

The cost-utility of treating anemia with continuous erythropoietin receptor activator or Epoetin versus routine blood transfusions among chronic hemodialysis patients

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Objective: The purpose of this study was to determine the cost-utility of treating anemic dialysis patients with continuous erythropoietin receptor activator (CERA) once monthly or Epoetin Beta (EpoB) thrice weekly compared with a reference strategy of managing anemia with red blood cell transfusion (RBCT).

Methods: Cost-utility analysis study design. Decision analysis model, National health care payer, over 1 year with the publicly funded health care system. Chronic hemodialysis patients with renal anemia were included. The outcome marker of this study was the incremental cost per quality-adjusted life-year (QALY) gained (incremental cost-utility ratio [ICUR]) of CERA or EpoB relative to RBCT.

Results: The total cost per patient (in US\$) was estimated at \$2,176.37, \$4,107.01, and \$4,356.69 for RBCT, CERA, and EpoB, respectively. The cost-utility ratio was calculated at 4,423.52, 6,955.50, and 7,406.38 \$/QALY for RBCT, CERA, and EpoB, with an ICUR of CERA and EpoB in relation to RBCT at 19,606.40 and 22,466.09 \$/QALY, respectively. In sensitivity analysis, the model was most sensitive to hospitalization costs, hospital stay, and annual number of RBCT units. Also, assuming utility and survival improvement with erythropoiesis stimulating agents use resulted in a decrease in ICUR at 13,429 \$/QALY for CERA and 15,331 \$/QALY for EpoB. In probabilistic sensitivity analysis, the main results of our model were unchanged; CERA and EpoB were more costly and more effective than RBCT below a threshold of 19,500 \$/QALY. CERA was the best option for a willingness to pay over 19,500 \$/QALY.

Limitations: Some model parameters were obtained from observational data, the comparator RBCT is not the standard of care.

Conclusion: Our study suggests that managing anemia in dialysis patients with CERA or EpoB may result in better outcomes with higher overall costs. Considering different assumptions, we found substantial variability in the estimates of the cost-utility and incremental of using CERA or EpoB.

Keywords: cost-utility, cost-effectiveness, anemia, dialysis, erythropoiesis stimulating agents, continuous erythropoietin receptor activator, epoetin

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Introduction

Anemia is a common complication of chronic kidney disease (CKD) because of decreased kidney production of erythropoietin. It is associated with adverse clinical outcomes and poor health-related quality of life (QOL).^{1,2} Treatment of anemia before the advent of erythropoiesis stimulating agents (ESAs) relied on routine blood transfusions.²⁻⁴



Early studies demonstrated a reduction in transfusions needed and an improvement in QOL in chronic hemodialysis patients (CHP) after the introduction of ESA in the market, compared with managing anemia without ESAs.^{4,5} Therefore, ESAs in routine clinical practice diffused rapidly and became the standard option.⁶ The class of ESA includes the short-acting forms Epoetin Alpha and Epoetin Beta (EpoB), and the long-acting ones: darbepoetin and the pegylated erythropoietin continuous erythropoietin receptor activator (CERA).⁷ Understanding the relative cost-utility of those treatments is of importance to both clinicians and health care reimbursement authorities, as the acquisition costs of all ESAs are relatively high and are among the top drug expenditures of hospitals, health care payers, and providers.^{7–10} Although all of previous health economic studies focused their analysis on short-acting ESA, CERA as the last one to be introduced in clinical practice has not been well studied yet.^{1,7,9,11}

The purpose of this study was to determine the cost-utility of treating dialysis patients with CERA once monthly or EpoB thrice weekly compared with a strategy of managing anemia without ESAs.

Patients and methods

Study design

We estimated the cost per quality-adjusted life-year (QALY) gained with treatment using two different ESAs to maintain hemoglobin level within the target 10.5–12 g/dL, compared with strategy of managing anemia without ESAs. A decision analytic model was constructed to model the cost and clinical outcomes in a cohort of Moroccan CHP. All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Treatment comparators

Three treatment strategies were compared: (1) CERA, (methoxy polyethylene glycol-EpoB; Mircera[®]; Hoffman-La Roche Ltd, Basel, Switzerland); (2) EpoB, (Recormon[®]; Hoffman-La Roche Ltd); and (3) management of anemia without ESAs (use of rescue red blood cell transfusions [RBCTs]).

