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Prevention of Respiratory Distress Syndrome

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Lucinactant for Prevention of Respiratory Distress Syndrome: Results From 2 Multicenter Randomized, Controlled Trials

Learning Objectives

Upon Completion of this course, you will be able to:

- Define “lucinactant”
- Define Respiratory Distress Syndrome
- Explain the impact of administration of lucinactant to infants at risk for RDS

ABSTRACT

BACKGROUND. The benefits of exogenous surfactants for prevention or treatment of respiratory distress syndrome are well established, but there is a paucity of long-term follow-up data from surfactant-comparison trials.

OBJECTIVE. We sought to determine and compare survival and pulmonary and neurodevelopmental outcomes through 1 year corrected age of preterm infants who received lucinactant and other surfactants in the SELECT (Safety and Effectiveness of Lucinactant Versus Exosurf in a Clinical Trial) and STAR (Surfaxin Therapy Against Respiratory Distress Syndrome) trials individually and, secondarily, from analysis using combined data from these 2 trials.

METHODS. All infants from both trials who were randomly assigned to administration of lucinactant (175 mg/kg), colfosceril palmitate (67.5 mg/kg), beractant (100 mg/kg), or poractant alfa (175 mg/kg) were prospectively followed through 1 year corrected age, at which point masked assessment of outcomes was performed for surviving infants. One-year survival was a key outcome of interest. Other parameters assessed included rates of rehospitalization and respiratory morbidity and gross neurologic status. Data were analyzed by comparing the different surfactants within each trial and, in secondary analysis, combining data from both trials to compare lucinactant versus the animal-derived surfactants (beractant and poractant) used in these trials. Survival rates over time were compared by using the Wilcoxon test for survival through 1 year corrected age and logistic regression for comparison of fixed time points.

The latter analyses were performed by using the prespecified approach, where loss to follow-up or withdrawal of consent was imputed as a death, and also using raw data. Other outcomes were analyzed by using the Cochran-Mantel-Haenszel test or logistic regression for categorical data, and analysis of variance on ranks was used for continuous data.

RESULTS. Very few cases were lost to follow-up in either trial (29 of 1546 enrolled in both trials [1.9%]). In the primary analysis of the SELECT trial comparing lucinactant to either colfosceril or beractant, there were no significant differences in the proportion of infants who were alive through 1 year corrected age. Fixed-time-point estimates of mortality at 1 year corrected age imputing loss to follow-up as a death were 28.1% for lucinactant, 31.0% for colfosceril, and 31.0% for beractant. By using raw data without imputing loss to follow-up as a death, mortality estimates at 1 year corrected age were computed to be 26.6%, 29.1%, and 28.3%, respectively. In the primary analysis of the STAR trial, significantly more infants treated with lucinactant were alive through 1 year corrected age compared with those who received poractant alfa. Fixed time estimates of mortality at 1 year corrected age imputing loss to follow-up as a death were 19.4% for lucinactant and 24.2% for poractant. These estimates using raw data that did not impute loss to follow-up as a death were 18.6% and 21.9%, respectively. In the combined analysis, survival through 1 year corrected age was higher for infants in the lucinactant group versus that of the infants in the animal-derived surfactants (beractant and poractant) group. The fixed-time-point estimates of mortality at 1 year corrected age imputing loss to follow-up as a death for lucinactant and animal-derived surfactants were 26.0% and 29.4%, respectively.

However, the 1-year-corrected-age estimates using combined raw data were 24.6% for the lucinactant group and 26.7% for the animal-derived surfactant group. The incidence of postdischarge rehospitalizations, total number of rehospitalizations, incidence of respiratory illnesses, and total number of respiratory illnesses were generally similar among those in the treatment groups. Neurologic status at 1 year corrected age was essentially similar between infants who received lucinactant and those who received all other surfactants used in these 2 trials.

CONCLUSIONS. Findings from this 1-year follow-up of both lucinactant trials indicate that this new peptide-based synthetic surfactant is at least as good, if not superior, to animal-derived surfactants for prevention of respiratory distress syndrome and may be a viable alternative to animal-derived products.

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Key Words: long-term survival • respiratory distress syndrome • surfactant • survival rate • 1-year outcome

Abbreviations: RDS—respiratory distress syndrome • SP—surfactant protein • BPD—bronchopulmonary dysplasia • SELECT—Safety and Effectiveness of Lucinactant Versus

Exosurf in a Clinical Trial • STAR—Surfaxin Therapy Against Respiratory Distress Syndrome • PMA—postmenstrual age • OR—odds ratio • CI—confidence interval

Intratracheal administration of animal-derived and synthetic exogenous surfactant preparations improves respiratory status and decreases mortality and morbidity rates among premature infants at risk of or with respiratory distress syndrome (RDS).[1] Currently available animal-derived surfactants from bovine or porcine sources contain phospholipids and variable, yet relatively small, quantities of surfactant proteins (SPs) B and C,[2] whereas currently available synthetic surfactants contain phospholipids but no SPs. Although these synthetic surfactants have potential safety advantages over animal-derived products, they seem to be inferior to animal-derived surfactants in improving clinical outcomes.[1]

A meta-analysis of 11 controlled trials that compared these 2 classes of surfactants demonstrated a marginally significant lower mortality rate and a lower risk of pneumothorax with animal-derived surfactants when surfactant was administered as a rescue therapy.[1] However, no reductions in the incidence of bronchopulmonary dysplasia (BPD) were demonstrated. None of these surfactant-comparison trials reported findings beyond the initial hospital stay in the NICU. The limitation of synthetic non–protein-containing surfactants has been attributed to the lack of SP-B and SP-C.[3–5] The absence of SP-B seems to be particularly important: animals or humans lacking SP-B because of a genetic mutation develop a fatal form of respiratory failure during the neonatal period.[4,5] In contrast, individuals with mutations in SP-C develop interstitial lung disease as adults rather than neonatal RDS.[6]

Lucinactant (Surfaxin; Discovery Laboratories, Inc, Warrington, PA) is a new-generation synthetic surfactant that contains phospholipids and a high concentration of the synthetic 21-amino acid hydrophobic peptide (sinapultide, also known as KL_4 peptide). This peptide resembles the hydrophobic-hydrophilic amino acid pattern of the tail end of SP-B.[7] The concentration of sinapultide in lucinactant is higher than the concentration of SP-B in current animal-derived products, which approximates the concentration of SP-B in normal lungs. Lucinactant has greater resistance to oxidation and peroxidation than the bovine-derived surfactant beractant (Survanta; Ross Products Division, Abbott Laboratories, Columbus, OH)[8] and has been shown to improve pulmonary function and alveolar expansion in an animal model of RDS[9] and in a pilot study that involved preterm infants with RDS.[10]

We recently reported the results of 2 multicenter, phase III, double-blind, randomized, controlled trials, which demonstrated the efficacy of lucinactant in the prevention of neonatal RDS.[11,12] The SELECT (Safety and Effectiveness of Lucinactant Versus Exosurf in a Clinical Trial) study compared lucinactant with the synthetic non–protein-containing surfactant, colfosceril palmitate (Exosurf; GlaxoSmithKline, Brentford, United Kingdom); beractant was used in the trial as a reference arm.[11] The STAR (Surfaxin Therapy Against Respiratory Distress Syndrome) trial compared lucinactant with the porcine-derived surfactant poractant alfa (Curosurf; Chiesi Farmaceutici, Parma, Italy).[12] Inclusion criteria, approach to surfactant administration, and time periods when the studies were conducted were fairly similar for both trials. In the SELECT trial, RDS-related mortality through 14 days of age was significantly ($P < .01$) reduced with lucinactant compared with both beractant and colfosceril palmitate, and proportionally more patients were alive at 36 weeks' postmenstrual age (PMA) compared with beractant (odds ratio [OR]: 0.67; 95% confidence interval [CI]: 0.45–1.00).

In the STAR trial, the primary outcome of alive without BPD at 28 days was not significantly different between lucinactant and poractant alfa.[12]
To evaluate outcomes beyond the initial hospital stay and examine further the safety of lucinactant, both trials included planned follow-up of participating infants to 1 year corrected age.

