CLINICAL INVESTIGATION

# A Cost Minimization Comparison of Two Surfactants—Beractant and Poractant alfa—Based Upon Prospectively Designed, Comparative Clinical Trial Data

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**OBJECTIVES** To compare the pharmacoeconomic profiles of beractant (Survanta®, Ross Laboratories, Columbus, Ohio) and poractant alfa (Curosurf®, DEY LP, Napa, CA) via a cost-minimization analysis.
**METHODS** This analysis was based upon clinical data from two previously published studies (Speer C, et al. Arch Dis Child 1995;72: F8-13; and Ramanathan R, et al. Am J Perinatol 2004; 21:109-19) where investigators found significant differences in the number of doses required to achieve a similar clinical response. Our analyses employed several models based upon single-use or multiple-use of single-use vial scenarios, average wholesale pricing, and costs computed on a per-patient basis. Model 1 involved single-dose vials and mean weight of the infants (both trials). Models 2 and 3, based on individual patient weights, assessed single-dose and multiple-use of single-dose vials cost scenarios, respectively. Individual patient weights allowed for statistical evaluation in Models 2 and 3.
**RESULTS** Model 1 savings with poractant alfa treatment was $949.67 (53%) based upon Speer and $617.90 (46%) based upon Ramanathan. Models 2 and 3 reported savings for poractant alfa of $220.50 (20%) ($P = 0.11$) and $180 (20%) ($P = 0.018$), respectively over beractant.
**CONCLUSIONS** These analyses would suggest poractant alfa may offer a less costly, clinically-equivalent option. Savings may vary with vial usage and mix, patient weight distribution, and how surfactants are used in practice. Institutions utilizing surfactants may wish to examine usage patterns, dosing protocols, and patient mix to determine what potential savings may exist.

**KEYWORDS:** beractant, pharmacoeconomics, poractant alfa, respiratory distress syndrome, surfactant

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## INTRODUCTION

Respiratory Distress Syndrome (RDS), also referred to as hyaline membrane disease, is a leading cause of infant mortality in the United States. The Centers for Disease Control's most recent United States live birth census estimates 4.05 million births between July 1, 2001 and July 1, 2002.[1] With an incidence of 11% premature live births,[1] this syndrome occurs in an estimated 40,000 to 50,000 infants in the United States each year.[2] RDS is caused by a deficiency of pulmonary surfactant in the alveolar spaces of the lungs of premature infants.[3,4] Symptoms occur in 60% to 80% of babies born before 28 weeks gestational age compared to only 5% of those born after 35 weeks gestational age.[2] Insufficient production and differentiation of pulmonary surfactant causes an

**ABBREVIATIONS** CMA, cost-minimization analysis; RDS, Respiratory Distress Syndrome

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increase in alveolar surface tension, decreased lung compliance, increased work of breathing, and inadequate gas exchange that requires the use of high ventilatory pressures.[5-7] The combination of high ventilatory pressures, large tidal volumes and exposure to oxygen in the setting of surfactant deficiency is responsible for lung injury.[5-7] Pulmonary surfactants reduce surface tension in the lung to stabilize alveoli at low lung volumes thereby allowing alveoli of all sizes to inflate.[8,9]

Morbidity and mortality figures for RDS have improved following the advent of surfactant therapy.[9,10] These agents improve lung function and promote faster weaning from ventilatory support during the acute phase of RDS, and generally produce these effects within the first 24 hours of the initial administration. There are two types of surfactants: synthetic and natural. Natural surfactants have been shown to produce greater clinical benefit than the synthetic surfactants.[7-12] Three natural surfactants are commercially available in the United States. These are beractant (Survanta®, Ross Labs, Columbus, OH), calfactant (Infasurf®, Forest Labs, NY, NY), and poractant alfa (Curosurf®, Dey LP, Napa, CA). Beractant and calfactant are both bovine-derived surfactants. Although calfactant has been available for several years, beractant is currently considered the predominant agent used in the American marketplace. Poractant alfa, a porcine-derived product, is the latest entry in this market and is considered to be the predominant surfactant used in Europe. These three surfactants appear to differ in their physiochemical makeup, with poractant alfa having the largest percentage of phospholipids, the major surface-active component.[8,13]