Population and data sources

ESA requirement, efficacy, and costs

We used the study of Maoujoud et al¹² to provide clinical and costing data for this model. Authors reported in this

prospective observational study the cost-effectiveness of CERA once monthly in comparison with EpoB thrice weekly to maintain hemoglobin within the range 10.5–12 g/dL. The study was conducted in a cohort of 75 Moroccan CHP. In this study, patients who complied with the inclusion criteria were selected for a follow-up over two periods: the first period during 6 months (month –6 to 0); maintaining prior treatment with EpoB thrice weekly; the second for 6 months (month 0–6), after changing treatment to CERA once monthly. The cost-effectiveness analysis was conducted from the health care payer perspective; and applied decision analytic techniques; key model inputs included clinically effectiveness measures, which was measured by the clinical success rate of treatment, defined as the proportion of patients successfully maintaining Hb within the range of 10.5–12 g/dL, in the first period on EpoB and in the second period on CERA therapy, as well as drug acquisition costs for both treatments considered.

Iron use

Mean intravenous iron requirement in maintenance therapy with ESA was estimated according to two Moroccan studies Maoujoud et al¹² and Benamar,¹³ which are in accordance with the recent data provided by the *Dialysis Outcomes and Practice Patterns Study* (DOPPS) reports.¹⁴ For our model, we adopted an average use of intravenous iron for in-center hemodialysis patients at 100–125 mg/month.

RBCT requirement

Transfusion requirement for patients not receiving ESAs was based on two Moroccan studies (Benamar et al¹⁵ and Bahadi et al¹⁶), also we considered for our analysis the data reported by Remak et al⁴ and Naci et al,¹⁷ according to those studies; the average number of RBCT/year needed was estimated in our model at 10 red blood cell units/year.

Quality of Life

QALY is the survival weighted by health-related QOL, it is calculated by multiplying survival with utility; which is a measure of the preference for a specific health outcome, and usually acts as a single marker of health-related QOL. Utility ranges from 0, representing the worst imaginable health, to 1, representing perfect health.^{7,18} Considering previous studies, there is a continuous improvement in QOL with the increase in Hb level using ESA,^{1,17,19} we determinate the QALYs in our model at three Hb ranges: low Hb range (9–10.5 g/dL), high Hb range (>12 g/dL), and intermediate Hb range (10.5–12 g/dL). For baseline analysis to obtain QALYs,

survival was multiplied by utility at the three ranges. The utility estimate for dialysis patients treated with ESA was based on the published meta-analysis, randomized trials, and cohorts studies comparing different Hb levels achieved^{7,19,20} and from recent studies evaluating QOL in CHP.¹⁷ The average utility score for CHP treated with ESA and achieving Hb in the range 10.5–12 g/dL was estimated at 0.64,^{7,17,21–23} and at 0.63 for patients in the lower Hb range.^{3,7,22} As there is no evidence that utility scores continue to improve, once Hb level rise above 12.0, we considered only one utility score for all Hb above 12 g/dL at 0.65.^{3,7,20} For hemodialysis patients not receiving ESA, the mean Hb level was estimated by the Moroccan society of nephrology at 8.25 g/dL in the national registry of renal disease Magredial.²⁴ Thus, we considered in our model this level of Hb; with a corresponding utility score at 0.54, considering previous studies that had evaluated the QOL in CHP receiving only RBCT.^{19,20,22,25}

