

# Economic Evaluation of Plerixafor for Stem Cell Mobilization

Steven M. Kymes, PhD; Iskra Pusic, MD; Dennis L. Lambert, PhD; Martin Gregory, BA; Kenneth R. Carson, MD; and John F. DiPersio, MD, PhD

**H**igh-dose chemotherapy in conjunction with autologous peripheral stem cell transplantation (ASCT) has emerged as a preferred treatment modality for a variety of hematologic malignancies including multiple myeloma (MM), non-Hodgkin lymphoma (NHL), and Hodgkin lymphoma (HL).<sup>1-3</sup> The 2 most commonly used mobilization regimens are the cytokine granulocyte colony-stimulating factor (G-CSF) and G-CSF plus chemotherapy.<sup>4</sup> However, failure rates with current mobilization regimens are estimated to be between 5% and 30%.<sup>5,6</sup> This failure adds substantially to the cost of this already costly procedure due to the need for multiple apheresis sessions, as well as the implementation of costly remobilization protocols.<sup>7</sup> An additional economic burden of this reduced efficacy is increased morbidity and mortality, as transplantation with suboptimal stem cell numbers may lead to prolonged hospitalization and increased transfusion requirement as fewer patients proceed to engraftment.

Plerixafor is a new agent for stem cell mobilization which is used in conjunction with G-CSF or on its own. Plerixafor is a direct inhibitor of the interaction between the stromal cell–derived factor 1, expressed on bone marrow stromal cells, and its receptor CXCR4, expressed on CD34+ stem cells. Several studies have shown that plerixafor, when used with G-CSF, results in successful stem cell mobilization in heavily pretreated patients with NHL, HL, and MM.<sup>8,9</sup> Investigators in 2 phase III, multicenter, randomized, double-blind, placebo-controlled studies, who compared G-CSF plus plerixafor (G+P) with G-CSF alone for mobilization of stem cells in patients with MM and NHL, reported that patients mobilized with G+P were significantly more likely to achieve the target CD34+ cell count with fewer apheresis sessions and less need for a rescue remobilization.<sup>10</sup> Thus, this increased efficacy reduces the required number of apheresis sessions, reduces the likelihood of remobilization, and increases the likelihood of successful engraftment. However, we are not aware of any previous group that has investigated this question using rigorous economic methods.

We conducted an economic evaluation of the cost utility of the use of G+P as a first-line treatment for stem cell mobilization in patients with NHL versus use of G-CSF alone. Data for the model came from the Washington Uni-

**Introduction:** Autologous peripheral stem cell transplantation (ASCT) with high-dose chemotherapy is a preferred treatment for relapsed non-Hodgkin lymphoma (NHL) patients. Estimated failure rates with current stem cell mobilization (SCM) regimens are 5% to 30%. Granulocyte colony-stimulating factor (G-CSF) with plerixafor (G+P) is superior to G-CSF alone for SCM in heavily pretreated NHL patients.

**Objectives:** To conduct a cost-utility evaluation of G+P versus G-CSF as a method for SCM in patients with diffuse large B-cell lymphoma (DLBCL), the most common subtype of NHL.

**Methods:** A Markov model simulated the care process of DLBCL patients undergoing ASCT using data from the Washington University site of the plerixafor phase III study. Other data and utilities were taken from the literature. Costs were Medicare allowable. Using microsimulation we estimated the incremental cost-utility ratio (ICUR) over the patient's remaining lifetime.

**Results:** The expected lifetime cost of providing care for DLBCL patients using G+P was \$25,567 more than G-CSF, but they accumulated 1.74 more quality-adjusted life-years (QALYs) for an ICUR of \$14,735 per QALY. In sensitivity analyses this result was robust to clinically relevant changes in assumptions.

**Conclusions:** Using G+P for SCM in ASCT of patients with DLBCL meets accepted standards of cost-effectiveness, primarily because of its effectiveness in SCM.

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**In this issue**

Take-Away Points / p34

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Full text and PDF

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eAppendix

**For author information and disclosures, see end of text.**

### Take-Away Points

Plerixafor with granulocyte colony-stimulating factor (G-CSF) has been shown to be superior to G-CSF alone for stem cell mobilization in heavily pretreated patients with non-Hodgkin lymphoma.