The primary objective for this study was to report the outcome results of the planned follow-up to 1 year corrected age of infants participating in the SELECT and STAR trials. Furthermore, given the similarity of these trials in the populations studied, treatment approach, end points, and contemporary nature, a secondary goal of this analysis was to compare the outcome of infants who received lucinactant versus those who received other classes of surfactants after combining data from both trials.

METHODS

Study Design

Methods for both RDS-prevention trials have been described previously in detail.[11,12] In summary, within 30 minutes of birth, infants between 600 and 1250 g were randomly assigned to receive lucinactant, colfosceril palmitate, or beractant in a 2:2:1 ratio in the SELECT trial and lucinactant or poractant alfa in a 1:1 ratio in the STAR trial. In both trials, infants were randomly assigned by stratification on the basis of birth weight at each site. Clinicians who were caring for participating infants remained blinded to the surfactant assigned at randomization throughout their stay in the NICU and up to 1 year corrected age for prematurity (i.e., chronologic age minus the number of weeks premature). Study protocols were approved by the institutional review boards of all participating centers, and signed informed consent was obtained for all participants. An independent data-safety board reviewed the study design and data for both trials. Both studies were conducted under the auspices of independent steering committees, which were chaired by the respective principal investigators.

From birth to 1 year corrected age, we recorded the occurrence of rehospitalization after discharge from the NICU, the number and type of respiratory illnesses that occurred after 36 weeks' PMA (e.g., wheezing, pneumonia, cough), and deaths. In addition, at the 1-year-corrected-age visit, weight, length, and head circumference were obtained and a physical examination, including a gross neurologic assessment, was performed. The neurologic examination assessed, at minimum, gross motor tone, reflex abnormalities, presence of unilateral or bilateral deafness, unilateral or bilateral blindness, and history of seizures that required treatment with anticonvulsant agents. The clinicians involved in the follow-up assessment phase of the studies also remained blind to the assigned surfactant treatment throughout the study.

Statistical Analyses

In this 1-year-corrected-age follow-up analysis, all randomly assigned infants were included on the basis of the intent-to-treat principle across both studies.

In the STAR trial, the short-term results through 36 weeks' PMA were previously reported on the basis of the per-protocol population (all infants who received any surfactant [$N = 243$]), which is typical for noninferiority studies.[13,14]

For all survival comparisons, we used a prespecified imputation approach, with which loss to follow-up or withdrawal of consent was counted as a death. However, we also compared survival between groups using raw data without imputing loss to follow-up or consent withdrawal as death. The overall survival rate through 1 year corrected age for all randomly assigned infants within each study was estimated by using a standard Kaplan-Meier approach for long-term survival analysis. The Kaplan-Meier curves for lucinactant versus animal-derived surfactants in the combined analysis were estimated by using meta-analysis methods in which the overall Kaplan-Meier curves were constructed on the basis of the weighted average of the individual curves from the studies, weighted by study size.[15] Also, when comparing lucinactant with animal-derived surfactants, we used meta-analysis methodology for analyzing data across studies with different sample sizes between and within these studies.[1,15] This statistical method was chosen to compare these surfactants because simple pooling of data from the STAR and SELECT trials is not appropriate given that the randomization ratios in the 2 studies were unequal (lucinactant/colfosceril palmitate/beractant, randomization ratio: 2:2:1 [SELECT]; lucinactant/poractant alfa, randomization ratio: 1:1 [STAR]). Survival rates through 1 year corrected age for individual studies and the meta-analysis were compared by using the Wilcoxon test adjusting for study, birth weight strata, country, gender, and race. In addition to using the standard Kaplan-Meier approach for survival comparisons, we determined fixed-time-point estimates of mortality by imputing loss to follow-up as a death and also using raw data and compared them by using logistic regression adjusting for pooled center and birth weight stratum.

The incidence of rehospitalizations was analyzed by using logistic regression, and the total number of postdischarge rehospitalizations was compared by using analysis of variance. Data on respiratory morbidity through 1 year corrected age were collected for those patients who were alive at 36 weeks' PMA. The incidence of respiratory illnesses was compared by using logistic regression. The total number of respiratory illnesses through 1 year corrected age was compared by using analysis of variance. Neurologic outcomes at 1 year corrected age were only assessed for surviving infants in whom the data were captured; the data were compared by using the Cochran-Mantel-Haenszel test. All analyses described above were adjusted for pooled center and birth weight stratum. No missing data imputation was performed unless clearly specified.

RESULTS

Patient Population and Disposition

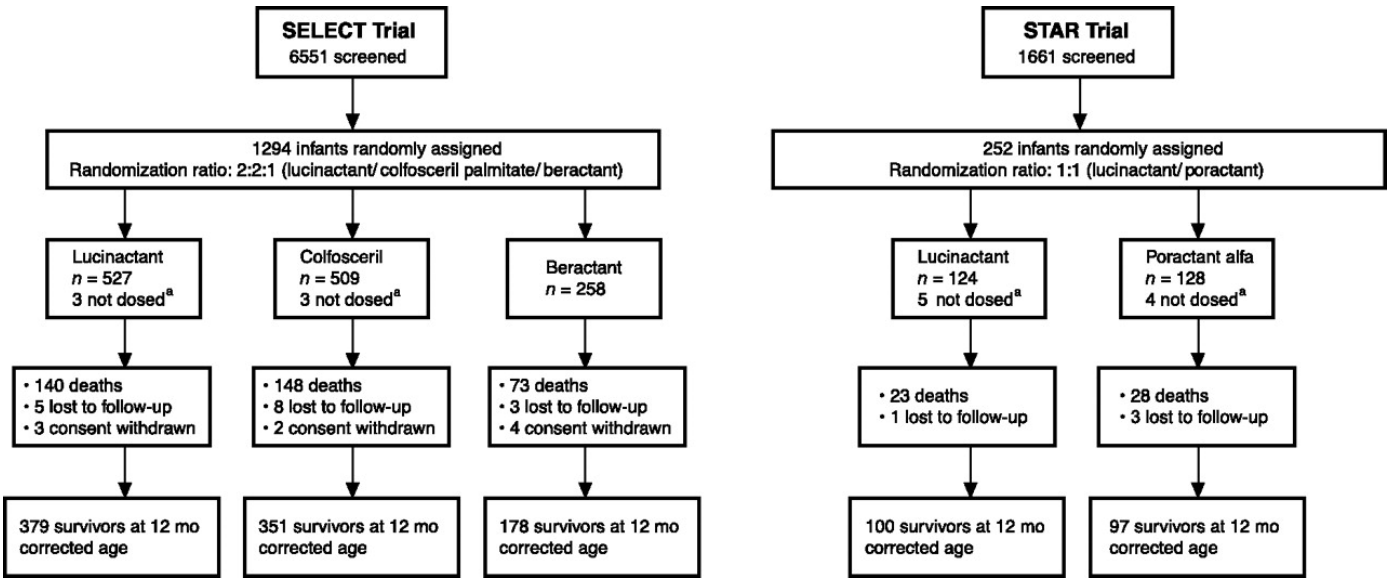
In the SELECT study, 527, 509, and 258 preterm infants between 24 and 32 weeks' gestational age and between 600 and 1250 g birth weight were randomly assigned to receive lucinactant, colfosceril palmitate, and beractant, respectively. In the STAR study, 124 and 128 preterm infants in the same weight range were randomly assigned to receive lucinactant and poractant alfa, respectively.

The upper limit for gestational age in the STAR trial was <29 weeks. Complete maternal and neonatal demographics for the STAR and SELECT study populations have been reported.[11,12] A summary of the main demographic characteristics of both studies is given in Table 1.
The study populations were fairly similar; small, nonsignificant differences in Apgar scores, birth weight, and prenatal steroid use were observed among infants enrolled in the 2 trials. In total, 651 infants were randomly assigned to lucinactant and 386 to animal-derived surfactants (beractant and poractant alfa).