Table 1 Baseline clinical, costs, and input assumptions

Variable	Base-case estimate	Reference source
CERA cost per year	\$3,030.19	12
EpoB cost per year	\$3,288.49	12
CERA dose per month	106.4±50.1 µg	12
EpoB dose per week	6,104±3,178 iu	12
IV iron dose per month	100 mg ^a	12,13
IV iron cost per year	\$163.60	ANAM
Annual number of hospitalization days		4,16,17,31,32
Patients receiving ESA	8.5	
Patients receiving RBCT	11.65	
Cost of 1 day hospitalization	\$107.50 ^b	ANAM
Annual cost of hospitalization days		ANAM
Patients receiving ESA	\$913.75	
Patients receiving RBCT	\$1,252.37	
Number of RCB units per year	10	4,15,16,33
Cost of one unit of RBCs	\$92.40 ^c	ANAM
Annual cost of RBCT per year	\$924	ANAM
Utility for dialysis patient receiving RBCT	0.48 ^d	3,24,25,33
Utility for dialysis patient receiving ESA		
Hb 10.5 g/dL	0.63	1–3
Hb 10.5–12 g/dL	0.64	1,2,4–6
Hb 12 g/dL	0.65	1,3,7
Annual risk of death for dialysis patients, Hb 10.5–12 g/dL	0.077	1,7,19
Relative risk of death for dialysis patients, no ESA vs intermediate or low Hb range	1.14	1,7,19
Relative risk of death for dialysis patients, High vs intermediate or low Hb range	1.12	7,26–28

Notes: All costs are in US\$. ^aAverage iron cost in maintenance therapy; ^bcost includes basic explorations without cost of treatments; ^ccost of one filtered unit, including compatibility testing, cross-match, and infusion in day-hospital; ^dconsidering mean Hb 8.25 g/dL in patients receiving RBCT only.

Abbreviations: CERA, continuous erythropoietin receptor activator; EpoB, Epoetin Beta; RBC, red blood cells; RBCT, red blood cell transfusion; ESA, erythropoiesis stimulating agent; Hb, hemoglobin; iu, international unit; ANAM, Moroccan National Agency on Medical Insurance; IV, intravenous; vs, versus.

Mortality

Annual mortality in CHP treated with ESA in comparison with RBCT was based on two systematic reviews^{1,19} and a health economic evaluation of ESA in CKD.⁷ Annual mortality rates for each of the three Hb ranges in CHP receiving ESA and patients receiving RBCT were obtained from the same studies. For our model as reported in the meta-analysis of Tonelli et al¹⁹ and in the study of Naci et al,¹⁷ we considered that ESA use is associated with better survival in comparison with RBCT, and that mortality rate in the intermediate Hb level (10.5–12 g/dL) and low (<9–10.5 g/dL) is similar. Also, we integrate in our model the results of randomized controlled trials that demonstrated an increase in mortality with higher Hb level^{6,26–28} in comparison with low and intermediate ranges.

Hospitalization

Data relative to hospitalization in Moroccan hemodialysis patients receiving ESA were extrapolated from four observational studies.^{29–32} In the absence of RCT investigating the relationship between ESA use or Hb level, and the risk or the duration of hospitalization, we assumed in our model that there is no difference in hospital stay for the three Hb ranges, this assumption is comforted by previous studies.^{17,20,33} Hospitalizations in patients receiving RBCT only in the model were based on Moroccan observational data reported by Bahadi et al,¹⁶ and the studies of Remak et al⁴ and Naci et al;¹⁷ considering those reports, ESA use in CHP is associated with a decrease in hospitalization estimated at –37% in comparison with patients receiving RBCT. Baseline clinical, costs and assumptions are reported in Table 1.

Economic analysis

In our analysis, we adopted the perspective of the National health care payer in Morocco, for a time horizon of 1 year. So, for CERA and EpoB, we considered direct medical cost including ESA acquisition cost, iron usage, and hospitalization. For RBCT, we based our estimation on the hospital cost of one unit of transfused filtered red blood cells, including compatibility testing, cross-matching, and the infusion in day hospital. All costs were obtained from the prices approved by the Moroccan National Agency on Medical Insurance (ANAM), they were collected every 3 months, reported in Moroccan dirhams (MAD) then converted to US dollar (\$) (in 2013; 1 US\$ = 9,297 MAD). A discount rate of 3% was applied to both costs and utilities, all analyses were performed using TreeAge Pro 2015 (TreeAge Software, Williamstown, MA, USA).