- Use of plerixafor plus G-CSF for stem cell mobilization in autologous stem cell transplantation of patients with diffuse large B cell lymphoma has a lifetime cost of \$25,576 more than G-CSF alone.
- Plerixafor plus G-CSF provides 1.74 more quality-adjusted life-years.
- It thus meets most accepted standards of cost-effectiveness.

versity School of Medicine, site of the plerixafor phase III study.<sup>11</sup> We constructed a decision-analytic model to replicate the series of events experienced by a patient undergoing stem cell mobilization, apheresis, and ASCT. We conducted these analyses taking a societal perspective and using a microsimulation approach to model estimation.

## METHODS

### Model Description and Data Sources

We constructed a Markov decision model using TreeAge software (TreeAge Software, Inc, Williamstown, Massachusetts) to compare the cost and effectiveness of using G+P for stem cell mobilization in patients undergoing hematopoietic stem cell transplantation for treatment of relapsed diffuse large B-cell lymphoma (DLBCL), the most common subtype of NHL, with those receiving only G-CSF for mobilization. Model estimation was performed using a microsimulation process.<sup>12</sup> The Markov model is a mathematical representation of an iterative process with a “Markov cycle” representing the length of the iterative process.<sup>13</sup> In this case, the iterative process describes the transplantation process from apheresis through transplant and beyond. Initially, in the first cycle, the individual enters the model at the apheresis arm and begins cell collection (see **Figure 1**). Continuing the first cycle, if cell collection is successful, the individual then enters the transplant arm and undergoes stem cell transplantation, subsequently entering the posttransplant cycle. The individual completes the first year of the process in the posttransplant cycle. In this part of the model, the individual cycles through the posttransplant cycle 1 year at a time, each year facing a probability of cancer recurrence and death from natural causes. The cycling through the posttransplant arm ends when the individual has a recurrence of DLBCL or dies from other causes (see explanation below). Microsimulation refers to a process where only 1 individual is sent through the model at a time, facing various probabilities for occurrences as he proceeds. Each individual completes all cycles before another individual enters the model. The model described here has 3 elements, 2 of which have distinct iterative processes:

- (1) the collection of stem cells for transplant (Markov cycle = apheresis session);
- (2) the engraftment process (noniterative); and
- (3) the post-engraftment period (Markov cycle = 1 year).