TABLE 1 Summary of the Main Demographic Characteristics

Characteristic	SELECT Trial			STAR Trial	
	Lucinactant (*N* = 527)	Colfosceril Palmitate (*N* = 509)	Beractant (*N* = 258)	Lucinactant (*N* = 124)	Poractant Alfa (*N* = 128)
Male, *n* (%)	263 (49.9)	254 (49.9)	129 (50.0)	60 (48.4)	66 (51.6)
Birth weight, mean (SD), g	974 (183)	971 (186)	967 (187)	932 (191)	937 (194)
Gestational age, mean (SD), wk	28.2 (1.9)	28.2 (2.0)	28.1 (2.1)	26.9 (1.2)	27.0 (1.4)
Apgar score at 5 min, median (range)	7 (3–10)	7 (4–10)	7 (4–10)	8 (3–10)	8 (3–10)
Prenatal steroid use, *n* (%)	415 (79.2)	394 (78.5)	191 (74.3)	109 (87.9)	107 (83.6)

In both trials and subsequent follow-up, 6 infants (0.9%) who received lucinactant and 8 (1.6%) and 6 (1.6%) infants who received colfosceril palmitate and an animal-derived surfactant, respectively, were lost to follow-up (Fig 1). Consent after randomization was withdrawn for 3 infants (0.5%) who received lucinactant and 2 (0.4%) and 4 (1.5%) infants who received colfosceril palmitate and an animal-derived surfactant, respectively. Per the prespecified rules (see "Methods"), these losses to follow-up were counted as deaths. Nonetheless, overall survival comparisons were also conducted only on infants for whom data were available (i.e., without imputation for loss to follow-up as a death).



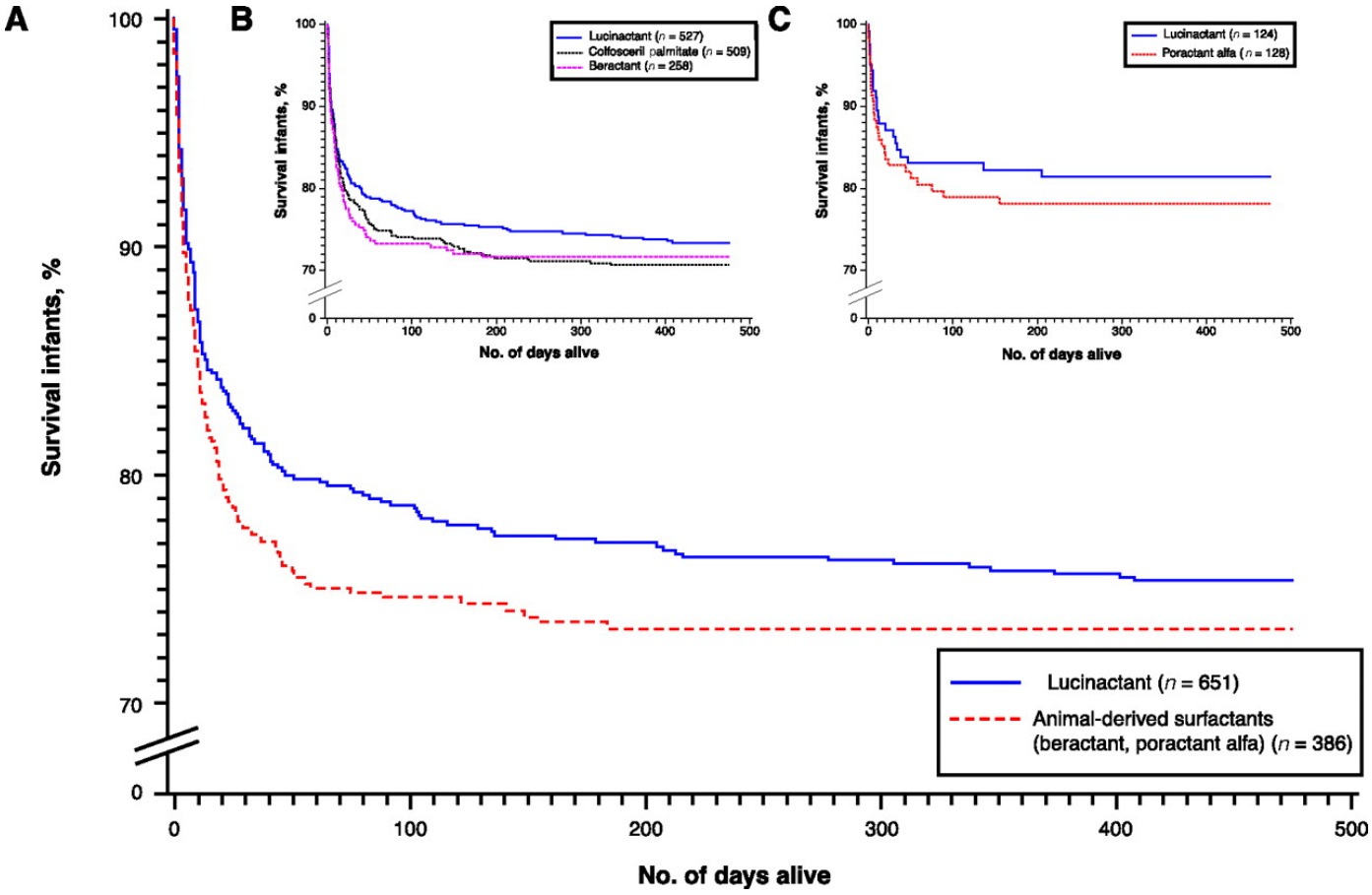
1 Enrollment and disposition of infants in the SELECT and STAR trials through 1 year corrected age. [a] Did not receive study medication.

Overall Survival

The Kaplan-Meier survival curves through 1 year corrected age for infants in the SELECT study, the STAR study, and the combined group of infants who received lucinactant compared with those who received animal-derived surfactants (beractant and poractant alfa) are presented in Fig 2 (A, B, and C, respectively). Comparisons of mortality data for lucinactant versus the individual comparator surfactants at both 28 days' and 36 weeks' PMA in the SELECT and STAR trials have already been provided in their original publications.[11,12] However, the findings of the combined analysis at 36 weeks' PMA represent new data and are mentioned briefly below, because they provide a reference point for the 1-year-corrected-age data. There were no significant differences in the proportion of infants who were alive through 1 year corrected age comparing those given lucinactant with those who received colfosceril and beractant (Fig 2A).

Fixed-time-point estimates of mortality at 1 year corrected age imputing loss to follow-up as a death were 28.1% for lucinactant, 31.0% for colfosceril, and 31.0% for beractant (OR: 0.81; 95% CI: 0.60–1.09 [lucinactant versus colfosceril]; OR: 0.84; 95% CI: 0.58–1.21 [lucinactant versus beractant]). In the STAR trial, significantly more infants who were treated with lucinactant were alive through 1 year corrected age compared with those who received poractant alfa ($P = .04$, Wilcoxon test; Fig 2B). Fixed-time-point estimates of mortality at 1 year corrected age imputing loss to follow-up as a death were 19.4% for lucinactant and 24.2% for poractant (OR: 0.64; 95% CI: 0.32–1.27). In the combined analysis, survival through 1 year corrected age of those infants who received lucinactant was higher compared with those who received animal-derived surfactants ($P = .05$, Wilcoxon test; Fig 2C). Fixed-time-point estimates using combined data from both trials imputing loss to follow-up as a death to compare lucinactant with the animal-derived surfactants demonstrated a lower mortality rate that favored infants who received lucinactant at 36 weeks' PMA (20.1% vs. 24.7%; $P = .045$; OR: 0.70; 95% CI: 0.50–0.99).

The fixed-time-point estimates of mortality at 1 year corrected age imputing loss to follow-up as a death for lucinactant and animal-derived surfactants were 26.0% vs. 29.4%, respectively (OR: 0.80; 95% CI: 0.58–1.09).