Cost-utility analysis

In order to calculate costs, QALYs and increments associated with CERA, EpoB, and RBCT alone, a decision analysis model was constructed in TreeAge Pro 2015 (TreeAge Software). Key model inputs included for CERA, EpoB, and RBCT; medical costs, survival, and utilities depending on Hb levels. Model outputs were expected cost-utility ratio and the incremental cost-utility ratio (ICUR), which represent the additional cost and utility obtained, when CERA or EpoB is compared with the RBCT regime. As there is no official incremental cost-utility threshold for willingness to pay (WTP) in Morocco; being considered as ideal for the acceptance of a given health intervention, we compared ICUR with different hypothetical WTPs.

Sensitivity analysis

Given the fact that our model involves some uncertainties and assumptions, we performed one-way sensitivity analysis; by varying baseline estimates within a range of potentially reasonable values, particularly the number of hospitalizations, the mean length of hospital stay, ESA costs, utilities, and survival estimations. Also, probabilistic sensitivity analysis was conducted by a Monte Carlo simulation; to better test the overall uncertainty in our model. We varied the input parameters used in clinical effectiveness, utility, and cost estimates. A normal distribution was used for clinical parameters, and a log-normal distribution was applied to the cost estimates.

Results

In Table 2, cost, QALYs, and incremental associated with CERA and EpoB administration, compared to treatment with RBCT, are summarized. The total cost per patient was estimated at \$2,176.37, \$4,107.01, and \$4,356.69 for RBCT, CERA, and EpoB, respectively. In our model, ESA administration was associated with an increase in patients' QOL by 0.1 QALYs per annum in average, compared to treatment with RBCT alone, with an incremental cost at \$1,930.64 for CERA and \$2,189.32 for EpoB. Therefore, the cost-utility ratio was calculated at 4,423.52, 6,955.50, and 7,406.38 \$/QALY for RBCT, CERA, and EpoB, with an ICUR of CERA

and EpoB in relation to RBCT at 19,606.40 and 22,466.09 \$/QALY, respectively. The cost-utility diagram is resumed in Figure 1.

For the one-way sensitivity analysis, the inputs in the model were allowed to vary within clinically plausible ranges. Table 3 shows sensitivity of the base-case ICUR of CERA and EpoB relative to RBCT in different scenarios tested. The model was most sensitive to hospitalization costs, hospital stay, and annual number of RBCT units, any increase in those parameters resulted in a decrease in ICURs as reported in Table 3. Assuming utility and survival improvement with ESA use while all costs remained the same resulted in a decrease in ICUR at 13,429 \$/QALY for CERA and 15,331 \$/QALY for EpoB. Testing the hypothesis of equal mortality rate between ESA use and RBCT; only resulted in an ICUR at 20,878 \$/QALY and 23,940 \$/QALY, respectively. Decreasing the acquisition cost of CERA and EpoB by 25% resulted in ICUR at 11,911 \$/QALY and 14,088 \$/QALY, respectively.

The probabilistic sensitivity analysis was performed using a second-order Monte Carlo simulation, for this analysis, 10,000 simulated trials were run. The main results of our model were unchanged; CERA and EpoB therapy was always more costly and more effective than RBCT as shown in the scatter plots of Figures 2 and 3. A cost-effectiveness acceptability curve was also obtained from the simulation (Figure 4). This graph indicates the probability that the use of CERA and EpoB being cost-effective compared with RBCT at different levels of a maximum acceptable threshold for WTP. At all WTP thresholds below 19,500 \$/QALY gained, RBCT was the cost-effective as compared with both ESAs, and a WTP at 19,666 \$/QALY resulted in a probability that CERA was cost-effective at 65%. Over this threshold, CERA was always the best option.

