

Cost-minimization Analysis of Treatment for Respiratory Distress Syndrome

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BACKGROUND:

Surfactant therapy has improved morbidity and mortality of respiratory distress syndrome (RDS) (1-3). Despite favorable economic impact versus non-treatment (4-7), product expenditures are of concern (mean annual institutional cost, \$113,000, and >\$300,000 in large NICUs) (8). Cost-minimization analysis would be helpful in comparing the relative economic impact of available respiratory surfactants.

Two comparative trials with clinical outcome and dosing data set the basis for our analysis comparing poractant alfa and beractant.

Study 1 (Speer C, et al) (9): 73 preterm infants were randomized to 200mg/kg poractant alfa (33) or 100mg/kg beractant (40). Both agents were effective, with similar reductions in oxygenation and ventilatory requirements. Infants treated with poractant alfa had a higher arterial:alveolar oxygen tension ratio and required a lower peak inspiratory pressure and mean airway pressure. (p<0.05–0.001). While AEs profiles were comparable, mortality was 3.0% in the poractant alfa group and 12.5% in the beractant group (NS). Less additional doses were required in the poractant alfa vs beractant infants: 52 vs 63%.

Study 2 (Ramanathan R, et al) (10): 293 infants were randomized in a controlled trial to an initial dose of 100 (96) or 200 (99) mg/kg of poractant alfa or 100 (98) mg/kg of beractant. Groups were comparable for birth weight gestational age, gender, race, and steroid exposure. Mean FiO₂ AUC₀₋₆ for both poractant alfa groups was lower than the beractant group (p < 0.005). Differences between the 200 mg/kg poractant alfa and 100mg/kg beractant group were noted in 36 week post conception mortality in ≤32 week gestation infants (3% vs. 11%) and fewer additional doses (27% vs. 49%, p < 0.002) based on continued ventilation and FiO₂ of ≥0.3 to maintain ≥88% O₂ saturation.

OBJECTIVE:

To compare the economic profiles of two surfactants, beractant and poractant alfa based upon average wholesale (AWP) pricing and FDA approved dosage.

METHODS:

A cost-minimization analysis (CMA) was used due to comparable clinical profiles.

Three models were used:

- **Model 1:** Single-dose/vial, mean infant weight (Speer, Ramanathan)
- **Model 2:** Single-dose/vial, individual infant weight (Ramanathan)
- **Model 3:** Multiple-dose/vial, individual infant weight (Ramanathan).

All models employed the following assumptions:

- Initial and follow up doses are per the approved FDA label for both products.
- Infants required a second, third and even fourth dose based upon the clinical data, to achieve a response.
- AWP (April, 2003)(11):

	Small Vial	Large Vial
Beractant:	\$454.80 (4mL)	\$804.96 (8mL)
Poractant alfa:	\$312.00 (1.5mL)	\$610.80 (3mL)

Models 1 and 2 involved single-dose (per FDA label) per vial with the remaining solution is wasted. Model 1 utilized mean infant weight from the Speer and Ramanathan studies.

Model 2 employed individual patient weights from the Ramanathan trial to more accurately calculate the number of vials based upon the actual patient dose and appropriate vial size with the least costly vial is selected for each patient based on exact weight dosing.

Model 3 utilized the same individual patient weights calculations from the Ramanathan trial. Rather than using one dose/vial, this model considered multiple doses per single vial. The analysis factored the number of mLs utilized to calculate cost. The large vial was as the least costly vial from which to draw doses.

Comparative analysis was presented as cost/patient and cost/cohort. Results from Models 2 and 3 were statistically evaluated utilizing a t-test of unequal variances. This was due to the availability of mean and SD infant weight data from the Ramanathan trial.