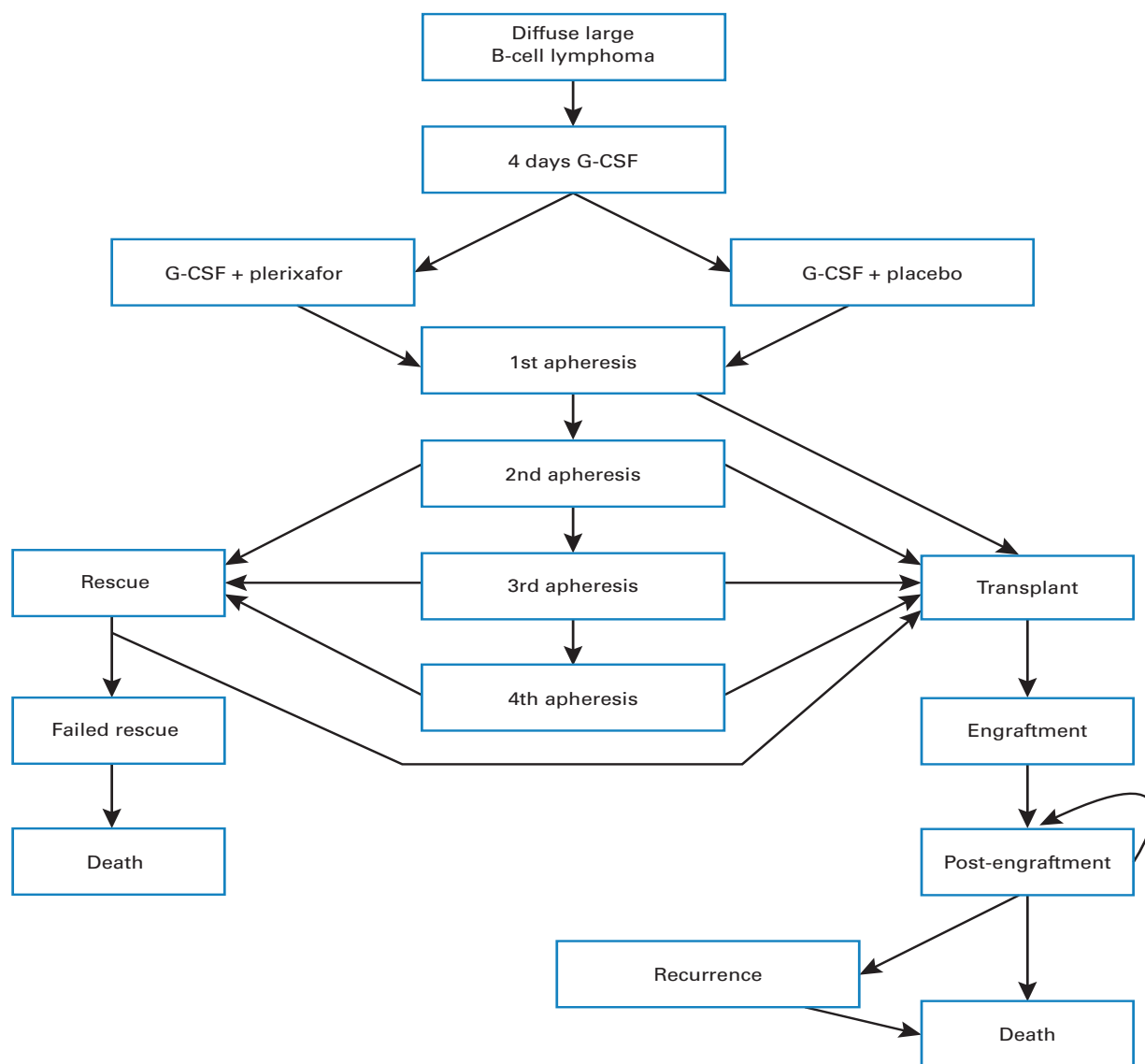
The data for the first part were taken from the participants randomized (N = 20) at Washington University School of Medicine as part of a phase III trial of plerixafor.<sup>11</sup> In the phase III trial, patients preparing to undergo ASCT were given 10 µg/kg of G-CSF for up to 8 days. Beginning on day 4, they were given either 240 µg/kg of plerixafor or the placebo daily for up to 4 days while undergoing apheresis. Apheresis began in the morning of day 5 and continued daily for up to 4 days or until at least  $5 \times 10^6$  CD34+ cells per kilogram were collected. Those patients who failed to collect at least  $0.8 \times 10^6$  CD34+ cells per kilogram after 2 apheresis sessions or at least  $2 \times 10^6$  CD34+ cells per kilogram in 4 apheresis sessions were given the option of entering an open-label rescue procedure. After a minimum 7-day rest period, the rescue patients received a course of G+P (240 µg/kg) identical to the treatment plan described above and underwent up to 4 sessions of apheresis. Those who failed to collect sufficient cells in rescue either went to transplant with a suboptimal number of cells or did not receive transplantation.

Transition probabilities for the Markov matrix were estimated as the probability that a person would require the next apheresis session and were calculated as the proportion of people in the current session who proceeded to the next apheresis session. This proportion was parameterized as a random variable using the mean and variance to estimate a beta distribution. Costs were estimated by applying Medicare-allowable charges to actual utilization of participants prior to undergoing the stem cell mobilization process. Anyone who did not proceed to the transplant arm (high-dose chemotherapy and engraftment after stem cell mobilization and apheresis) was considered to have died and not to have generated any additional costs or benefits for the model.

In the model, participants “wait” for stem cell engraftment after transplantation. During that time they require transfusion support and remain at high risk for infections, likely requiring antibiotics. Costs during this period were based upon the resources used by patients enrolled in the clinical trial, and costs were those that were Medicare allowable in Eastern Missouri.

After successful engraftment, “participants” in the model entered the post-ASCT segment of the model. For the first 3 years posttransplant, participants face a probability of re-

■ **Figure 1.** Schematic of the Markov Model



G-CSF indicates granulocyte colony-stimulating factor.

currence of lymphoma, based on the report by Fenske and colleagues.<sup>14</sup> This probability is 38% in the first year, with a total probability over 3 years of 50% (see [eAppendix](#) at [www.ajmc.com](#)).