Discussion

This cost-utility analysis shows that treating anemia in CHP with CERA or EpoB is associated with a substantial clinical benefit and results in significant additional cost relative to RBCT. Elaborate sensitivity analyses revealed that the health care payer should be willing to pay

Table 2 Expected costs, QALYs, and incremental

Intervention	Average cost (\$)	Incremental cost (\$)	Average QALY	Incremental QALY	Cost-utility ratio	ICUR (\$/QALY)
RBCT	2,176.37	–	0.491	–	4,423.52	–
CERA	4,107.01	1,930.64	0.591	0.1	6,955.50	19,606.4
EpoB	4,365.69	2,189.32	0.591	0.1	7,406.38	22,466.09

Abbreviations: CERA, continuous erythropoietin receptor activator; EpoB, Epoetin Beta; RBCT, red blood cell transfusion; ICUR, incremental cost-utility ratio; QALY, quality-adjusted life-year.

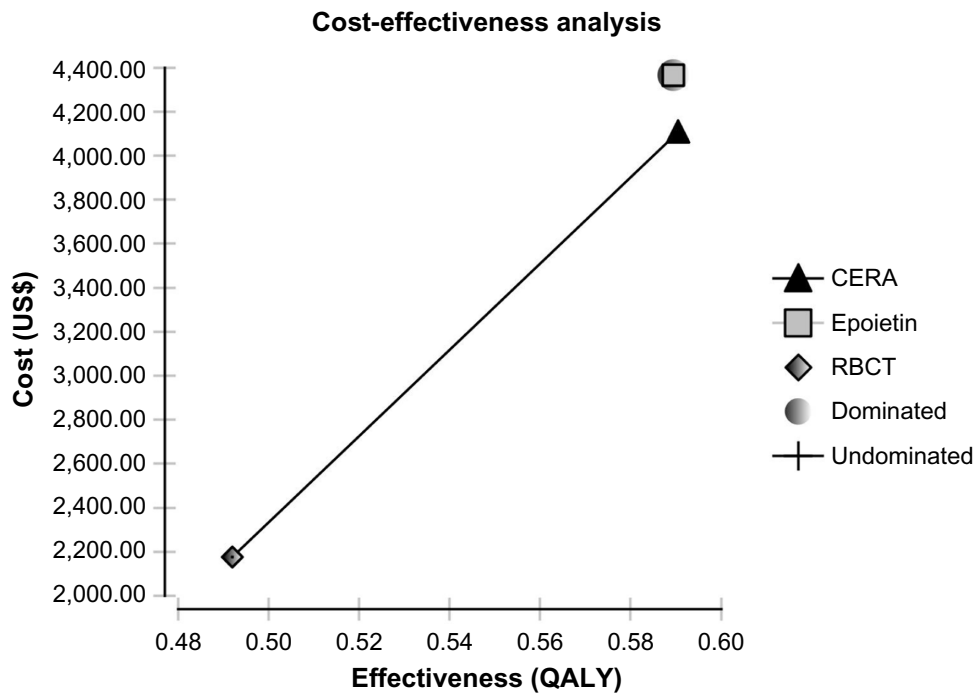


Figure 1 Cost-utility diagram.

Notes: The diagonal line represents the cost-utility ratio for CERA compared with management of anemia with RBCT. Treatment with EpoB above the line is ruled out by simple dominance (less effective and more costly compared with CERA).

Abbreviations: CERA, continuous erythropoietin receptor activator; EpoB, Epoetin Beta; RBCT, red blood cell transfusion; QALY, quality-adjusted life-year.

at least \$19,666 per additional QALY for CERA to become cost-effective compared with a strategy without ESA use. In Morocco, there is no official adopted threshold value of the WTP; as almost all emerging countries. The World Health Organization consider an incremental cost per QALY gained or an incremental cost-effectiveness ratio of a medical intervention below one time of the gross domestic product (GDP) per capita as maximum cost-effective, between 1 and 3 times of GDP per capita as cost-effective, and more than 3 times of GDP per capita as not cost-effective.³⁴ According to the World Bank,³⁵ the 2013 Moroccan GDP per capita was estimated at \$3,092, considering this value, a threshold of 9,276 \$ would be adopted as maximum limit for a health procedure to be considered as being cost-effective; therefore, CERA and EpoB would be considered technically as not cost-effective in our model. But this is a misinterpretation of the main results of our study. Indeed, the comparison between ESA and RBCT in the management of anemia has been considered as counter-factual;¹⁷ considering the fact that the use of ESA as a treatment of anemia in dialysis patients is now unanimously considered as the standard of care;³⁶⁻³⁹ following international clinical practice guidelines for anemia management in CKD⁴⁰ and Moroccan national guidelines,⁴¹ as RBCT is linked to transfusion-transmitted infections, immunologic sensitization complicating transplantation, and