The efficacy and safety of surfactants have been studied extensively in large clinical trials.[14-18] Likewise, the pharmacoeconomic impact of surfactant therapy has been evaluated in several studies.[2,19-22] When compared to non-treatment (placebo), surfactant has been reported to reduce overall costs, cost per case day, cost per comparable life year, and cost per survivor.[2,19-22] These studies present encouraging data which supports the premise that surfactants offer not only significant clinical benefit, but economic value when compared to non-treatment of RDS. Nonetheless, surfactant therapy represents a significant expense for any healthcare institution. The average annual hospital expenditure for surfactants is approximately $113,000; however, institutions with large neonatal units or specialty pediatric hospitals can spend more than $300,000 per annum.[23]

Beractant is the market leader among the surfactants used in the United States. Against this background, we compare the pharmacoeconomics of poractant alfa to those of beractant. To establish the basis for our assessment, we reviewed the surfactant literature for prospectively-designed, comparative trials that provided clinical results in the treatment setting. We found two published, IRB-approved studies that would allow assessment of usage data, dosing, patient weight, and similar clinical outcomes based upon FDA approved dosing guidelines for beractant and poractant alfa (Table 1).[17,18] Using these data we evaluated cost differences between the two surfactant therapies.

## METHODS

In order to compare beractant and poractant alfa we developed three pharmacoeconomic models. Since the two comparative trials[17,18] yielded results that would allow one to conclude that poractant alfa is as efficacious as beractant, a cost-minimization analysis (CMA) was employed. We were unable to conduct a full cost-effectiveness analysis because we did not have the necessary data from one trial[17] and cost data was not collected as part of the second study.[18]

CMA compares the overall expense of use between agents, including acquisition, administration, and adverse effects.[24] Since the adverse event profile of poractant alfa and beractant are similar, the costs associated with an event should be comparable; therefore, expenses incurred by adverse effects were omitted from analysis. Costs associated with administration were not factored into the models since both surfactant products are given in the same fashion and require similar resources for administration. Therefore, the only costs to consider between medications for this particular CMA are the cost of initial and subsequent doses.

We developed three cost models based upon single-use or multiple-use of single-use vials (use of all surfactant available in the vial), FDA approved doses, and the total number of doses needed to achieve a response. For all models, average wholesale price (AWP, April 2003) was used. Beractant and poractant alfa are both available from the manufacturers in two vial sizes: 4 mL and 8 mL for beractant (25 mg/mL) and 1.5 mL and 3 mL for poractant alfa (80 mg/mL). At the time of our

**Table 1.** Comparative Trials to Establish the Basis for Pharmacoeconomic Evaluation

| Category | Study 1* (n = 73) | Study 2† (n = 293) |
|---|---|---|
| Inclusion Criteria | RDS and $FiO_2 \geq 0.4$ requiring artificial ventilation | RDS; Infants 750-1750 g and < 35 weeks gestation |
| Dosing | Poractant alfa 200 mg/kg and Beractant 100 mg/kg | Poractant alfa 100 mg/kg; Poractant alfa 200 mg/kg; and Beractant 100 mg/kg |
| Follow-up dosing criteria | Continued artificial ventilation with an $FiO_2 \geq 0.3$ | Continued artificial ventilation with an $FiO_2 \geq 0.3$ |
| % requiring follow-up dosing | 63% of beractant group and 52% of poractant alfa group | 49% of beractant group and 27% of poractant alfa 200 mg/kg group |
| Outcome | Rapid reductions in oxygen and ventilatory requirements with poractant alfa compared to beractant; Mortality was 3% in poractant alfa and 12.5% in beractant (P = NS) | Mean $FiO_2$ $AUCs_{0\text{-}6}$ significantly lower with poractant alfa compared to beractant ($P < 0.01$); Mortality in infants $\leq$ 32 weeks gestation given 200 mg/kg poractant alfa was significantly lower than those given 100 mg/kg beractant (P = 0.03) |
| Adverse Effects | Similar between groups | Similar between groups |

*Reference 17
†Reference 18

analyses, the AWP for the vials were $454.80, $804.96, $312.00, and $610.80, respectively.[25]

All models calculated comparative costs by multiplying the cost of a dose by the total number of doses within each treatment arm. Since unequal numbers of patients were enrolled in the beractant and poractant alfa treatment arms, we adjusted the final cost to eliminate differences in sample size. Total cohort costs were divided by the comparative, or normalized, number of patients to obtain a per-patient cost. Sensitivity analyses were then performed to investigate the range of possible cost differences.