If a participant had a recurrence, we made the conservative assumption that it would be fatal. We also assumed that if the participant survived for 3 years posttransplant, her annual mortality rate reflected that of the general public. This assumption was tested in sensitivity analyses.

Key model probabilities, costs, and utility values are summarized in [Table 1](#) and detailed in the eAppendix.

### Measuring the Benefit of Treatment

In valuing the outcomes of a medical intervention, quality of life is often a key outcome, assuming survival is achieved.<sup>15</sup> In our investigation, we measured quality of life using “utility,” which, in contrast to clinical measures, is a preference-based measure that quantifies the person’s perception of the importance of functional limitation. Utility is measured on a scale from 0.0 to 1.0, with zero indicating the value of a state of health comparable to death and 1.0 the value for perfect health. The methods by which utility is measured have been described in detail elsewhere.<sup>16</sup>

■ METHODS ■

■ **Table 1.** Model Probabilities, Costs, and Utility Values

Variable	Value	Range for Sensitivity Analysis
<b>Probability of collecting &gt;2 × 10<sup>6</sup> cells</b>		
After 1st apheresis in plerixafor arm	0.30	
After 2nd apheresis in plerixafor arm	0.00	
After 3rd apheresis in plerixafor arm	0.29	
After 4th apheresis in plerixafor arm	0.80	0.5-1
After 1st apheresis in placebo arm	0.00	
After 2nd apheresis in placebo arm	0.00	
After 3rd apheresis in placebo arm	0.17	
After 4th apheresis in placebo arm	0.75	
<b>Probability of rescue</b>		
After 1st apheresis in plerixafor arm	0.00	
After 2nd apheresis in plerixafor arm	0.00	
After 3rd apheresis in plerixafor arm	0.00	
After 4th apheresis in plerixafor arm	0.00	0-1
After 1st apheresis in placebo arm	0.00	
After 2nd apheresis in placebo arm	0.36	
After 3rd apheresis in placebo arm	0.20	
After 4th apheresis in placebo arm	0.00	
<b>Transplant costs (\$)</b>		
Cost of hospital admission (HCPCS 99223)	206.74	
Cost of apheresis—procedure (HCPCS 38206)	804.99	
Cost of apheresis—processing (HCPCS 86890)	49.77	
Cost of stem cell infusion (HCPCS 99241)	132.89	
Nursing charge for injection (HCPCS 96372)	22.74	
Cost of discharge (HCPCS 99238)	73.13	
Cost of transplant (MS-DRG-9)	45,721 <sup>a</sup>	
Daily physician charge	96.08	
G-CSF cost	Weight (kg) × 10 × 0.69871	
Plerixafor cost	Weight (kg) × 240 × 0.26851	
<b>Resource utilization posttransplant</b>		
Antivirals		
Valacyclovir	5.572 <sup>b</sup>	
Acyclovir	0.2885 <sup>b</sup>	
Red blood cells (P9021)	136.82	
Platelets (P9019)	73.25	
Hospital days	1096 <sup>c</sup>	
<b>Quality of life</b>		
Day before transplant	0.75	
14 days posttransplant	0.53	
3 months posttransplant	0.78	
<b>Posttransplant survival</b>		
Annual risk of death	2004 life table	
Probability of recurrence—3 years	0.5	0.75-0.909

G-CSF indicates granulocyte colony-stimulating factor; HCPCS, Healthcare Common Procedure Coding System; MS-DRG-9, Medicare Severity-Related Groups, Bone Marrow Transplant.  
<sup>a</sup>MS-DRG-9 charge for cost of transplant: Personal communication with Rebecca Rakers, Senior Financial Analyst, May 2009.  
<sup>b</sup>Average retail price in May 2010. See eAppendix at www.ajmc.com.  
<sup>c</sup>Estimate by St. Louis Business Health Coalition, 2009.