iron overload.^{1,2} In our model, it was mandatory to include RBCT as a reference procedure; because at our knowledge, this is the first cost-utility analysis of ESA including CERA.^{9,11} None of the previous cost-utility or cost-effectiveness studies had considered the last long-acting ESA for anemia in such population. Also, in Morocco, our study is the first to evaluate ESA at all. As reported recently by Schmid,⁹ there are few pharmaco-economic studies evaluating the cost-utility of CERA; in 18 publications included in his analysis, only one study published as an abstract, reported data about the cost and QALY relative to CERA use in Brazilian dialysis patients;⁴⁰ using a model of a hypothetical cohort of CHP treated with CERA or epoetin, the analysis showed that epoetin treatment was more cost-effective than CERA treatment. Unfortunately, it was not possible to compare this study with our results since the access was limited to an abstract. We evaluated the robustness of the main finding in extensive sensitivity analysis, and found that our model was sensitive to hospitalizations length and cost, number of RBCT units, and utility estimates. These parameters have been highlighted in previous studies as major drivers of cost variations among chronic dialysis patients.^{1,7,17,33} In addition, wherever uncertainty exists, we have made some assumptions favorable to RBCT, as we did not consider the costs relative to complications of blood transfusion, and hospitalization costs were based only on the minimum daily

Table 3 Results of one-way sensitivity analysis

Variable	Range of variations			Corresponding ICUR of CERA and EpoB relative to RBCT	
	Low	Base-case	High	Low	High
Annual number of hospital days of patients receiving RBCT	-25%	11.65	+25%	CERA: 22,494 EpoB: 25,384	15,954 18,775
Mean number of RBCT units per year	-25%	10	+25%	CERA: 22,961 EpoB: 25,856	17,254 20,089
Cost of RBCT (one unit)	-30% ^a	\$92.40	+30% ^b	CERA: 22,484 EpoB: 25,373	14,664 17,472
Cost of hospitalization per 1 day	-40% ^c	\$107.50	+200% ^d	CERA: 20,650 EpoB: 23,240	12,530 15,120
Average monthly use of iron	50 mg	100 mg	200 mg	CERA: 18,754 EpoB: 21,622	21,246 24,140
Average utility score for patients on RBCT	0.42 ^e	0.50	0.56 ^f	CERA: 9,305 EpoB: 10,604	23,992 27,555
Average utility score for patients on ESA	-0.05	0.64	+0.05	CERA: 37,297 EpoB: 43,099	13,429 15,331
Odds ratio of death RBCT vs ESA	1 ^g	1.14	1.2 ^h	CERA: 20,878 EpoB: 23,940	17,014 19,469
Average cost of ESA	-25% ⁱ	Mean cost of CERA/EpoB	+25%	CERA: 11,911 EpoB: 14,088	27,295 30,902

Notes: All costs are in US\$. ^aCost of standard unit; ^bIncluding cost of 1 day hospitalization; ^cexcluding costs of basic investigations; ^dincluding cost of biologic and radiologic investigations and basic treatments; ^eassuming the worst quality of life associated with RBCT; ^fassuming the best quality of life associated with RBCT; ^gconsidering the same survival in ESA and RBCT; ^hconsidering best survival associated with ESA; ⁱconsidering standard market variations.