### *Model 1: Single-dose Use of Vials and Mean Weight*

The first model involved single-dose use of vials and mean weight of the infants from both the Speer[17] and Ramanathan[18] trials. This model was developed with the following assumptions: 1) A single-dose (per FDA label) is withdrawn from the vial and any solution remaining in the vial is discarded; 2) the dose given is the volume based upon a dose of 100 mg/kg or 200 mg/kg in accordance with FDA approved dosing schedules for both products; 3) Infants required a second, third, and even fourth dose to achieve desired treatment outcome; 4) Analysis was done to compare FDA approved schedules for each product, 100 mg/kg for both initial and follow up doses with beractant and 200 mg/kg for initial and 100 mg/kg for follow up doses with poractant alfa.

We looked at how many initial and subsequent doses were administered in both studies. The Speer study observed that fewer additional doses with poractant alfa were required than with beractant. The criteria for re-treatment (poractant alfa at 12 hours and beractant at 6 hours after initial dose) in the Speer study was based upon the infant remaining on a ventilator and requiring an $FiO_2$ of $\geq 0.3$ to maintain $PaO_2 \geq 50$ mmHg ($\geq 6.7$ kPa). For poractant alfa (n = 33), 16 received a single dose, 11 two doses, and six received three doses. For beractant (n = 40), 15 received only an initial dose, 9 a second, 8 a third, and 8 a fourth dose. In sum, for poractant alfa there were 33 (200 mg/kg) doses and 23 (100 mg/kg) doses, while there were 89 (100 mg/kg) beractant doses.

In the Ramanathan study, the need for more than one dose of surfactant was also significantly lower in infants initially treated with 200 mg/kg poractant alfa than those in the other two groups (P = 0.002). In this study, the criteria for additional doses (poractant alfa at 12 hours and beractant at 6 hours after initial dose) was based on the infant's continued reliance on ventilation and an $FiO_2$ of $\geq 0.3$ to maintain oxygen saturation by pulse oximetry of $\geq 88\%$. For poractant alfa (n = 99) 72 received a single dose, 19 two doses, 7 three doses, and 1 a fourth dose. For beractant (n = 98), 50 received an initial dose, 33 a second, 11 a third, and 4 a fourth dose. In sum, for poractant alfa 99 (200 mg/kg) doses and 36 (100 mg/kg) doses were given for the treatment arm employing an initial dose of 200 mg/kg. For beractant, 165 (100 mg/kg) doses were given.

Calculation of vials was based upon the mean weight multiplied by the specific dose required for initial and follow-up treatment. The mean in-

**Table 2.** Results of Economic Model 1 (Single-dose Vials and Mean Weight of Patients)

| Parameter | Reference 17 | | Reference 18 | |
|---|---|---|---|---|
| | Poractant (n = 33) | Beractant (n = 40) | Poractant (n = 99) | Beractant (n = 98) |
| **Mean Weight** | 1.095 kg | 1.082 kg | 1.15 kg | 1.19 kg |
| **Average dose level** | | | | |
| 100 mg/kg (cost) | 109.5 ($312) | 108.2 ($805) | 115 ($312) | 119 ($805*) |
| 200 mg/kg (cost) | 219 ($624*) | NA | 230 ($624) | NA |
| **No. of Doses** | | | | |
| 100 mg/kg (cost) | 23 | 89 | 36 | 165 |
| 200 mg/kg (cost) | 33 | NA | 99 | NA |
| **Treatment cost** | $33,658† | $71,645† | $73,745‡ | $135,536‡ |