The utility measure is used to calculate a quality-adjusted life-year (QALY). The QALY is a measure of a person's expected life span that is weighted by the quality of life enjoyed during those years. For example, assume that living with congestive heart failure is found to have an associated utility loss of 0.35 (or 35%), for a final utility of 0.65. Each year the person would experience a quality of life that is 0.65 of a year spent in perfect health, or a QALY of 0.65. If they live for 5 years they would accumulate 3.25 QALYs, compared with the 5.0 QALYs of someone living in perfect health. In the context of this study, the QALYs accumulated would represent the years of survival of those patients who undergo high-dose chemotherapy and engraftment, multiplied by the quality of life they experience during treatment and after engraftment. There have been a number of studies that examined the utilities for patients with NHL, but few have looked specifically at patients who underwent ASCT. Van Agthoven et al compared the utility for patients undergoing peripheral blood stem cell transplantation with that for patients undergoing autologous bone marrow transplant.<sup>17</sup> They estimated the utility for NHL patients the day before ASCT, 14 days post-ASCT, and 3 months post-ASCT to be 0.75, 0.53, and 0.78, respectively. We validated these estimates by comparing them with similar work by other investigators. Doorduijn et al examined patients undergoing cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone (CHOP) chemotherapy for NHL.<sup>18</sup> They estimated utility scores for NHL patients at the time treatment was initiated as 0.74 for patients with an International Prognostic Index score of 0 to 1 and 0.44 for an International Prognostic Index score of 2 to 3. Patient-reported utility returned to pretherapy scores at 3 months. Uyl-de Groot et al elicited utility scores for NHL patients in remission after undergoing autologous bone marrow transplant at 6 months, 12 months, and 24 months to be 0.63, 0.84, and 0.91, respectively.<sup>19</sup> Therefore, in our model, patients were assigned a utility score of 0.75 while undergoing apheresis, 0.53 during high-dose chemotherapy and engraftment, and 0.78 postengraftment (see Table 1). We believe that estimation of an annual utility score of 0.78 for people who are asymptomatic following ASCT is very conservative since this is comparable to the utility reported by people with severe macular degeneration<sup>20</sup> and reflects more utility loss than recent stroke victims (0.145).<sup>21</sup> However, we believe that this conservative approach is appropriate given that the expected benefit of treatment with plerixafor is to increase the probability of progression to ASCT (and thus survival), and to overestimate the benefit of survival would be to favor treatment with plerixafor.

Our time frame for this evaluation was the patient's lifetime, the perspective of the analysis was societal, and all costs and utilities were discounted at 3%.

## Estimation of the Model

Our primary outcome in estimation of this model was the incremental cost-utility ratio (ICUR):

$$\frac{\text{Cost}_P - \text{Cost}_G}{\text{QALY}_P - \text{QALY}_G}$$

where *P* denotes the average cost accrued (and QALYs gained) for someone who receives G+P as first-line treatment, and *G* denotes the cost and QALYs for those who received G-CSF alone as first-line treatment. The ICUR represents the cost of "buying" 1 additional year of perfect health. Cost-effectiveness of an intervention is determined by comparing the ICUR with the policy maker's willingness to pay (WTP) to gain a QALY.

We estimated the model using a microsimulation approach.<sup>12</sup> Microsimulation is a method of mathematical modeling in which all sources of uncertainty are recognized and incorporated into the estimation. Conceptually, individual participants proceeded through the model 1 at a time, accumulating costs and benefits (ie, QALYs) as they progress through the tree. Each time they approach a "fork" in the pathway (ie, a probability node), the path they choose from there is determined by a random drawing from the distribution at that node. For instance, in the model presented here, a participant who has completed engraftment must proceed to the probability node to determine whether he will have a relapse. At that node there is a 38% probability that he will have a relapse; therefore (again conceptually), the participant "flips a coin" to determine the direction in which he will proceed. After this participant has made his way through the model, the next one takes her turn. After all participants in the cohort have completed their journey, the ICUR is estimated by taking the average of the cost and benefits of these participants. Our primary estimation of the model was conducted using a Monte Carlo microsimulation with 500,000 trials (participants).

The influence of uncertainty on model results was evaluated in 2 ways. First, we performed 1-way sensitivity analyses to determine for which parameters a change in the base value resulted in a change in the cost-effectiveness decision (ie, if plerixafor was found to be cost-effective in the base case, the change in the value would result in it not being cost-effective, or vice-versa).<sup>22</sup> For this purpose we used WTPs of \$50,000 and \$100,000 per QALY as our thresholds for determination of cost-effectiveness. In order to evaluate the overall stability of the model, we conducted a probabilistic sensitivity analysis using a Monte Carlo simulation to estimate net-benefit acceptability curves.<sup>23</sup> All variables in the model were parameterized as distributions for this purpose.