Abbreviations: CERA, continuous erythropoietin receptor activator; EpoB, Epoetin Beta; RBCT, red blood cell transfusion; ICUR, incremental cost-utility ratio; ESA, erythropoiesis stimulating agent.

cost allowed by the National Agency of Medical Insurance without considering medications and investigation costs. Not surprisingly, when assuming higher costs of hospital stay per day, ESA use become more cost-effective, as reported in the systematic review of Ferguson et al.¹ Our analysis has

several strengths. This is the first cost-utility study of ESA in the management of anemia in CHP that consider CERA; to be published in peer-review journal. Also, our results are as close to real practice as possible; as CERA and EpoB doses, costs, and efficacy were derived from our previous prospective

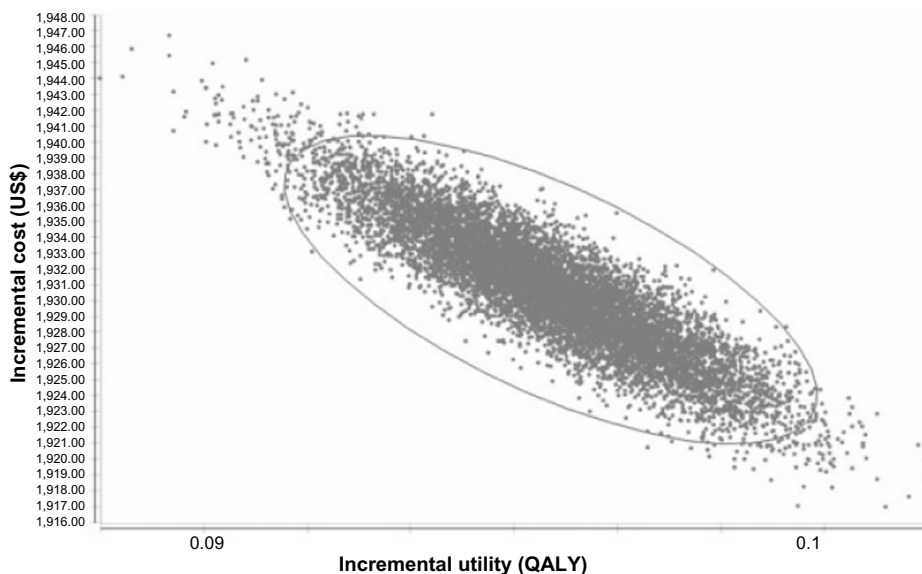


Figure 2 Results of probabilistic sensitivity analysis of CERA vs RBCT.

Notes: This figure shows the incremental cost and QALY for CERA vs RBCT based on 10,000 iterations, CERA is more expensive and more effective than RBCT (the scatter-plot is in the northeast quadrant).

Abbreviations: CERA, continuous erythropoietin receptor activator; RBCT, red blood cell transfusion; QALY, quality-adjusted life-year; vs, versus.

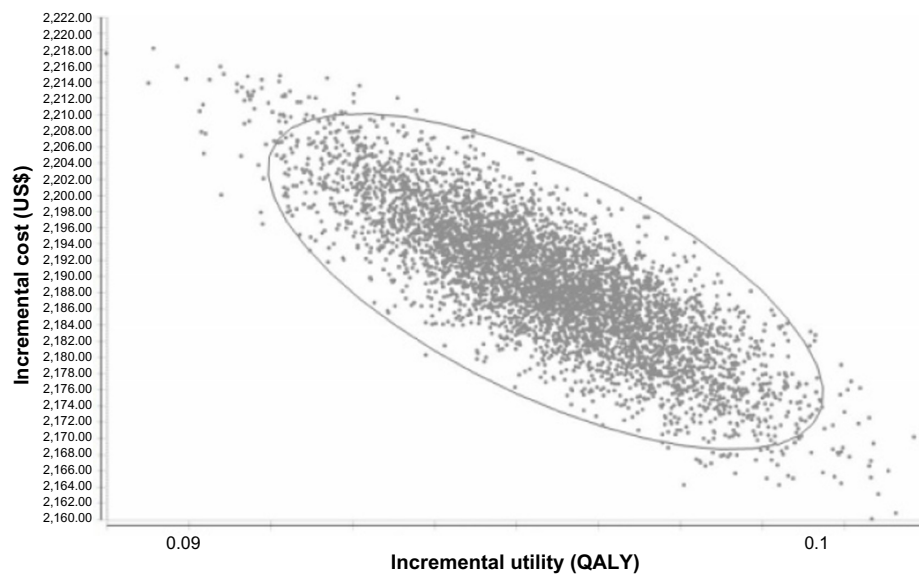


Figure 3 Results of probabilistic sensitivity analysis of EpoB vs RBCT.

