Cost-minimization Analysis of Two Surfactant Treatments for Respiratory Distress Syndrome

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INTRODUCTION:

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

COMPARATIVE TRIALS:

Study 1 (*Speer C, et al.*)[9]: Seventy-three 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 AE profiles were comparable for both products, mortality was 3.0% in the poractant alfa group and 12.5% in the beractant group (NS). Fewer additional doses were required in poractant alfa vs. beractant infants, 23 vs. 49.

Study 2 *(Ramanathan R, et al.)*[10]: Two hundred and ninety-three 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. All groups were comparable for birth weight gestational age, gender, race, and steroid exposure. Mean FiO2 AUC_{0-6} for both poractant alfa groups was lower in than in the beractant group (p < 0.005). Post conception mortality at 36 weeks in the ≤ 32 week gestation infants was lower in the 200 mg/kg poractant alfa group vs. the 100mg/kg beractant group: 3% vs. 11%. Fewer additional doses (based on continued ventilation and FiO_2 of ≥0.3 to maintain ≥88% 02saturation) were needed in the 200 mg/kg poractant alfa group compared with the 100mg/kg beractant group, 36 vs. 67 (p < 0.002).

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 employed:

- **Model 1:** Single-use per vial, mean infant weight (Speer, Ramanathan)
- **Model 2:** Single-use per vial, individual infant weight (Ramanathan)
- **Model 3:** Multiple-use per 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. Additional 100mg/kg doses were as follows:

	Poractant alfa	Beractant
Speer:	**23**	**49**
Ramanathan:	**36**	**67**

- AWP (April, 2003)[11]:

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

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. Two 1.5 mL poractant alfa vials were used in the analysis.

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 weight calculations from the Ramanathan trial. Rather than using one use per vial, this model considered multiple uses per single vial. The analysis factored the number of mL utilized to calculate cost. The large vial was used as the least costly vial from which to draw doses.

Comparative analysis was presented as cost/patient and cost/cohort (normalized for 40 infants for Speer and 100 infants for Ramanathan). Results from Models 2 and 3 were statistically evaluated utilizing a t-test of unequal variances and a Mann Whitney U. 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 Infants for Speer or 100 for Ramanathan 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**

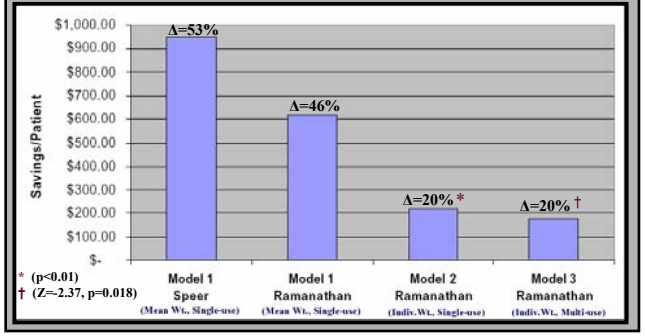
Model 2 (Single-use, Individual Weight)

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)



* (p<0.01)
† (Z=-2.37, p=0.018)

DISCUSSION:

All models found poractant alfa to be less costly than beractant. This was based upon dosing schedule per product package inserts, AWP, and comparative trial data.

Per patient savings varied from $949 (53%) to $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 GPO 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 suggests that poractant alfa may offer cost savings. The amount (and direction) of savings can vary with multiple factors. Further evaluation of institutional level data will allow us to validate this initial analysis. 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:

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