■ **Table 2.** Cost-Utility and Cost-Effectiveness Results

Strategy	Total Cost, \$	Incremental Cost, \$	Total Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	Incremental Cost-Effectiveness Ratio (Cost per QALY), \$
G-CSF alone		67,730		5.05	
G-CSF plus plerixafor	93,180	25,450	6.80	1.75	14,574

G-CSF indicates granulocyte colony-stimulating factor; QALY, quality-adjusted life-year.

## RESULTS

### Summary of Results of Phase III Trial at Washington University School of Medicine

Twenty participants with DLBCL were randomized at Washington University (N = 20). Ten were randomized to receive G+P as a first-line regimen for stem cell mobilization, and 10 were randomized to G-CSF + placebo (with plerixafor as part of the rescue protocol). In the G+P arm all patients (10/10) achieved the minimal goal of CD34+ cells after initial mobilization and proceeded to ASCT, while in the G-CSF + placebo arm only 5 of 10 achieved the minimal goal and proceeded directly to ASCT. Of the 5 remaining patients in the G-CSF + placebo arm, 1 was considered to be a poor candidate for rescue and did not proceed to ASCT. Four patients underwent the rescue protocol with G+P, but only 2 of 4 achieved the minimal CD34+ cell count required and went to ASCT. Therefore, 3 of 10 patients (30%) from the original G-CSF + placebo arm failed the mobilization process and did not proceed to ASCT.

### Summary of Cost-Utility and Cost-Effectiveness Analysis

The results of our analysis are presented in **Table 2**. The expected cost of providing care to patients with relapsed DLBCL referred to autologous transplant over their lifetime was \$93,180 when G+P was used as a first-line treatment for stem cell mobilization. This was \$25,450 more than the expected cost of using G-CSF alone as the first-line treatment. People who received G+P as a first-line treatment had an expected benefit of 6.80 QALYs following treatment. That was 1.75 QALYs more than people who had G-CSF alone as their first-line treatment. This was largely the result of the improved likelihood of proceeding to ASCT following mobilization and apheresis. The ICUR for use of G+P as a first-line mobilization regimen was \$14,574 per QALY.

As this intervention primarily affected the stem cell mobilization process, we also evaluated the cost-effectiveness of having an additional patient proceed to ASCT as a secondary outcome (taking the payer’s perspective). We found that mobilization using G+P as a first-line treatment cost \$18,113

more per patient than did G-CSF alone. As 100% of G+P participants progressed to ASCT versus 70% of those treated with G-CSF alone, the incremental effectiveness of plerixafor was 30%. This yielded an incremental cost-effectiveness ratio of \$60,377. In other words, it cost an additional \$60,377 for each incremental patient who progressed to ASCT using G+P versus those who progressed to ASCT relying on a stimulation protocol with G-CSF alone.

### One-Way Sensitivity Analysis

As our base case finding was that the ICUR for plerixafor was well below our critical WTP value for evaluation of cost-effectiveness (\$14,574 per QALY vs \$50,000 per QALY), we focused primarily on identifying those factors which, when varied across a clinically relevant range, would result in use of plerixafor as a first-line treatment not meeting our most stringent standard for cost-effectiveness (\$50,000). The factors that were found to be most influential were those related to stem cell mobilization/apheresis, such as the probability of progression to rescue as well as the probability of failure to progress to ASCT. Specifically, we found that if the probability of rescue for G+P participants was more than 40% (vs 0%), or if the probability of failure to progress to ASCT for G+P participants was greater than 23% (vs 0% in the base model), then G+P would not meet the standard for cost-effectiveness at a WTP of \$50,000. Similarly, if the probability of disease recurrence in the first year was greater than 87% (vs 38% in the base model), the incremental cost-effectiveness ratio would be greater than \$50,000 per QALY (and thus not meet the standard for cost-effectiveness).

### Probabilistic Sensitivity Analysis

The net benefit acceptability curve for the model is presented in **Figure 2**. The distinctive “S” shape, which quickly becomes asymptotic to “1,” indicates that the model is very stable to assumptions concerning relative effectiveness of plerixafor, despite our small sample, if decision makers have a WTP in excess of \$36,000 per QALY. At a WTP less than \$10,000 per QALY, G-CSF alone would be the preferred treatment.