Because very few infants from both trials were either lost to follow-up or had their consent withdrawn, estimations of overall survival using raw data without imputation for loss to follow-up as a death introduced minor variations to the findings described above but did not modify the trend of the results. Using raw data without imputing loss to follow-up as a death, fixed-time-point estimates of mortality at 1 year corrected age were 26.6%, 29.1%, and 28.3%, respectively (OR: 0.83; 95% CI: 0.61–1.12 [lucinactant versus colfosceril]; OR: 0.89; 95% CI: 0.61–1.32 [lucinactant versus beractant]). In the STAR trial, there was no loss to follow-up or withdrawal of consent before 36 weeks' PMA; therefore, estimates using raw data did not differ from those using a worst-case scenario approach.[12] However, at 1 year corrected age, overall mortality estimates using raw data not imputing loss to follow-up as a death were 18.6% for the lucinactant group and 21.9% for the poractant group (OR: 0.69; 95% CI: 0.34–1.40). Mortality estimates using combined raw data at 1 year corrected age not imputing loss to follow-up as a death were 24.6% for the lucinactant group and 26.7% for the animal-derived surfactant group (OR: 0.85; 95% CI: 0.62–1.18).

Postdischarge Rehospitalization and Respiratory Morbidity

Although between one third and one half of the infants in both studies were rehospitalized during the first year, in general, readmission to the hospital occurred only once for most of them (Table 2). The incidence of postdischarge rehospitalization did not differ between surfactant groups in the SELECT trial (lucinactant: 43.4%; colfosceril: 43.4%; beractant: 50.8%) or the STAR trial (lucinactant: 34%; poractant alfa: 34.7%). Likewise, the number of postdischarge rehospitalizations through 1 year corrected age for all discharged infants did not differ between groups. Data on the number of respiratory illnesses (coughing, wheezing, and pneumonia) through 1 year corrected age were collected for infants from both studies who were alive at 36 weeks' PMA. There were no significant differences between the groups (Table 2).

TABLE 2 Postdischarge Rehospitalizations and Respiratory Illnesses From 36 Weeks' PMA to 1 Year Corrected Age

	SELECT Trial			STAR Trial	
	Lucinactant	Colfosceril Palmitate	Beractant	Lucinactant	Poractant Alfa
No. of postdischarge rehospitalizations					
n/N (%)[a]	173/399 (43.4)	159/366 (43.4)	91/179 (50.1)	34/100 (34.0)	34/98 (34.7)
Mean (SD)	0.8 (1.4)	1.0 (1.7)	1.1 (1.8)	0.8 (1.4)	0.8 (1.6)
Median (range)	0.0 (0.0–8.0)	0.0 (0.0–8.0)	1.0 (0.0–8.0)	0.0 (0.0–8.0)	0.0 (0.0–8.0)
No. of respiratory illnesses					
n/N (%)[b]	281/406 (69.2)	263/375 (70.1)	130/178 (73.0)	70/101 (69.3)	61/99 (61.6)
Mean (SD)	1.9 (2.3)	2.1 (2.1)	2.1 (2.2)	1.7 (1.9)	1.5 (1.8)
Median (range)	1.0 (0.0–26.0)	2.0 (0.0–13.0)	1.0 (0.0–12.0)	1.0 (0.0–10.0)	1.0 (0.0–9.0)

[a] *N* = all discharged infants through 1 year corrected age.

[b] *N* = all infants alive as of 36 weeks' PMA with available data.

Neurologic Assessment

Neurologic evaluations at 1 year corrected age were performed for most surviving infants from the 2 studies. In the SELECT trial, 731 (81%) of the 908 infants alive at 1 year corrected age had neurologic evaluations (lucinactant: 306; colfosceril palmitate: 279; beractant: 146). In the STAR trial, neurologic evaluations were performed in 190 (96%) of the 197 infants alive at 1 year corrected age (lucinactant: 98; poractant alfa: 92; Table 3).

TABLE 3 Abnormal Gross Neurologic Findings: All Randomly Assigned Evaluated Survivors in Each Trial

	SELECT Trial			STAR Trial	
Neurologic Finding	Lucinactant (*N* = 306)	Colfosceril Palmitate (*N* = 279)	Beractant (*N* = 146)	Lucinactant (*N* = 98)	Poractant Alfa (*N* = 92)
Gross tone or reflex abnormality, *n* (%)	30 (9.8)	45 (16.1)[a]	25 (17.1)[a]	8 (8.2)	9 (9.8)
Gross motor delay, *n* (%)	30 (9.8)	42 (15.1)[a]	15 (10.3)	3 (3.1)	4 (4.4)
Unilateral or bilateral deafness, *n* (%)	10 (3.3)	7 (2.5)	1 (0.7)	0 (0.0)	0 (0.0)
Unilateral or bilateral blindness (or registered as blind), *n* (%)	8 (2.6)	10 (3.6)	2 (1.4)	1 (1.0)	2 (2.2)
Seizures requiring anticonvulsant agents, *n* (%)	7 (2.3)	7 (2.5)	5 (3.4)	1 (1.0)	1 (1.1)

[a] $P \leq .05$ versus lucinactant. No other comparisons were significant.

Among survivors examined from the SELECT and STAR trials, there were generally no significant differences between groups with very few exceptions (Table 3).

There were fewer muscle-tone abnormalities in the infants in the lucinactant group compared with those in the colfosceril and beractant groups and also a lower incidence of gross motor delay compared with the colfosceril group. There were no major differences in neurologic outcomes at 1 year corrected age when comparing infants who received lucinactant with those who received animal-derived surfactants (Table 4) despite the greater number of survivors in the lucinactant group.

TABLE 4 Pooled Analysis of Abnormal Gross Neurologic Findings: All Randomly Assigned Evaluated Survivors

Neurologic Finding	Lucinactant (*N* = 404)	Animal-Derived Surfactants (*N* = 238)
Gross tone or reflex abnormality, %	9.4	15.3[a]
Unilateral or bilateral deafness, %	2.5	0.5
Unilateral or bilateral blindness (or registered as blind), %	2.2	1.6
Seizures requiring anticonvulsants, %	2.0	2.9

No comparisons were significant:

[a] *P* = .055 versus lucinactant.

DISCUSSION

Surfactant therapy is associated with an absolute reduction of ~5% to 7% in neonatal mortality among preterm infants compared with those who receive placebo.[16,17] This reduction in mortality rate translates into ~1 life saved for every 14 to 20 infants who receive surfactant. The other major benefit consistently shown in trials that have compared surfactant administration with placebo is a marked decrease in the occurrence of air leaks. On the basis of these findings, surfactant therapy has become widely used for the prevention and treatment of RDS.

There have been many randomized trials that compared the 2 major classes of surfactants, namely synthetic preparations devoid of SPs and animal-derived surfactants that contain variable amounts of SP-B and SP-C, although most have used a treatment rather than a prophylactic approach. Soll and Blanco[1] conducted a systematic review of 11 trials and compared animal-derived surfactants versus synthetic surfactants. Ten of the trials included in that review compared colfosceril with beractant (7 trials),[18–24] calfactant (2 trials),[25,26] or poractant alfa (1 trial),[27] whereas only 1 trial compared pumactant to poractant.[28]

These authors concluded that both types of surfactants are effective in the treatment and prevention of RDS. They also concluded that when taken together, use of animal-derived surfactants resulted in fewer deaths, greater early improvement in the requirement for ventilatory support, and a lower overall incidence of pneumothorax than synthetic products that contain only phospholipids. However, none of the studies that compared beractant to colfosceril, including large, well-conducted trials, have shown a significant difference in overall mortality rate favoring either surfactant, either singly or in combination. Furthermore, in the only trial that compared poractant alfa and colfosceril, the overall mortality rate was higher in the poractant group (20%) than in the colfosceril group (13%), but this difference was not significant, probably because of the relatively small sample size of the study ($N = 228$).[27] No advantages in terms of reduction in the incidence of BPD were described in this systematic review or in any of the individual trials included in it. In addition, a small but significant increase in the incidence of intraventricular hemorrhage among infants who were treated with animal-derived surfactants was reported.

We recently reported the results of 2 multicenter, randomized, double-blind trials that compared the new-generation synthetic surfactant lucinactant, which contains a peptide that mimics the main function of human SP-B, with other synthetic or animal-derived surfactants for the prevention of RDS.[11,12] In the largest of these trials, the SELECT study, lucinactant was shown to decrease the incidence of RDS, RDS-related mortality, and BPD compared with colfosceril, but no reduction in overall mortality rate compared with this surfactant was observed.[11] These findings supported the hypothesis that the addition of a peptide that mimics the main action of SP-B to surfactant phospholipids improves short-term clinical outcomes compared with using a surfactant that contains only phospholipids. In this study, a reference arm of infants who were randomly assigned to receive beractant was included. Lucinactant reduced RDS-related deaths and the overall mortality rate at 36 weeks' corrected age compared with beractant, but there was no difference in BPD. It is notable that this is the only study to date that has compared prophylactic administration of colfosceril and beractant.