**AWP for 200mg/kg dose based on use of two 1.5mL vials of poractant alfa. If a single 3 mL vial of poractant alfa was utilized, then the treatment cost normalized to 40 patients would be $33,138.18, resulting in a $38,506.82 (54%) difference versus beractant for this size cohort.*
*†Costs were normalized for equivalent beractant cohort size of 40 patients. Cost of poractant alfa for 33 patients was $27,767.85.*
*‡Costs were normalized for equivalent cohort size of 100 patients. Cost of poractant alfa for 99 patients was $73,008 and 98 beractant patients $132,825.*

fant weight in each treatment arm was utilized. In the Speer trial, it was 1.095 kg for poractant alfa and 1.082 kg for beractant, while in the Ramanathan trial, it was 1.15 kg for poractant alfa and 1.19 kg for beractant. The number of vials calculated was a result of the mean dose for each agent divided into the number of milligrams per vial: 120 mg in a 1.5 mL and 240 mg in a 3.0 mL vial for poractant alfa and 100 mg in a 4.0 mL and 200 mg in an 8.0 mL vial for beractant. We chose the 8.0 mL vial versus two 4.0 mL vials as the less costly option for beractant doses greater than 100 mg. For the Speer trial, poractant alfa would require 33 (3.0 mL) vials for the 200 mg/kg dose and 23 (1.5 mL) vials for the 100 mg/kg doses, while beractant needed 89 (8.0 mL) vials. In the Ramanathan trial, poractant alfa would require 99 (3.0 mL) vials for the 200 mg/kg dose and 36 (1.5 mL) vials for the 100 mg/kg doses (99 patients), while beractant needed 165 (8.0 mL) vials. In these analyses, we used AWP of two 1.5 mL vials of poractant alfa ($624) for 200 mg/kg dose. Finally, we divided total costs by the number of patients treated to obtain a cost per patient and then adjusted this number to represent an equivalent cost per cohort, which was 40 patients for the Speer study and 100 for the Ramanathan trial.

### *Model 2: Single-dose Use of Vials and Actual Infant Weight*

The second model uses the same assumptions, dose requirements, and cost calculations as the previous model. Because we were able to use actual infant weights from the Ramanathan trial, we could more accurately calculate the number of vials. This calculation was based upon the actual patient dose and selection of the vial size (small or large) that would be most appropriate for each individual patient. Patients administered poractant alfa would require 108 vials containing 3 mL while 67 vials containing 1.5 mL would be necessary for the 99 infants assigned to the 200 mg/kg initial dose cohort. Seventy-two vials of the 4 mL product and 93 vials of the 8 mL product would be required for beractant. With these figures, we calculated comparative cost per patient and cost per cohort.

### *Model 3: Multiple-dose Use of Vials and Actual Infant Weight*

Components of the third model were similar to those reported for Model 2. Using the actual infant weights, we calculated the total volume needed to treat all infants in each cohort. This model involved multiple-uses from a single vial, which is not consistent with the FDA approved package insert for either product. We applied the costs of the smaller size vial. The 99 infants given the 200 mg/kg dose of poractant alfa would require 342 mL. This compares to 776 mL in the 98 infants treated with beractant. Again, we calculated comparative cost per patient.

### *Statistical Analysis*

Statistical differences between cost per patient and cost per cohort were determined using the Mann Whitney U test. Statistical significance was defined as $P \leq 0.05$.

## RESULTS

### *Model 1*

Table 2 summarizes the economic analyses from

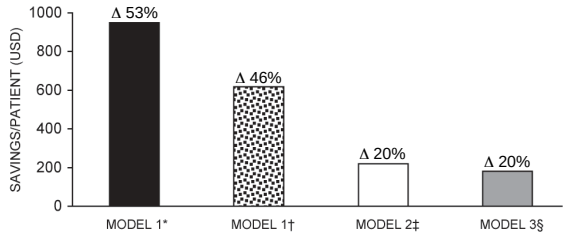


**Figure 1.** Comparison of Cost Differences for the Three Models.
*Reference 17 (mean weight, single-use vial).
†Reference 18 (mean weight, single-use vial).
‡Reference 18 (individual weight, single-use vial); P < 0.01.
§Reference 18 (individual weight, multiple-use vial); z = -2.37; P = 0.018.
P-values reflect Mann Whitney U tests for difference between groups.

