected life-time costs and outcomes with each iron-chelating treatment in patients requiring regular blood transfusion therapy. The results were presented as an incremental cost per QALY gained for deferoxamine versus deferiprone, deferoxamine versus deferasirox, and deferiprone versus deferasirox.

A separate analysis was performed for thalassaemia patients receiving low blood transfusion therapy since the dose regimens for the three therapeutic options are different in such patients from those receiving regular blood transfusions. The recommended doses for these patients are: deferoxamine 40 mg/kg/day, 5 days a week; deferiprone 50 mg/kg/day, daily; and deferasirox 20 mg/kg/day, daily.[41,42] We assumed these recommended regimens for patients with low blood transfusion had comparable efficacy. This assumption was based on the results of two clinical trials[15,16] showing deferasirox 20 mg/kg/day is non-inferior to deferoxamine 40 mg/kg/day in patients with low blood transfusion. However, as there were no studies comparing the efficacy of deferoxamine 40 mg/kg/day with deferiprone 50 mg/kg/day, we assumed dose regimens used in low blood transfusion patients would have similar efficacy to the regimens used in regular transfusion patients. The time horizon in the model was set to start from the age of 20 years until death due to the fact that these groups of patients required chelating therapy in the second to third decade of their life. The risks of death, cardiac complications and adverse events of neutropenia associated with using deferiprone in patients with low blood transfusion were assumed to be the same as for patients receiving regular blood transfusions.

One-way sensitivity analyses were performed to investigate the effects of altering parameters within plausible ranges including all costs, utilities and discount rates. We also calculated the cost effectiveness of deferiprone when the cost of generic deferiprone locally made in Thailand (GPO-L-One®) was used instead of the cost of deferiprone imported from India (Kelfer®). The cost of deferasirox required to hypothetically make the product cost effective under the willingness to pay (WTP) value of between one and three times gross domestic product (GDP) per capita[43] ($US2902 and $US8707, respectively, per QALY) was also determined. Probabilistic sensitivity analyses were undertaken to capture the effects of uncertainty around all parameters varied simultaneously within the model. Cost-effectiveness acceptability curves were also constructed based on the 10 000 sets of the simulation. The Markov model was constructed and analysed using Microsoft Excel 2003 (Redmond, WA, USA).

Results

Base-Case Analyses

Our base-case analysis showed the estimated total life-time costs of using deferoxamine, deferiprone and deferasirox were $US157 940, $US66 823 and $US680 804, respectively, while the estimated QALYs were 14.04, 14.04 and 19.81, respectively (table II). The major costs of all interventions were drug costs, which represented 93.21%, 90.01% and 99.03% of all costs for deferoxamine, deferiprone and deferasirox, respectively.

Compared with deferoxamine, the most commonly used iron-chelating therapy in Thailand, the incremental cost per QALY gained for defer-

Table II. Outcome measures following base-case analyses: individual treatment groups

Outcome measure	Deferoxamine	Deferiprone	Deferasirox
Costs ($US, year of costing 2009)			
Direct medical costs			
drug costs	147 218.14	60 146.96	674 213.96
other costs	7 157.24	3 516.95	3 477.90
Direct non-medical costs	2 744.83	2 339.38	2 291.81
Indirect costs	820.15	820.15	820.15
Total costs	157 940.36	66 823.44	680 803.82
QALYs	14.04	14.04	19.81

QALY = quality-adjusted life-year.

asirox was $US90 648. Deferiprone was dominant with a life-time cost saving of $US91 117 per patient compared with deferoxamine (table III). Because deferiprone was a dominant strategy, an incremental analysis of deferasirox compared with deferiprone was performed. The incremental cost-effectiveness ratio for deferasirox compared with deferiprone was $US106 445 per QALY.

Analysis in patients receiving low blood transfusions showed that deferiprone was dominant with a life-time cost saving of $US76 492 per patient compared with deferoxamine. Incremental costs per QALY gained for deferasirox compared with deferoxamine and deferiprone were $US68 018 and $US84 707, respectively.