Although this was not the comparison of primary interest in the SELECT trial, the findings of a lower incidence of RDS at 24 hours and more rapid weaning with beractant than with colfosceril parallel those of previous randomized comparison trials of these 2 types of surfactants for the treatment of established RDS.[18,19] Similar to all previous trials that compared colfosceril and beractant, the SELECT trial did not demonstrate superiority of beractant over colfosceril in terms of BPD or overall mortality rate. The smaller of the 2 randomized trials of lucinactant, the STAR study, compared this surfactant with poractant alfa.[12] This trial is the second largest study published to date to compare poractant alfa to another surfactant. In this trial, the phospholipid doses of both surfactants were similar (175 mg/kg) but were also higher than in other comparison trials of surfactants (for doses and administration in both trials, see the original publications[11,12]). Furthermore, both poractant alfa and lucinactant contain more SP-B (or its equivalent as sinapultide) than beractant. The primary outcome of being alive without BPD at 28 days was observed to be more frequent in the lucinactant group (37.8%) than in the poractant alfa group (33.1%), but without statistical significance. No differences in other secondary outcomes between groups were identified.

In these 2 lucinactant trials there were far fewer differences in study design and the populations studied than between those studies included in the systematic review by Soll and Blanco.[1]

Furthermore, most outcomes evaluated in the lucinactant trials were within the ranges reported in those studies included in the review by Soll and Blanco and data from the Vermont Oxford Network.[29] In view of the relatively similar design of the lucinactant trials and considering that lucinactant is a different class of surfactant than previous synthetic and animal-derived preparations, we sought to compare overall survival between infants who received lucinactant versus those who received the other types of surfactants, not only within each trial but also by using combined data from both trials.

We elected to present overall survival data by using the standard Kaplan-Meier approach, because it allows for comparison of survival between groups through the entire observation period (up to 1 year corrected age) and also because this methodology was used to report survival through 36 weeks' PMA in both of the original publications of the lucinactant trials.[11,12] Using a similar approach to report the 1-year survival curves should facilitate comparison with previous data. Kaplan-Meier survival estimates do not falsely amplify treatment differences with respect to survival. Rather, they generally reveal unbiased estimates of survival rates for each treatment, hence yielding unbiased estimates of treatment differences. Nonetheless, because most of the surfactant benefit in mortality occurs in the neonatal period, in our survival analysis comparing treatments through 1 year corrected age we used the Wilcoxon test, which emphasizes earlier treatment differences. Using this approach for analysis, lucinactant administration resulted in better survival through 1 year corrected age than poractant in the STAR trial but no difference with colfosceril or beractant in the SELECT trial. In the combined analysis there was better survival at 1 year corrected age for lucinactant versus the animal-derived surfactants (beractant and poractant), which was of borderline statistical significance but potentially of clinical importance.

We also calculated fixed estimates of mortality at defined time points to allow for crude estimations of the relative magnitude of change and its CIs by using both the prespecified worst-case scenario approach (imputing loss to follow-up as a death) and raw data. The impact of imputations on treatment differences is uncertain and depends on variations in the rate of censoring among treatment groups. When there are premature withdrawals from a study before the end of follow-up, a raw incidence estimate may be biased (i.e., counting premature withdrawals as death will generally overestimate the event rate, whereas counting premature withdrawals as survival will generally underestimate the event rate). Not unexpectedly, results of the fixed-time-point estimates of mortality depended on whether imputation was used. Regardless of the methodology used, mortality estimates for infants who received lucinactant were either comparable or significantly lower than those observed for the other surfactants. Unfortunately, only short-term mortality data from the previously published surfactant-comparison trials are available, none of which evaluated survival at 1 year corrected age.

Several randomized trials that compared different animal-derived surfactants for prevention and treatment of RDS have been conducted in the past decade.[30–34] Some of these surfactants contain more SP-B (calfactant, poractant) or have used higher doses of phospholipids than when beractant is administered.[2,3] Therefore, it is not surprising that a faster improvement in oxygenation versus beractant has been observed in some of them.[30,33,34] However, no differences in overall mortality rate have been reported in the 2 large RDS-prevention or -treatment trials that compared calfactant and beractant.[30,31] Several relatively small trials have compared poractant with beractant only for treatment of RDS.[35]

These studies administered poractant using either a higher initial dose of phospholipids (200 mg/kg) or a similar amount (100 mg/kg) compared with beractant. In a preliminary meta-analysis of these trials, Halliday[35] suggested that administration of poractant resulted in a lower neonatal mortality rate than beractant primarily when the higher initial dose was given, because no difference in mortality rate versus beractant was found in those trials that administered 100 mg/kg poractant initially. Using this lower initial dose for treatment of RDS, poractant administration resulted in a higher mortality rate (20%) than colfosceril (13%), although this difference did not achieve statistical significance, probably because of the study's sample size.[27]

At present, it is impossible to differentiate whether any potential benefits of the higher initial dose of poractant are a result of administration of more phospholipids, a higher amount of SP-B, a higher volume of drug (2.5 vs. 1.25 mL/kg), which may improve lung distribution, or other alternative explanations. Nonetheless, Halliday concluded that for infants with moderate-to-severe RDS, the larger dose of poractant is more effective, but for prophylaxis a lower dose may be appropriate; however, this hypothesis has yet to be tested prospectively in a clinical trial.[35] In keeping with this notion and because, to our knowledge, no randomized comparison of these 2 surfactants for prevention of RDS using any dose has ever been conducted, we combined data from infants who received beractant and poractant in both of the lucinactant trials for analysis. Furthermore, we used appropriate methodology for analyzing data across studies with different sample sizes and randomization schemes.[1,15]

To our knowledge, previous surfactant-comparison trials have not reported outcomes that were prospectively collected beyond the neonatal period. This may limit the ability to draw conclusions related to the impact of surfactants in long-term survival and other morbidity frequently observed in preterm infants after discharge from neonatal intensive care. Nonetheless, published follow-up data from studies that compared various surfactants with placebo demonstrate that the improved survival observed resulting from surfactant treatment is not associated with increased subsequent morbidity.[36] Because lucinactant is a new-generation surfactant, we sought to determine postdischarge morbidity and outcome up to 1 year corrected age of infants who received this as well as the other surfactants used in these 2 trials. We successfully collected this information in nearly all of the participants or survivors from both trials. Our data indicate that rehospitalization of preterm infants after discharge from neonatal intensive care remains a frequent event and confirm the findings from previous follow-up studies of surfactant therapy.[37] When we examined the incidences of respiratory morbidity and rehospitalization in each trial, no differences were detected between infants given the various surfactant preparations, including lucinactant. Similarly, neurologic assessment of these infants showed essentially no differences except for a lower occurrence of muscle-tone abnormalities and gross motor delay favoring the lucinactant group, even with a higher number of survivors in the lucinactant group. Although our data on neurologic evaluations have limitations, most infants from both trials were assessed at 1 year corrected age. In fact, the proportion of infants we were able to follow was similar or higher than many of the previous follow-up studies of infants treated with surfactant.[38,39] An additional strength of these evaluations is that they were conducted by physicians who were unaware of group assignment.

CONCLUSIONS

The findings of this 1-year follow-up study, as well as data from the original reports of the lucinactant trials, strongly suggest that administration of lucinactant to infants at risk for RDS results in neonatal survival that is at least comparable with, if not superior to, that of infants given the animal-derived surfactants beractant and poractant alfa. Furthermore, these data demonstrate that there is no difference in morbidity through 1 year corrected age in infants given lucinactant versus other animal-derived surfactants despite the proportionally higher number of survivors. These findings strongly support the long-term safety of using lucinactant for the prevention of neonatal RDS.