Model 1 for both trials. When using the Speer data,[17] the total cost for poractant alfa (n = 33) was $27,767.85 and $71,645 for beractant (n = 40). The cost per patient was $841.45 for poractant alfa and $1,791.12 for beractant. The total cost to treat 40 infants with 100 mg/kg of poractant alfa was $33,658 compared to $71,645 for the same dose of beractant.[17] Using data from Ramanathan,[18] the normalized cost for 100 infants given poractant alfa was $73,745 compared to $135,536 for those who received beractant. The cost per patient was $737 and $1,355 for poractant alfa and beractant, respectively.

Both of the above scenarios point to savings with poractant alfa. Cost savings using poractant alfa instead of beractant would be $38,000 (53%) for a 40 patient cohort ($950/patient)[17] and about $61,800 (46%) for the 100 patient cohort ($618/patient) from the Ramanathan[18] trial (Figure 1). Since Model 1 results are affected by mean patient weight, a sensitivity analysis was performed. Based upon the volume of a vial of beractant, the ideal mean patient weight would be 1 kg, as the entire vial would be consumed without any left-over solution. When the mean patient weight was lowered to 1 kg, the cost savings for poractant alfa using the Speer[17] data was decreased to $12,683. Once the mean weight was lowered to 1 kg the cost savings for poractant alfa using the Ramanathan[18] data was reduced to $2,800.

### *Model 2*

Table 3 summarizes the economic analysis for Model 2, which used the actual weight for each individual from the Ramanathan et al.[18] The total cost to treat 100 patients was $87,770 for poractant alfa and $109,821 for beractant. The average cost to treat a patient with poractant alfa was $878 (95% CI $811–$944) while the average cost to treat a patient with beractant was $1,098 (95% CI $992–$1204) (Figure 2). The apparent cost savings observed with poractant alfa was $22,051 for the 100-patient cohort. The difference in mean costs/patient was $220 (20%) (Figure 1) ($z = 1.65$, $P = 0.11$).

**Table 3.** Results of Economic Model 2 (Single-dose Vials and Actual Weight of Infants)[18]

| | Poractant alfa (n = 99) | Beractant (n = 98) |
|---|---|---|
| **Number of Doses** | | |
| 100 mg/kg | 36 | 165 |
| 200 mg/kg | 99 | NA |
| **Number of Vials** | | |
| Small (cost/vial) | 67 ($312) | 72 ($455) |
| Large (cost/vial) | 108 ($611) | 93 ($805) |
| **Treatment Costs** | $87,770* | $109,821* |

*Costs were adjusted for equivalent cohort size of 100 patients.

### *Model 3*

This model employed a multiple-dose vial scenario that used the actual infants' weights. The use of a multi-dose vial model assumes that no product is wasted. Results using Model 3 were consistent with the previous two models and found poractant alfa to be less costly than beractant (Table 4). The total cost to treat 100 patients based upon the data was $71,970 for poractant alfa compared with $90,025 for beractant. The cost/patient of poractant alfa and beractant using Model 3 are reported in Figure 2. The mean cost/patient for poractant alfa was $720 (95% CI $665–$775) compared to $900 (95% CI $811–$989) for beractant. After normalizing the data for a cohort size of 100 patients the apparent cost savings of poractant alfa over beractant was $18,055. The difference in costs/patient between the two products ($180; 20%) (Figure 1) was statistically significant ($z = -2.37$, $P = 0.018$).

## DISCUSSION

The purpose of our economic analysis was to determine the presence of any cost differences between poractant alfa and the market leader, beractant. In our analysis, we found poractant alfa to be less costly than beractant based upon dosing schedule per FDA approved product package inserts, AWP, and comparative trial data in the treatment setting. In all models poractant alfa