Sensitivity Analyses

A series of one-way sensitivity analyses showed that the most influential parameter was discount rate. When the discount rate was varied from 3% to 0% and 6%, the life-time cost saving with use of deferiprone for one patient compared with use of deferoxamine was shifted to $US54 242 and $US186 023, respectively. For analysis of deferiprone compared with deferoxamine, varying the dose and cost of deferoxamine or deferiprone also resulted in substantial changes in cost-saving values, as shown in figure 2.

In the analyses of deferasirox compared with deferoxamine and deferiprone, the most influential parameter in both cases was the utility of using deferasirox. Varying the utility of using deferasirox from 0.85 to 0.76 and 0.94 (±10%), the incremental cost-effectiveness ratio (ICER) was shifted to $US128 231 and $US70 102 when compared with deferoxamine, and to $US150 577 and $US82 319 when compared with deferiprone, respectively.

The result of 10 000 simulations of probability sensitivity analysis for each pair of the analyses (deferoxamine vs deferiprone, deferoxamine vs deferasirox, and deferiprone vs deferasirox) showed that deferiprone was estimated to have a total cost less than deferoxamine while the mean utility was almost the same. Deferasirox was estimated to have a higher total cost and greater effectiveness than deferoxamine and deferiprone (figure 3). Cost-effectiveness acceptability curves showed that at the threshold values of $US2902 and $US8707, deferasirox had zero probability of being cost effective when compared with both deferoxamine and deferiprone (figure 4). The cost saving associated with the use of deferiprone was $US145 416 when the total cost of deferiprone locally made in

Table III. Outcome measures following base-case analyses: treatment group comparisons

Outcome measure	Deferiprone vs deferoxamine	Deferasirox vs deferoxamine	Deferasirox vs deferiprone
Costs ($US, year of costing 2009)			
Direct medical costs			
drug costs	−87 071.19	526 995.82	614 067.00
other costs	−3640.30	−3679.35	−39.05
Direct non-medical costs	−405.45	−453.02	−47.57
Indirect costs			
Total costs	−91 116.94	522 863.45	613 980.38
QALYs gained	0	5.77	5.77
Cost per QALY gained ($US)	Deferiprone dominant	90 648.37	106 445.23

QALY = quality-adjusted life-year.

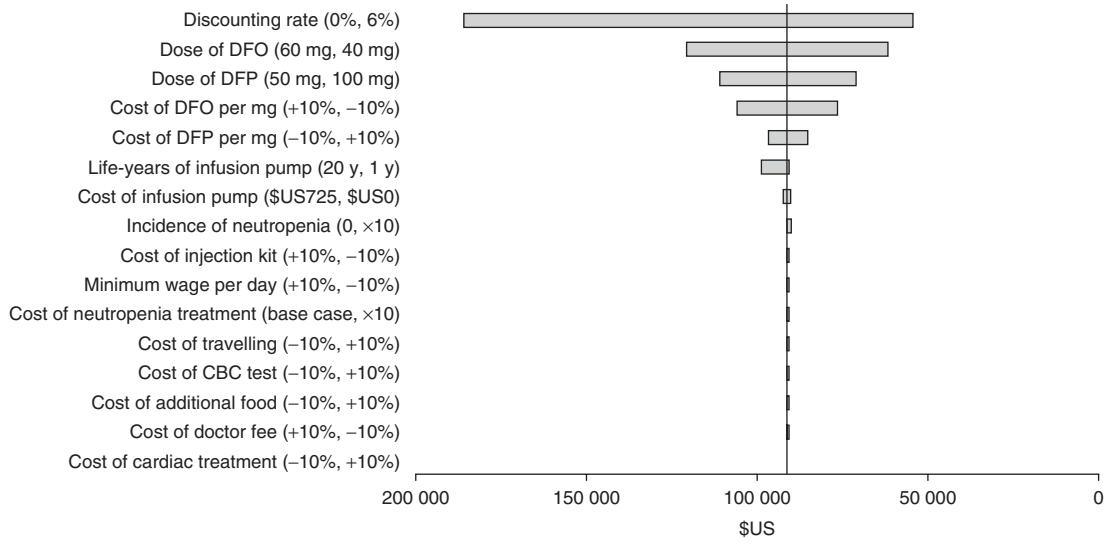

Fig. 2. Tornado diagram showing a series of one-way sensitivity analyses for cost saving comparing deferiprone (DFP) with deferoxamine (DFO) [year of costing 2009]. **CBC** = complete blood count.