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Glossary of Terms

Acute: Of abrupt onset, in reference to a disease. Acute often also connotes an illness that is of short duration, rapidly progressive, and in need of urgent care.
See the entire definition of Acute

Acute respiratory distress syndrome: Better known as ARDS. See: ARDS .
See the entire definition of Acute respiratory distress syndrome

Adverse effect: A harmful or abnormal result. An adverse effect may be caused by administration of a medication or by exposure to a chemical and be indicated by an untoward result such as by illness or death.
See the entire definition of Adverse effect

Alveolar: Pertaining to the alveoli, the tiny air sacs in the lungs. The exchange of oxygen and carbon dioxide takes place in the alveoli which look like cells in a honeycomb.
See the entire definition of Alveolar

Alveoli: The plural of alveolus. The alveoli are tiny air sacs within the lungs where the exchange of oxygen and carbon dioxide takes place.
See the entire definition of Alveoli

Analysis: A psychology term for processes used to gain understanding of complex emotional or behavioral issues.
See the entire definition of Analysis

Anteroposterior: From front to back. When a chest x-ray is taken with the back against the film plate and the x-ray machine in front of the patient it is called an anteroposterior (AP) view. As opposed to from back to front (which is called posteroanterior).
See the entire definition of Anteroposterior

Antibiotic: A drug used to treat infections caused by bacteria and other microorganisms. Originally, an antibiotic was a substance produced by one microorganism that selectively inhibits the growth of another. Synthetic antibiotics, usually chemically related to natural antibiotics, have since been produced that accomplish comparable tasks.
See the entire definition of Antibiotic

Anxiety: A feeling of apprehension and fear characterized by physical symptoms such as palpitations , sweating, and feelings of stress . Anxiety disorders are serious medical illnesses that affect approximately 19 million American adults. These disorders fill people's lives with overwhelming anxiety and fear. Unlike the relatively mild, brief anxiety caused by a stressful event such as a business presentation or a first date, anxiety disorders are chronic, relentless, and can grow progressively worse if not treated.
See the entire definition of Anxiety

ARDS: Acute Respiratory Distress Syndrome . A fulminant lung condition in which trauma to the lungs leads to inflammation of the lungs, accumulation of fluid in the alveolar air sacs, low blood oxygen, and respiratory distress.
See the entire definition of ARDS

Artery: A vessel that carries blood high in oxygen content away from the heart to the farthest reaches of the body. Since blood in arteries is usually full of oxygen, the hemoglobin in the red blood cells is oxygenated. The resultant form of hemoglobin (oxyhemoglobin) is what makes arterial blood look bright red.
See the entire definition of Artery

Aspiration: Removal of a sample of fluid and cells through a needle. Aspiration also refers to the accidental sucking in of food particles or fluids into the lungs.
See the entire definition of Aspiration

Bacterial: Of or pertaining to bacteria . For example, a bacterial lung infection .
See the entire definition of Bacterial

Bilateral: Having, or relating to, two sides. Bilateral is as opposed, for example, to unilateral (which means having, or relating to, one side).
See the entire definition of Bilateral

Blood: The familiar red fluid in the body that contains white and red blood cells , platelets , proteins , and other elements. The blood is transported throughout the body by the circulatory system . Blood functions in two directions: arterial and venous. Arterial blood is the means by which oxygen and nutrients are transported to tissues while venous blood is the means by which carbon dioxide and metabolic by-products are transported to the lungs and kidneys, respectively, for removal from the body.
See the entire definition of Blood

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Blood count: The calculated number of white or red blood cells (WBCs or RBCs) in a cubic millimeter of blood.
See the entire definition of Blood count

Blood pressure: The blood pressure is the pressure of the blood within the arteries. It is produced primarily by the contraction of the heart muscle . It's measurement is recorded by two numbers. The first (systolic pressure) is measured after the heart contracts and is highest. The second (diastolic pressure) is measured before the heart contracts and lowest. A blood pressure cuff is used to measure the pressure. Elevation of blood pressure is called " hypertension ".
See the entire definition of Blood pressure

Blood transfusion : The transfer of blood or blood components from one person (the donor) into the bloodstream of another person (the recipient). This may be done as a lifesaving maneuver to replace blood cells or blood products lost through bleeding. Transfusion of your own blood

(autologous) is the safest method but requires advance planning and not all patients are eligible. Directed donor blood allows the patient to receive blood from known donors. Volunteer donor blood is usually most readily available and, when properly tested has a low incidence of adverse events. Blood conserving techniques are an important aspect of limiting transfusion requirements.
See the entire definition of Blood transfusion

Breathing: The process of respiration, during which air is inhaled into the lungs through the mouth or nose due to muscle contraction, and then exhaled due to muscle relaxation.
See the entire definition of Breathing

Bronchoscopy : A procedure that permits the doctor to see the breathing passages through a lighted tube.
See the entire definition of Bronchoscopy

Carbon dioxide: A gas which is the byproduct of cellular metabolism and which collects in the tissues, is cleared from the tissues by the blood within the veins, is carried by the hemoglobin in the red blood cells, and removed from the body via the lungs in the exhaled air. Abbreviated CO2.
See the entire definition of Carbon dioxide

Cardiac: Having to do with the heart.
See the entire definition of Cardiac

Catheter: A thin, flexible tube . For example, a catheter placed in a vein provides a pathway for giving drugs, nutrients, fluids, or blood products. Samples of blood can also be withdrawn through the catheter.
See the entire definition of Catheter

Central venous catheter: See: Catheter, central venous .
See the entire definition of Central venous catheter

Chest: The area of the body located between the neck and the abdomen . The chest contains the lungs , the heart and part of the aorta . The walls of the chest are supported by the dorsal vertebrae , the ribs , and the sternum .
See the entire definition of Chest

Chest X-ray: Commonly used to detect abnormalities in the lungs, but can also detect abnormalities in the heart, aorta, and the bones of the thoracic area. Metallic objects, such as jewelry are removed from the chest and neck areas for a chest x-ray to avoid interference with x-ray penetration and improve accuracy of the interpretation.
See the entire definition of Chest X-ray

Complete blood count : A set values of the cellular (formed elements) of blood. These measurements are generally determined by specially designed machines that analyze the different components of blood in less than a minute.
See the entire definition of Complete blood count

Condition: The term "condition" has a number of biomedical meanings including the following:

1. An unhealthy state, such as in "this is a progressive condition."
2. A state of fitness, such as "getting into condition."
3. Something that is essential to the occurrence of something else; essentially a "precondition."
4. As a verb: to cause a change in something so that a response that was previously associated with a certain stimulus becomes associated with another stimulus; to condition a person, as in behavioral conditioning.

See the entire definition of Condition

Critical care: Intensive care. The specialized care of patients whose conditions are life-threatening and who require comprehensive care and constant monitoring, usually in intensive care units.
See the entire definition of Critical care

CT scan: Computerized tomography scan. Pictures of structures within the body created by a computer that takes the data from multiple X-ray images and turns them into pictures on a screen. CT stands for computerized tomography.
See the entire definition of CT scan

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Dehydration : Excessive loss of body water. Diseases of the gastrointestinal tract that cause vomiting or diarrhea may, for example, lead to dehydration. There are a number of other causes of dehydration including heat exposure, prolonged vigorous exercise (e.g., in a marathon), kidney disease, and medications (diuretics).
See the entire definition of Dehydration

Diagnosis: 1 The nature of a disease ; the identification of an illness. **2** A conclusion or decision reached by diagnosis. The diagnosis is rabies . **3** The identification of any problem. The diagnosis was a plugged IV.
See the entire definition of Diagnosis

Discharge: 1. The flow of fluid from part of the body, such as from the nose or vagina.
2. The passing of an action potential, such as through a nerve or muscle fiber .
3. The release of a patient from a course of care. The doctor may then dictate a discharge summary.
See the entire definition of Discharge

Dysfunction: Difficult function or abnormal function.
See the entire definition of Dysfunction

Edema: The swelling of soft tissues as a result of excess water accumulation.
See the entire definition of Edema