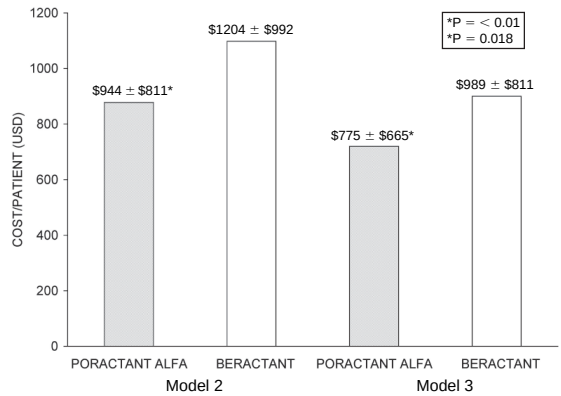


**Figure 2.** Model 2 & 3 comparison of the average cost to treat a patient with poractant alfa and beractant with individual patient weights (Model 2 = single use; Model 3 = multiple use).

appeared less costly than beractant, but with a substantial difference in Model 1. These savings varied on a per-patient basis from a low of $180 (20%) to $949.67 (53%). Since Models 2 and 3 utilized individual patient weights, we were able to apply statistical tests to determine significance of our results. While the lowest figure was 20%, this difference may represent a significant savings to some institutions. The variance depended upon the basis of analysis; the greatest was seen with single-use and mean weight with the Speer data and the least with multi-use exact weight dosing from the Ramanathan study.

The primary driver for cost savings seen within these economic models can be attributed to the fact that fewer additional doses of poractant alfa were necessary than were beractant. Another contributor to cost savings in the single-dose-vial scenarios is the larger amount of drug (and a higher concentration of phospholipids per mL) in the poractant alfa than in the beractant vial (120 mg/1.5 mL and 240 mg/3 mL with poractant alfa, versus 100 mg/4 mL, 200 mg/8 mL with beractant) for the same body weight. The greatest benefit here might be seen in infants in whom only one vial of poractant alfa is needed; two small vials or the larger vial would be needed with beractant.

While the FDA approved labeling for each agent is for single-use vials, we realize from anecdotal reports that some facilities, preparing large numbers of doses in well-controlled sterile environments, may engage in multiple entries into a single-dose vial (although this is an uncommon practice). For this reason and as a hypothetical example, we included an economic model utilizing multiple use of single-dose vials. As expected, the cost difference between agents was the lowest

**Table 4.** Results of Economic Model 3 (Multiple-dose Scenario and Actual Weight of Infants)[18]

| | Poractant alfa (n = 99) | Beractant (n = 98) |
|---|---|---|
| 100 mg/kg* | 36 | 165 |
| 200 mg/kg* | 99 | NA |
| mL used | 342 | 776 |
| Cost/mL (USD)† | $208.00 | $113.70 |
| Treatment cost (USD)‡ | $72,000§ | $90,000¶ |

**Number of doses*
*†Small vial*
*‡Costs normalized for equivalent cohort size of 100 patients*
*§Cost of poractant alfa for 99 patients was $71,280*
*¶Cost of beractant for 98 patients was $88,225*

for this model. In the single-use scenarios, some of the additional expenses for beractant could be attributed to the need for an additional vial. By allowing multi-dosing and not wasting residual solution, the cost savings with poractant alfa due to secondary doses was less.

Another consideration affecting cost relates to the criteria for subsequent doses. In these two trials, the threshold for additional doses was $FiO_2$ of $\geq 0.3$ to maintain oxygen saturation by pulse oximetry of $\geq 88\%$. Other practitioners and institutions may utilize a higher threshold such as a $FiO_2$ of $\geq 0.4$ which may lessen the need for a subsequent surfactant dose. Kattwinkel et al. evaluated this issue in 2,484 infants; 1,267 met criteria for conventional re-treatment and were randomized to low or high thresholds ($FiO_2$ 0.3 or 0.4).[26] These investigators observed significantly higher mortality for infants with complicated RDS who were retreated in accordance with the higher threshold strategy and concluded that these patients should be treated with the lower threshold approach, which is consistent with surfactant product package inserts and recent trends favoring lower oxygen concentration and exposure.[27-29]