Thailand (GPO-L-One) was used. The cost of deferasirox that made it cost effective compared with deferiprone was $US1.68 and $US2.41 per 250 mg tablet when setting the WTP as $US2902 and $US8707 per QALY gained, respectively.

Discussion

To the best of our knowledge, this is the first economic study evaluating deferiprone in comparison with deferoxamine and deferasirox, while most other published studies compared deferasirox with deferoxamine.[25,44] This cost-effectiveness study revealed that using deferiprone resulted in lower total life-time costs than deferoxamine, saving over $US91 117 per patient. Our results also demonstrated that from the societal perspective, deferiprone is the most cost-effective iron-chelating agent, and that deferasirox is not cost effective compared with deferoxamine and deferiprone, with ICERs of $US90 648 and $US106 445 per QALY, respectively, which are greater than the threshold value recommended by WHO.[43] According to this recommendation, an intervention would be cost effective when an ICER falls between one to three times GDP per capita, which is approximately $US2902–8707.[43,45]

The cost saving associated with the use of deferiprone was robust in a series of sensitivity analyses. Furthermore, the magnitude of cost saving was even greater when the locally made generic version of deferiprone (GPO-L-One®) was included in the analysis. We believe these cost-saving findings stem mainly from two factors. The first is that the cost of deferiprone is substantially lower than the cost of deferoxamine; the second is that drug cost is the cost driver because it accounts for over 90% of the total cost.

The finding that deferasirox is not cost effective in the Thai context differs from what has been reported in the current literature.[25,44] Two previously published economic evaluation studies conducted in the US[25] and UK[44] settings found that deferasirox was cost effective compared with deferoxamine. The differences in these findings might be explained by the fact that the differences in drug cost between deferasirox and deferoxamine in the Thai setting are much larger than the differences reported in the two previously published studies. In Thailand, the difference in drug costs when changing from deferoxamine to deferasirox resulted in an increase of over 400% while the drug cost increased only 100% in both US and UK settings.

The validity of our findings for deferasirox might be questioned because of the use of utility values based on the international literature.[38] Most importantly, sensitivity analyses revealed that the utility values were the most influential parameter in the model. However, when the upper bound utility value of deferasirox was used in the model, deferasirox was still not cost effective with the incremental cost per QALY remaining far in excess of the acceptable threshold. It is important to note that 'borrowing' utility values from the literature is not an uncommon practice.[46,47] Indeed, there is no evidence to show that conducting a utility study locally would be a cost-effective decision.

The assumption of a lack of difference in clinical efficacy among the three products (deferoxamine, deferasirox and deferiprone) was based on the findings of a Cochrane systematic review and several current RCTs,[14-18] these being the most reliable sources for data on the treatment effects of interventions. Current evidence shows these three options have comparable efficacy in preventing iron overload when liver and ferritin iron levels are used as surrogate outcomes.[14-18] Moreover, some studies[18,48] have reported that deferiprone has greater efficacy than deferoxamine in removing cardiac iron using the T2* imaging technique as an indicator.