## DISCUSSION

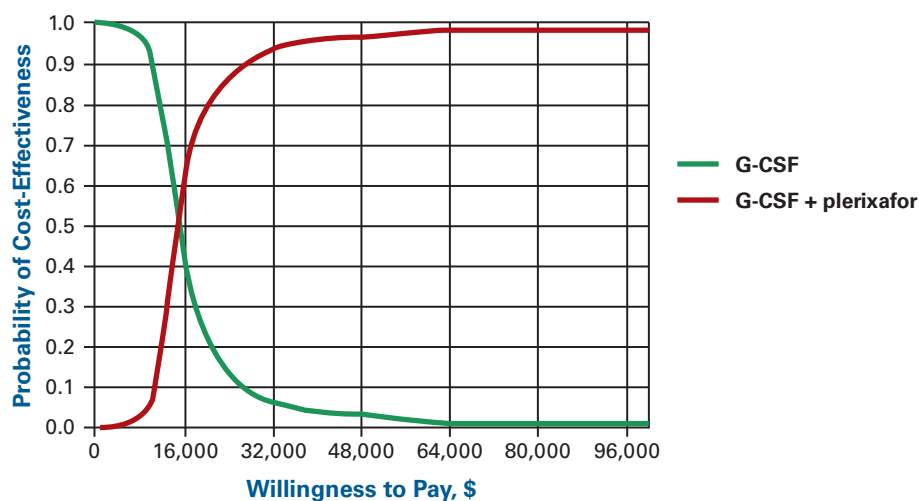
In this economic evaluation of the use of G+P as a first-line treatment for stem cell mobilization in people with relapsed DLBCL, we found that addition of plerixafor increased the cost of treatment, but at the same time resulted in greater benefit, resulting in an ICUR of \$14,574 per QALY. When examining only the cost-effectiveness of plerixafor in the stem cell mobilization/apheresis stage, we found that the addition of plerixafor cost \$60,377 for each additional patient who proceeded to ASCT over those who proceeded when only G-CSF was used.

There is very little consensus among policy makers in the United States concerning the societal WTP for a QALY, and we are aware of no standards at all in the oncology community of the WTP for successful stem cell mobilization in an individual and a subsequent ASCT. However, health authorities outside the United States have set WTP thresholds for the QALY. In the United Kingdom, the National Institute for Health and Clinical Excellence has established a standard of £30,000 per QALY (approximately \$50,000).<sup>24</sup> In Canada, the Canadian Agency for Drugs and Technology in Health operates with an informal standard of \$50,000 (Canadian, approximately \$49,000 US).<sup>25</sup> In the United States, some commentators have suggested that there is an informal standard between \$50,000 and \$100,000,<sup>26</sup> while others have suggested (based on empirical studies of coverage decisions) that the actual standard is well over \$200,000.<sup>27</sup> Regardless of the standard chosen, we have shown that the use of plerixafor as a part of the initial stem cell mobilization regimen meets even the most stringent standard for cost-effectiveness when compared with G-CSF alone. This was demonstrated in our ICUR estimates, deterministic sensitivity analysis, and probabilistic sensitivity analysis.

### Previous Economic Evaluation Studies in Non-Hodgkin's Lymphoma

In the past several years, there have been a number of economic evaluation studies of the treatment of NHL with and without ASCT. Virtually every one of these studies has concerned the cost-effectiveness of the addition of rituximab to the CHOP protocol,<sup>28-33</sup> although others have considered

■ **Figure 2.** Net Benefit Acceptability Curve



G-CSF indicates granulocyte colony-stimulating factor.

the cost of treatment of NHL<sup>34</sup> and the overall cost-effectiveness of high-dose chemotherapy with ASCT for treatment of NHL.<sup>35</sup> Our report is the first to investigate the cost-effectiveness of changes in the stem cell mobilization process.