Treatment for RDS has improved over the years. It is now common practice to administer prenatal steroids and better manage ventilator support. This is reflected in the trials used for this analysis. There is greater use of steroids in the Ramanathan study than in the Speer trial reflecting the newer treatment algorithm. While the outcomes are improving for RDS, the increased use of steroids does not impact the economic analysis as the use of steroids was equally distributed between the beractant and poractant alfa groups within the trials. Newer clinical trials should be performed to adequately measure the improvements in RDS therapy upon ultimate infant outcomes. In terms

of ventilator support, neonatal practice has evolved to extubating preterm infants to nasal continuous positive airway pressure (CPAP) after the first dose of surfactant. A large percent of preterm infants treated with 200 mg/kg of poractant alfa as the initial dose in the Ramanathan trial did not meet the criteria for redosing during the next 48 hours when compared to infants treated with beractant using the same redosing criteria. Thirty-six percent of infants randomized to poractant alfa 200 mg/kg received two or more doses of surfactant compared to 68% in the beractant group. It is likely that infants treated with poractant alfa 200 mg/kg as the initial dose may be safely extubated to nasal CPAP as this practice has been observed with success by several investigators.[30,31]

There are some limitations to our economic analysis. The most significant was the use of AWP. Most hospitals have a direct or a group-purchasing organization price that should be lower than AWP for these agents. Therefore, institutions should have a lower expenditure overall. Another institution-related consideration is that the data for the cost analyses were drawn from well-controlled clinical trials and might not be fully reflective of "real world" institutional practices. This observation could present an additional opportunity for testing these models in the practice setting. This effort would provide for a broader base of site-specific data including patient weights and contracted product costs. Obtaining a larger sample would allow more rigorous testing of the models.

Together these "real world" issues could be addressed as part of our future work evaluating surfactants and their economic impact and profiles. By asking practical questions, we could better evaluate a variety of issues, including the prevalence and safety of various dosing practices (e.g., multi-dosing and/or dose-rounding per vial), how these practices may be factored into determining cost savings, and perhaps the practical implications of a different dosing regimen in making a therapeutic switch. Furthermore, continued evaluation of these models utilizing institution-level data would provide for a statistically stronger and an even more relevant data set. Finally, these considerations should be incorporated into future prospective, controlled studies to more accurately assess the pharmacoeconomic impact associated with surfactant treatment.

While this evaluation was a cost analysis based upon primary trial endpoints and overall outcomes, it may be worthwhile to point out differences in other clinical outcomes. In the Ramanathan trial, the investigators observed a lower mortality rate in infants born at $\leq$ 32 weeks gestation ($>$ 90% of the study population) who were treated with poractant alfa 200 mg/kg than those treated with beractant. Mortality at 36 weeks post-conceptional age for infants born $\leq$ 32 weeks gestation was 3% in the 200 mg/kg poractant alfa group as compared to 11% each in the 100 mg/kg poractant alfa ($P = 0.046$) and beractant treated infants ($P = 0.034$). In another clinical trial, Baroutis et al[27] found no statistical difference in mortality and NICU-related morbidities between poractant alfa and beractant. The disparity between these two clinical outcomes may relate to the use of an initial dose of 100 mg/kg, as Ramanathan et al. also failed to see a mortality difference between poractant alfa and beractant when both were administered at an initial dose of 100 mg/kg. Baroutis et al. did show, however, that infants treated with poractant alfa required significantly less days on mechanical ventilation and supplemental oxygen and spent fewer days in the hospital than infants treated with beractant. Besides, any cost differences as a result of the mortality and morbidity outcome differences would favor poractant alfa, which already was shown to be less expensive than beractant; thus, it would have only widened the cost differential. However, it might be interesting to examine the economic impact associated with these mortality and morbidity differences as part of further randomized comparative trials in the future.

## CONCLUSIONS

While surfactants offer clinical benefit in the treatment of RDS, they represent a significant expenditure for institutions. This may be particularly important to those institutions that maintain a large neonatal intensive care unit and treat infants who may require additional or larger vials based upon body weight requirements. Based upon our cost-minimization approach, poractant alfa may offer institutions significant cost savings. This benefit could vary from 20% to 53%, based upon vial usage and the mix and distribution of patient weights. Additionally, institutions may see a different percentage and direction in savings based upon the actual contract acquisition prices of these agents. While these initial observations

are quite promising, we plan to further evaluate and validate these models utilizing institution-level data. Considering these observations, we would encourage institutions utilizing surfactants to examine their surfactant usage patterns and patient mix more closely to investigate potential savings.

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