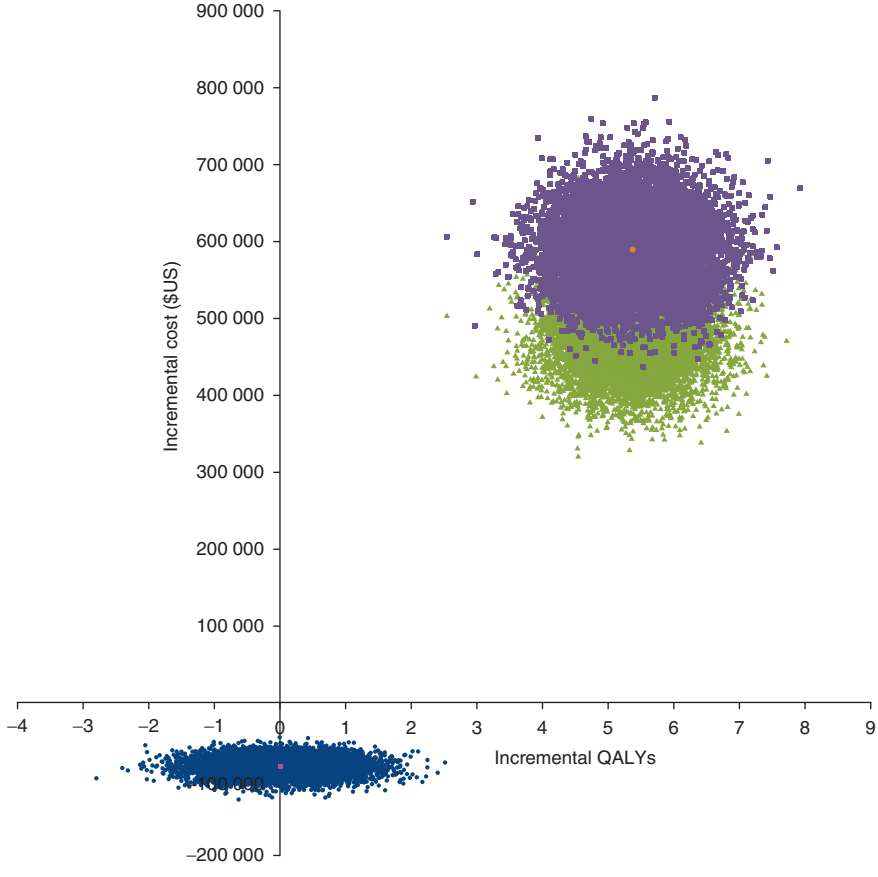

Fig. 3. Probabilistic sensitivity analysis of the incremental cost vs quality-adjusted life-years (QALYs) for three sets of analyses, deferoxamine (DFO) vs deferiprone (DFP) [blue], DFO vs deferasirox (DFX) [green], and DFP vs DFX (purple) presented on a cost-effectiveness plane [year of costing 2009].

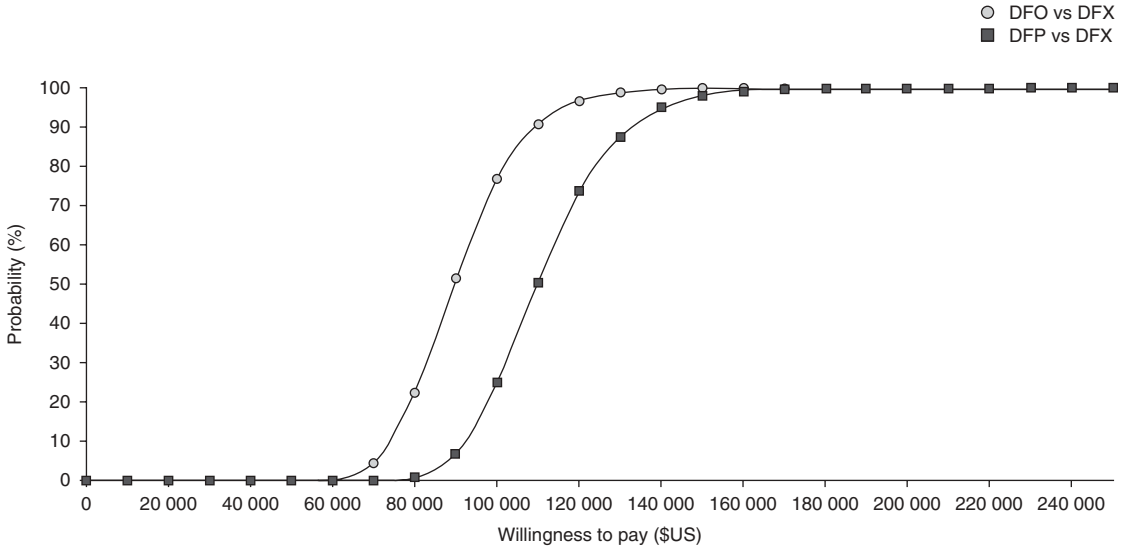

Fig. 4. Cost-effectiveness acceptability curve showing the probability that using deferasirox (DFX) is cost effective compared with deferoxamine (DFO) vs deferiprone (DFP) [year of costing 2009].