Notes: This figure shows the incremental cost and QALY for EpoB vs RBCT based on 10,000 iterations, EpoB is more expensive and more effective than RBCT (the scatter-plot is in the northeast quadrant).

Abbreviations: EpoB, Epoetin Beta; RBCT, red blood cell transfusion; QALY, quality-adjusted life-year; vs, versus.

observational real-life study.¹² Indeed, we have tried to deal with uncertainties and assumptions in our model with sensitivity analysis. Other economic evaluations did not fully test the assumptions though sensitivity analysis. There are some limitations to our study. Considering the lack of data on

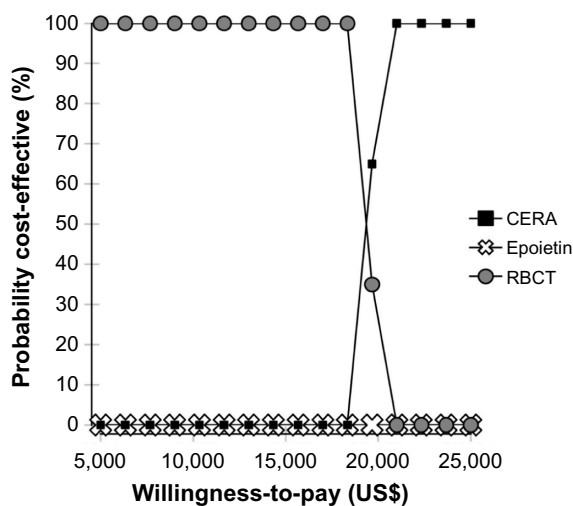


Figure 4 Cost-effectiveness acceptability curve (CEAC) of CERA and EpoB compared with RBCT.

Notes: This figure shows the probability that CERA or RBCT is the most cost-effective treatment for different willingness to pay (WTP). A WTP is the price that a society that is willing to pay for a QALY. Overall CERA is more costly and more effective than RBCT, which means that if the WTP increases, the probability that CERA becomes the most effective treatment increases. A WTP at 19,666 \$/QALY resulted in a probability that CERA was cost-effective at 65%. Over this threshold, CERA was always the best option.

Abbreviations: CERA, continuous erythropoietin receptor activator; EpoB, Epoetin Beta; RBCT, red blood cell transfusion; QALY, quality-adjusted life-year.

some epidemiological parameters such as mortality rate and utility scores in Moroccan hemodialysis patients, we based our analysis on results of randomized controlled trials and systematic reviews that have been conducted on this topic; to limit this potential bias. Also, our baseline estimates of hospitalizations rates and duration are based on some Moroccan retrospective studies,^{15,16,24,29-31} for this reason, we have also consider the results of previous cohort studies and analysis conducted in other countries. We did not include indirect costs such as loss of productivity and travel costs. Given the fact that the perspective was that of a health care payer, and not a societal one, and in the absence of evidence that ESA use increases employment rates in hemodialysis patients. Makes it unlikely that adopting societal perspective would have changed our results.^{1,7,17,19,33} The results of our analysis have several potential implications for clinical practice, health policy, and futures research. Our study shows the cost-utility associated with CERA and EpoB in a clinical and market context close to real-life. Also, we believe that our analysis would inform policy makers about optimal planning relative to ESA use.

Conclusion

In conclusion, our study suggests that managing anemia in dialysis patient with ESA may results in better outcomes with higher overall costs. Considering different assumptions, we found substantial variability in the estimates of the cost-utility and incremental of using CERA or EpoB, nevertheless, our

findings can help future investigators to design better cost-effectiveness and cost-utility studies.

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Disclosure

The authors report no conflicts of interest in this work.

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