### Uncertainty and Cost-Effectiveness

The phase III clinical trial of plerixafor showed clear superiority of G+P used as a first-line regimen for stem cell mobilization in people with NHL versus the use of G-CSF alone. In our modeling we found that this increased efficacy justified the increased cost of providing plerixafor to patients. Our sensitivity analysis further supported this finding, as we showed that clinically unlikely reductions in efficacy would be required to change the cost-effectiveness decision. A deterministic approach, as presented above, provides decision makers with information concerning parameter uncertainty (ie, what impact the choice of value for a parameter might have on the cost-effectiveness decision). A probabilistic approach provides decision makers with information on the sampling uncertainty (ie, what impact does uncertainty in parameter estimates have on the decision). In essence, the probabilistic sensitivity analysis is analogous to estimating the confidence interval, as is done in traditional frequentist statistical analyses.

While our findings were robust in both the deterministic and probabilistic analyses, we remain concerned that our findings are based upon the results of a single center with 20 participants. With a study size of 20 participants, the sampling error in our distributions is very large. As such, in spite of the strong evidence we have from our sensitivity analysis, the generalizability of these findings is limited by the size of the study on which we have based our probability estimates. It should be noted that our sample is drawn from a larger clinical

trial.<sup>11</sup> Future studies based upon the trial, should they confirm these findings, might provide policy makers with additional confidence in our findings.

### Limitations

In this study we examined only the treatment of relapsed DLBCL, the most common type of NHL. NHL encompasses a wide variety of cancers, widely varying in prognosis. However, DLBCL represents approximately 30% of NHL cases and also is among the most aggressive of NHL cancers. As such, our team was able to identify epidemiologic evidence to support the development of this model by focusing on this cancer. To the extent that other varieties of NHL would have a prognosis similar to that of DLBCL and a similar response to plerixafor, our results would be generalizable to those cancers. However, where the prognosis or response to plerixafor would be expected to differ substantially from those for DLBCL, a revised model would be necessary to estimate an unbiased ICUR.

In this model we took the societal perspective in our primary analyses, but did not consider the high indirect costs that would be associated with the treatment of NHL (eg, caregiver burden, productivity loss, loss of function). We were restricted in our ability to consider these costs due to the paucity of evidence in the literature on this subject for patients undergoing ASCT with NHL. However, it should be noted that given our very robust findings in deterministic sensitivity analyses, it is unlikely that inclusion of these costs (which would be likely to strengthen our findings) would change the cost-effectiveness decision.

Finally, in conducting this evaluation we considered only 1 initial DLBCL treatment regimen (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone; R-CHOP) and 1 ASCT conditioning regimen (carmustine or BCNU; etoposide cytarabine melphalan; BEAM). We did not consider the possibility of an interaction between plerixafor used for stem cell mobilization and the ASCT conditioning regimen. This was because we had only the results from a single clinical trial on which to base our findings. While it does not seem likely that such an interaction would exist, or would substantially change our findings if it did, if an interaction were identified we would need to conduct a new analysis.

### CONCLUSIONS

In this study, we found that the use of G+P for stem cell mobilization in patients with relapsed DLBCL is cost-effective as a result of the superior efficacy of the regimen in ensuring that patients progress to ASCT. While our modeling was based on a small sample size, our results were robust to clinically

meaningful changes in model assumptions. However, future evaluations that benefit from enriched data sets will increase policy maker confidence in these conclusions.

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**Author Affiliations:** From Center for Economic Evaluation in Medicine (SMK, DLL, MG), Washington University School of Medicine, St. Louis, MO; Center for Health Policy (SMK), Washington University, St. Louis, MO; Siteman Cancer Center (IP, KRC, JFD), Washington University School of Medicine, St. Louis, MO.

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**Authorship Information:** Concept and design (SMK, IP, KRC); acquisition of data (SMK, IP, JFD); analysis and interpretation of data (SMK, DLL, MG, KRC); drafting of the manuscript (SMK, MG, KRC, JFD); critical revision of the manuscript for important intellectual content (SMK, IP, DLL, KRC, JFD); statistical analysis (SMK, DLL, MG); provision of study materials or patients (IP, JFD); obtaining funding (JFD); and administrative, technical, or logistic support (SMK, DLL, MG).

**Address correspondence to:** Steven M. Kymes, PhD, Washington University Medical School, Center for Economic Evaluation in Medicine, 660 S. Euclid Ave, Campus Box 8096, St. Louis, MO 63110-1093. E-mail: kymes@wustl.edu.

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