With regard to drug safety, our meta-analysis of two studies[17,18] demonstrated that the incidence of neutropenia associated with deferiprone was as low as 3%. It might be argued that the true incidence might be greater in real-world practice but currently there is no evidence to support such a claim. Despite the low incidence of neutropenia, all deferiprone users should adhere to the guideline suggesting close blood monitoring.[39] This intensive assessment increases the likelihood of neutropenia being detected earlier and potentially facilitates commencement of appropriate neutropenia management in a timely fashion. The consequence is a relatively low neutropenia-related mortality in patients taking deferiprone, which justifies the lack of incorporation of mortality from this adverse effect in the model.

We believe that our findings are highly valid for several reasons. Importantly, we used local data in the analysis, making the results highly applicable in the local context. All cost data were acquired from reliable sources, i.e. the national reimbursement rate specified by MOPH and the Drugs and Medical Supplies Information Center (DMSIC), Ministry of Public Health. Moreover, our study was conducted in accordance with the pharmacoeconomic guidelines for Thailand.[23] The societal perspective used in our analysis is the most widely recommended perspective. The model used a life-time horizon with a 3% discount rate for both costs and outcomes. Furthermore, because we incorporated the age-specific mortality rate of the Thai population[24] in our analyses, the average life expectancy of patients with β-thalassaemia derived from the model was consistent with the reported average life expectancy of 30 years in the Thai literature.[49] This cross validation leads us to believe the findings of our analysis are valid.

Our study had several limitations. For example, the transition probabilities used in the model were derived from the international literature.[13,26,27] These parameters may therefore be different from those of the Thai population due to differences in ethnicity. Another potential limitation was that, in the absence of published evidence, we had to assume that the risk of having a cardiac complication and death in low transfusion patients was similar to that in patients receiving regular blood transfusions. Next, there was no utility value for deferiprone in the published literature. As only the utility values of using deferasirox

and deferoxamine[38] were available, we conservatively assumed the utility of deferiprone to be as low as that of deferoxamine. This might have resulted in an underestimation of the benefits of deferiprone. In addition, our analyses did not address the different compliance rates among the products. This may have led to an underestimation of the benefits of an oral regimen compared with subcutaneous infusion in relation to long-term treatment and patients' outcomes. However, in comparisons between the oral regimens, the degree of difference in the compliance rate would be minimal. This study also addressed the question of which single agent was the most cost-effective drug therapy from the national policy viewpoint; it did not assess combination regimens. Lastly, it is also important to note that our study did not determine the cost effectiveness of products in specific subgroups (e.g. patients of different ages, patients with specific clinical characteristics such as pre-existing neutropenia associated with bone marrow disorder, or patients who could not take deferoxamine or deferiprone).

Our findings were consistent with the policy decision taken in 2008 to include deferiprone in the Thai National List of Essential Medicines.[50] The use of deferiprone was further promoted through the collaboration of the NHSO, The Government Pharmaceutical Organization (GPO) and the Thalassaemia Foundation of Thailand.[50] Under this collaboration, the GPO is responsible for the production of deferiprone at an affordable cost, thereby ensuring access to iron-chelating therapy for thalassaemia patients in Thailand. Our results showing cost savings in association with use of deferiprone instead of deferoxamine provide the missing piece of information that strongly supports the policy decision made in relation to use of this product.

Conclusion

In summary, deferiprone is a cost-saving iron-chelating therapy for the treatment of transfusion-dependent β-thalassaemia patients with either regular or low blood transfusion in the Thai population when compared with the conventional treatment of deferoxamine. These findings are in accordance with and strongly support the policy implementation of promoting deferiprone to the National List of Essential Medicines in 2008. In addition, this model analysis revealed that using deferasirox instead of deferoxamine or deferiprone was not cost effective given the very high cost per QALY relative to Thailand's threshold value. The cost of deferasirox is the key component in determining whether to use this agent as the standard regimen.

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