Endotracheal tube: A flexible plastic tube that is put in the mouth and then down into the trachea (the airway). The doctor inserts the tube under direct vision with the help of a laryngoscope. The procedure is called endotracheal intubation . The purpose is to ventilate the lungs.
See the entire definition of Endotracheal tube

Event: A set of outcomes. Cardiovascular events might include a heart attack and gastrointestinal events a GI bleed. The use of the term "event" in medicine comes from probability theory.
See the entire definition of Event

Fever : Although a fever technically is any body temperature above the normal of 98.6 degrees F. (37 degrees C.), in practice a person is usually not considered to have a significant fever until the temperature is above 100.4 degrees F (38 degrees C.).
See the entire definition of Fever

Film: Slang shortening of X-ray film, an X-ray, a radiograph.
See the entire definition of Film

Fracture: A break in bone or cartilage. Although usually the result of trauma, a fracture can be caused by an acquired disease of bone such as osteoporosis or by abnormal formation of bone in a disease such as osteogenesis imperfecta ("brittle bone disease"). Fractures are classified according to their character and location as, for example, a greenstick fracture of the radius.
See the entire definition of Fracture

Fungal: Pertaining to a fungus . For example, a fungal skin infection.
See the entire definition of Fungal

Heart: The muscle that pumps blood received from veins into arteries throughout the body. It is positioned in the chest behind the sternum (breastbone; in front of the trachea, esophagus, and aorta; and above the diaphragm muscle that separates the chest and abdominal cavities. The normal heart is about the size of a closed fist, and weighs about 10.5 ounces. It is cone-shaped, with the point of the cone pointing down to the left. Two-thirds of the heart lies in the left side of the chest with the balance in the right chest.
See the entire definition of Heart

Hospital: It may seem unnecessary to define a "hospital" since everyone knows the nature of a hospital. A hospital began as a charitable institution for the needy, aged, infirm, or young.
See the entire definition of Hospital

Infection: The growth of a parasitic organism within the body. (A parasitic organism is one that lives on or in another organism and draws its nourishment therefrom.) A person with an infection has another organism (a "germ") growing within him, drawing its nourishment from the person.
See the entire definition of Infection

Inflammation: A basic way in which the body reacts to infection , irritation or other injury, the key feature being redness, warmth, swelling and pain . Inflammation is now recognized as a type of nonspecific immune response .
See the entire definition of Inflammation

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Injury: Harm or hurt. The term "injury" may be applied in medicine to damage inflicted upon oneself as in a hamstring injury or by an external agent on as in a cold injury . The injury may be accidental or deliberate, as with a needlestick injury . The term "injury" may be synonymous (depending on the context) with a wound or with trauma .
See the entire definition of Injury

Intensive care: See critical care .
See the entire definition of Intensive care

Internal medicine: A medical specialty dedicated to the diagnosis and medical treatment of adults. A physician who specializes in internal medicine is referred to as an internist. A minimum of seven years of medical school and postgraduate training are focused on learning the prevention, diagnosis, and treatment of diseases of adults. Subspecialties of internal medicine include allergy and immunology, cardiology (heart), endocrinology (hormone disorders), hematology (blood disorders), infectious diseases, gastroenterology (diseases of the gut), nephrology (kidney diseases), oncology (cancer), pulmonology (lung disorders), and rheumatology (arthritis and musculoskeletal disorders).
See the entire definition of Internal medicine

Low blood pressure : Any blood pressure that is below the normal expected for an individual in a given environment. Low blood pressure is also referred to as hypotension.
See the entire definition of Low blood pressure

Lungs: The lungs are a pair of breathing organs located with the chest which remove carbon dioxide from and bring oxygen to the blood. There is a right and left lung.
See the entire definition of Lungs

Mechanical ventilation: Use of a machine called a ventilator or respirator to improve the exchange of air between the lungs and the atmosphere.
See the entire definition of Mechanical ventilation

Medication: 1. A drug or medicine. **2.** The administration of a drug or medicine. (Note that "medication" does not have the dangerous double meaning of "drug.")
See the entire definition of Medication

Membrane: A very thin layer of tissue that covers a surface.
See the entire definition of Membrane

Mortality: A fatal outcome or, in one word, death. The word "mortality" is derived from "mortal" which came from the Latin "mors" (death). The opposite of mortality is, of course, immortality. Mortality is also quite distinct from morbidity (illness).
See the entire definition of Mortality

Nutrition : 1) The science or practice of taking in and utilizing foods. 2) A nourishing substance, such as nutritional solutions delivered to hospitalized patients via an IV or IG tube.
See the entire definition of Nutrition

Organ: A relatively independent part of the body that carries out one or more special functions. The organs of the human body include the eye , ear , heart , lungs , and liver .
See the entire definition of Organ

Organ failure: The failure of an essential system in the body. Multiple organ failure is the failure of two or more systems, such as the cardiovascular , and renal systems, and is a common consequence of sepsis (the presence of bacteria in the bloods) and of shock (very low blood pressure).
See the entire definition of Organ failure

Oxygen: A colorless, odorless and tasteless gas that makes up about 20% of the air we breathe (and at least half the weight of the entire solid crust of the earth) and which combines with most of the other elements to form oxides. Oxygen is essential to human, animal and plant life.
See the entire definition of Oxygen

Pancreatitis : Inflammation of the pancreas. Of the many diverse causes of pancreatitis , the most common are alcohol and gallstones .

See the entire definition of Pancreatitis

Pathogenic: Causing disease or capable of doing it.
See the entire definition of Pathogenic

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Pharmacy: A location where prescription drugs are sold. A pharmacy is, by law, constantly supervised by a licensed pharmacist.
See the entire definition of Pharmacy

Pulmonary: Having to do with the lungs. (The word comes from the Latin pulmo for lung).
See the entire definition of Pulmonary

Pulmonary artery: One of the two vessels which are formed as terminal branches of the pulmonary trunk and convey unaerated blood to the lungs. The two pulmonary arteries differ in length and anatomy.
See the entire definition of Pulmonary artery

Pulmonary artery catheter: Also called a Swan-Ganz catheter. A light flexible balloon-tipped tube that is introduced into the pulmonary artery (the artery from the right ventricle of the heart to the lungs). See; Catheter, Swann-Ganz.
See the entire definition of Pulmonary artery catheter

Pulmonary edema: Fluid in the lungs.
See the entire definition of Pulmonary edema

Pulmonary medicine: The branch of medicine that deals with the causes, diagnosis, prevention and treatment of diseases affecting the lungs .
See the entire definition of Pulmonary medicine

Quality of life: An important consideration in medical care, quality of life refers to the patient's ability to enjoy normal life activities. Some medical treatments can seriously impair quality of life without providing appreciable benefit, while others greatly enhance quality of life.
See the entire definition of Quality of life

Residual: Something left behind. With residual disease, the disease has not been eradicated.
See the entire definition of Residual

Respiratory: Having to do with respiration, the exchange of oxygen and carbon dioxide. From the Latin re- (again) + spirare (to breathe) = to breathe again.
See the entire definition of Respiratory

Respiratory failure: Inability of the lungs to perform their basic task of gas exchange , the transfer of oxygen from inhaled air into the blood and the transfer of carbon dioxide from the blood into exhaled air. The basis of respiratory failure may be failure of the exchange of oxygen and carbon dioxide within the tiny air sacs (alveoli) in the lungs; failure of the muscles required to expand the lungs; or failure of the brain centers controlling respiration.
See the entire definition of Respiratory failure

Respiratory therapy: Exercises and treatments designed to help patients maintain and recover lung function, such as with cystic fibrosis and after surgery .
See the entire definition of Respiratory therapy

Risk factor: Something that increases a person's chances of developing a disease.
See the entire definition of Risk factor

SARS: Severe acute respiratory syndrome. A severe form of pneumonia which appeared in outbreaks in 2003. See: Severe acute respiratory syndrome .
See the entire definition of SARS

Scan: As a noun, the data or image obtained from the examination of organs or regions of the body by gathering information with a sensing device.
See the entire definition of Scan