Total Comparative Cost for Single-Use Models

**Curosurf®
(FDA Approved Doses):** Cost/200mg/kg Dose x # of 200mg/kg Doses
Plus
Cost/100mg/kg Dose x # of 100mg/kg Doses

**Survanta®
(FDA Approved Doses):** Cost/100mg/kg Dose x # of 100mg/kg Doses

Adjust for Equivalent Patient Cohort Size (40 or 100 Infants)

RESULTS:

Model 1 (Single-use, Mean Weight)

Speer Data	Mean Weight (kg)	Dose Per 100mg/kg	Dose Per 200mg/kg	Cost Per 100mg/kg	Cost Per 200mg/kg	# of 100mg/kg doses	# of 200mg/kg doses	Cost/ 40 infants
Poractant alfa	1.095	109.5	219	\$312	\$624	23	33	\$33,658
Beractant	1.082	108.2	NA	\$805	NA	89	NA	\$71,645
Ramanathan Data	Mean Weight (kg)	Dose Per 100mg/kg	Dose Per 200mg/kg	Cost Per 100mg/kg	Cost Per 200mg/kg	# of 100mg/kg doses	# of 200mg/kg doses	Cost/ 100 infants
Poractant alfa	1.15	115	230	\$312	\$624	36	99	\$73,745
Beractant	1.19	119	NA	\$805	NA	165	NA	\$135,535

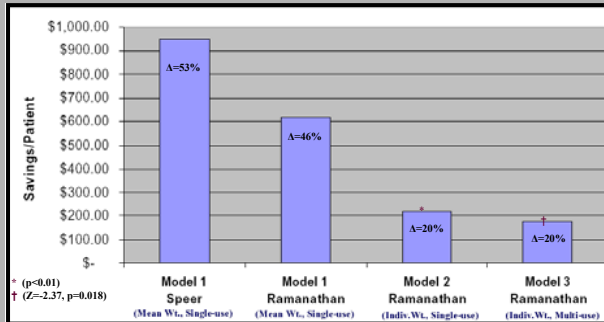
Model 2 (Single-use, Individual Weight)

Ramanathan Data	# of 100mg/kg doses	# of 200mg/kg doses	# of small vials needed	# of large vials needed	Cost / small vial	Cost / large vial	Cost / 100 infants
Poractant alfa	36	99	67	108	\$312	\$611	\$87,770
Beractant	165	NA	72	93	\$455	\$805	\$109,821

Model 3 (Multi-use, Individual Weight)

Ramanathan Data	# of 100mg/kg doses	# of 200mg/kg doses	# of mL used	Cost / mL (large vials)	Cost / 100 infants
Poractant alfa	36	99	340.55	\$203.60	\$70,036
Beractant	165	NA	777.92	\$100.62	\$79,871

Comparative Cost Savings (Based Upon Model)



DISCUSSION:

This analysis found poractant alfa to be less costly than beractant, based upon dosing schedule per product package inserts, AWP, and comparative US trial data. This observation was consistent among all models.

Per patient savings varied from as much as \$949 (53%) to as little as \$98.71 (20%). These differences can be accounted for based upon patient weight and dose scenario, vial selection, and dosing practice (single or multi-use). Even the low figure may represent a significant savings to some institutions.

Multiple factors may contribute to these observations:

- Fewer additional doses
- Larger amount of drug per vial (with respect to dose)
- Wasted drug per vial
- Initial dose of surfactant
- Product physiochemical make up
- Infant weight distribution
- Product prices

This analysis did not take into account a number of "real world" considerations:

- Most hospitals have a direct or a group-purchasing organization price lower than AWP.
- Well-controlled clinical trial data might not fully reflect institutional infant mix (and weights), threshold for additional doses, and dosing practices.
- Future work is planned to obtain a broader base of site-specific data to address these issues and allow us to more rigorously test this model.

This analysis did not fully consider all potential clinical benefits (e.g. faster weaning, and a lower mortality in <32 week population) from Ramanathan et al. Future work will focus on evaluating these from a cost-effectiveness perspective.

CONCLUSION:

This analysis, utilizing AWP and dosing data from two comparative trials suggests poractant alfa might offer cost savings. The amount (and direction) of savings can vary based upon vial usage and mix, distribution of patient weight, and actual contract acquisition prices of these agents. Further evaluation of institutional level data will allow us to validate this initial observation. It would be reasonable for institutions to examine their respiratory surfactant usage patterns and patient mix more closely to assess potential savings.

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DISCLOSURES:

W Marsh, Ph.D., J Smeeding, RPh, MBA: None
K Sekar, MD, R Ramanathan, MD: Dey LP Research and Speaker Bureau.
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