Sepsis: Commonly called a "blood stream infection." The presence of bacteria (bacteremia) or other infectious organisms or their toxins in the blood (septicemia) or in other tissue of the body. Sepsis may be associated with clinical symptoms of systemic (bodywide) illness, such as fever , chills, malaise (generally feeling "rotten"), low blood pressure , and mental status changes. Sepsis can be a serious situation, a life threatening disease calling for urgent and comprehensive care.
See the entire definition of Sepsis

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Septic: Infected, or denoting infection. For example, septic shock is shock caused by infection.
See the entire definition of Septic

Severe acute respiratory syndrome: A severe form of pneumonia . Abbreviated SARS . A term applied to outbreaks of a mysterious illness in Asia beginning February 1, 2003.
See the entire definition of Severe acute respiratory syndrome

Shock: In medicine, shock is a critical condition brought on by a sudden drop in blood flow through the body. There is failure of the circulatory system to maintain adequate blood flow. This sharply curtails the delivery of oxygen and nutrients to vital organs. It also compromises the kidney and so curtails the removal of wastes from the body. Shock can be due to a number of different mechanisms including not enough blood volume (hypovolemic shock) and not enough output of blood by the heart (cardiogenic shock). The signs and symptoms of shock include low blood pressure (hypotension), overbreathing (hyperventilation), a weak rapid pulse, cold clammy grayish-bluish (cyanotic) skin, decreased urine flow (oliguria), and mental changes (a sense of great anxiety and foreboding, confusion and, sometimes, combativeness).
See the entire definition of Shock

Stomach: 1. The sac-shaped digestive organ that is located in the upper abdomen, under the ribs. The upper part of the stomach connects to the esophagus, and the lower part leads into the small intestine.
See the entire definition of Stomach

Stress: Forces from the outside world impinging on the individual. Stress is a normal part of life that can help us learn and grow. Conversely, stress can cause us significant problems.
See the entire definition of Stress

Subclavian: Under the clavicle (the collar bone), as the subclavian artery or the subclavian vein .
See the entire definition of Subclavian

Syndrome: A set of signs and symptoms that tend to occur together and which reflect the presence of a particular disease or an increased chance of developing a particular disease.

Therapy: The treatment of disease .

Transfusion: The transfer of blood or blood products from one person (the donor) into another person (the recipient's) bloodstream. In most situations, this is done as a lifesaving maneuver to replace blood cells or blood products lost through severe bleeding. Transfusion of your own blood (autologous) is the safest method but requires planning ahead and not all patients are eligible. Directed donor blood allows the patient to receive blood from known donors. Volunteer donor blood is usually most readily available and, when properly tested has a low incidence of adverse events.

Trauma: Any injury , whether physically or emotionally inflicted. "Trauma" has both a medical and a psychiatric definition. Medically, "trauma" refers to a serious or critical bodily injury, wound, or shock . This definition is often associated with trauma medicine practiced in emergency rooms and represents a popular view of the term. In psychiatry , "trauma" has assumed a different meaning and refers to an experience that is emotionally painful, distressful, or shocking, which often results in lasting mental and physical effects.

Ultrasound : High-frequency sound waves. Ultrasound waves can be bounced off of tissues using special devices. The echoes are then converted into a picture called a sonogram. Ultrasound imaging, referred to as ultrasonography, allows physicians and patients to get an inside view of soft tissues and body cavities, without using invasive techniques. Ultrasound is often used to examine a fetus during pregnancy . There is no convincing evidence for any danger from ultrasound during pregnancy.

Vena cava: The superior vena cava is the large vein which returns blood to the heart from the head, neck and both upper limbs. The inferior vena cava returns blood to the heart from the lower part of the body.

Ventilation: The exchange of air between the lungs and the atmosphere so that oxygen can be exchanged for carbon dioxide in the alveoli (the tiny air sacs in the lungs).

Viral: Of or pertaining to a virus. For example, "My daughter has a viral rash ."

Vital: Necessary to maintain life. Breathing is a vital function.

Windpipe: The trachea, a tube-like portion of the respiratory (breathing) tract that connects the larynx (the voicebox) with the bronchial parts of the lungs.

X-ray: 1. High-energy radiation with waves shorter than those of visible light. X-rays possess the properties of penetrating most substances (to varying extents), of acting on a photographic film or plate (permitting radiography), and of causing a fluorescent screen to give off light (permitting fluoroscopy). In low doses X-rays are used for making images that help to diagnose disease, and in high doses to treat cancer . Formerly called a Roentgen ray. **2.** An image obtained by means of X-rays.

Exam

Select the ***best*** answer to each of the following items. Mark your responses on the Answer form.

1. Lucinactant is a new-generation _____ surfactant that contains phospholipids and a high concentration of the synthetic 21-amino acid hydrophobic peptide (sinapultide, also known as KL_4 peptide).

a. anabolic
b. synthetic
c. liquid
d. None of the above

2. A secondary goal of the analysis reviewed in this course was to compare the outcome of infants who received lucinactant versus those who received other classes of _____ after combining data from both trials.

a. steroids
b. analgesics
c. surfactants
d. None of the above

3. Within _____ of birth, infants between 600 and 1250 g were randomly assigned to receive lucinactant, colfosceril palmitate, or beractant in a 2:2:1 ratio in the SELECT trial and lucinactant or poractant alfa in a 1:1 ratio in the STAR trial.

a. 30 minutes
b. 1 to 2 hours
c. one day
d. none of the above

4. The neurologic examination in these studies assessed, at minimum _____ unilateral or bilateral blindness, and history of seizures that required treatment with anticonvulsant agents.

a. gross motor tone
b. presence of unilateral or bilateral deafness
c. reflex abnormalities
d. All of the above

5. Neurologic status at 1 year corrected age was essentially similar between infants who received lucinactant and those who received all other surfactants used in these 2 trials.

a. True
b. False

6. In addition to using the standard Kaplan-Meier approach for survival comparisons, the authors of the study here [determined] fixed-time-point estimates of mortality by imputing loss to follow-up as a death and also using raw data and compared them by using logistic regression adjusting for pooled center and birth weight stratum.

a. True
b. False

7. There were significant differences in the proportion of infants who were alive through 1 year corrected age comparing those given lucinactant with those who received colfosceril and beractant.

a. True
b. False

8. In the STAR trial, significantly more infants who were treated with lucinactant were alive through 1 year corrected age compared with those who received poractant alfa ($P = .04$).

a. True
b. False

9. Because _____ infants from both trials were either lost to follow-up or had their consent withdrawn, estimations of overall survival using raw data without imputation for loss to follow-up as a death introduced minor variations to the findings described above but did not modify the trend of the results.

a. none of the
b. very few
c. so very many
d. None of the above

10. Although between one third and one half of the infants in both studies were rehospitalized during the first year, in general, readmission to the hospital occurred _____ for most of them.

a. only once
b. twice
c. multiple times
d. None of the above

11. Neurologic evaluations at 1 year corrected age were performed for most surviving infants from the 2 studies. In the SELECT trial, 731 (81%) of the 908 infants alive at 1 year corrected age had neurologic evaluations (lucinactant: 306; colfosceril palmitate: 279; beractant: 146).

a. True
b. False

12. Surfactant therapy is associated with an absolute reduction of ~5% to 7% in neonatal mortality among preterm infants compared with those who receive placebo. This reduction in mortality rate translates into ~1 life saved for every 14 to 20 infants who receive surfactant.

a. True
b. False

13. The authors of this study concluded that both types of surfactants are effective in the treatment and prevention of RDS. They also concluded that when taken together _____ and a lower overall incidence of pneumothorax than synthetic products that contain only phospholipids.

a. fewer deaths
b. greater early improvement in the requirement for ventilatory support
c. use of animal-derived surfactants resulted in
d. All of the above

14. Kaplan-Meier survival estimates do not falsely amplify treatment differences with respect to survival. Rather, they generally reveal unbiased estimates of survival rates for each treatment, hence yielding unbiased estimates of _____.

a. protocol
b. patient differences
c. treatment differences
d. None of the above

15. The findings of this 1-year follow-up study, as well as data from the original reports of the lucinactant trials, strongly suggest that administration of lucinactant to infants at risk for RDS results in neonatal survival that is at least comparable with, if not superior to, that of infants given the animal-derived surfactants beractant and poractant alfa.

a. True
b. False

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