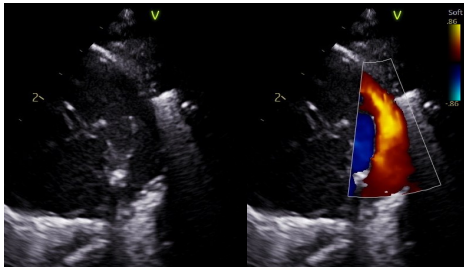
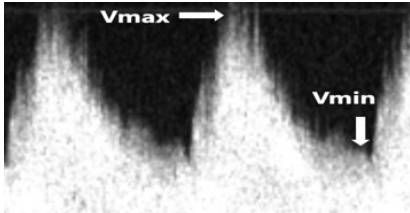
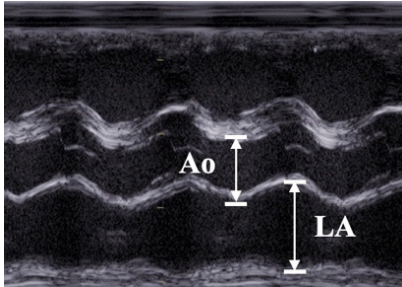
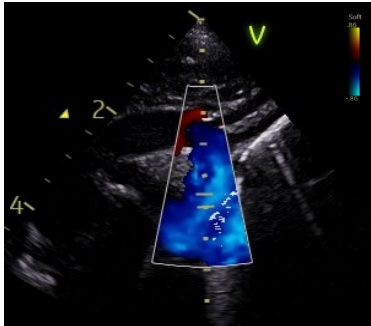


Table S1 Echocardiographic parameters and key measurement protocols for the assessment of PDA

Echocardiographic parameter	Recorded results	Key measurement protocols
Diameter	__mm	<ul style="list-style-type: none"> • Suprasternal or high parasternal view • Measured at the narrowest point on 2D imaging 
Ductal blood flow direction and velocity	__Purely left-to-right, Vmax__m/s, Vmin__m/s __Predominantly left-to-right __Bidirectional shunt __Purely right-to-left	<ul style="list-style-type: none"> • Pulsed wave Doppler (if peak velocity <2 m/s) • Continuous wave Doppler (if peak velocity \geq2 m/s) • Flow direction is determined by observing Doppler waveform direction 
Left atrium to aortic root ratio (LA/Ao)	LA__cm Ao__cm LA/Ao__	<ul style="list-style-type: none"> • Parasternal long-axis view • M-mode, with the cursor placed through the aortic root and left atrium, perpendicular to the aortic root 
Diastolic flow direction in descending aorta	__Antegrade (forward) flow __Absent flow __Retrograde (reversed) flow	<ul style="list-style-type: none"> • Suprasternal long-axis view of the aortic arch • Pulsed wave Doppler, with sample volume placed in the descending aorta post-ductally (at the level of the diaphragm or slightly above) • Keep the Doppler beam as parallel as possible to the direction of flow 

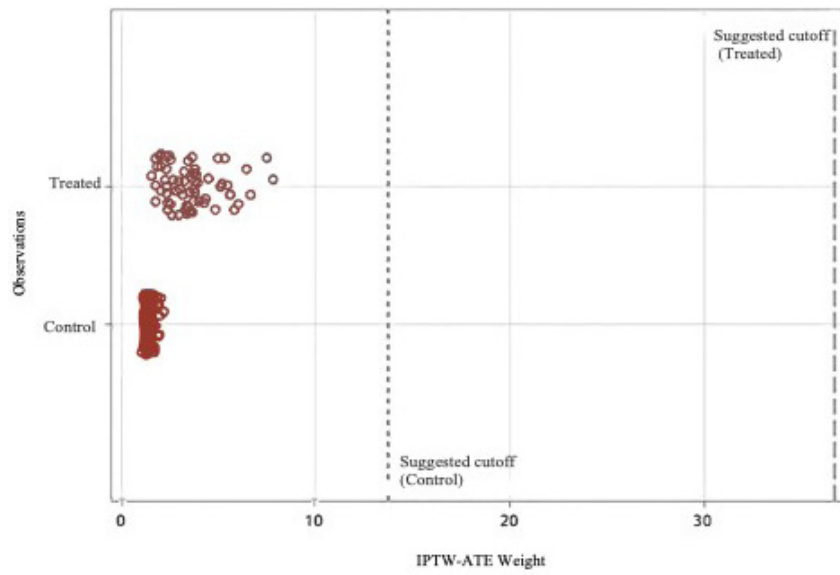


Figure S1 Distribution of inverse probability of treatment weighting (IPTW) weights.

Table S2 Maternal and neonatal baseline characteristics in the observational (unweighted) and emulated trial (IPTW-weighted) cohorts among the tolerant subgroup

Characteristic	Observational cohort (unweighted)				Emulated trial cohort (IPTW-weighted)			
	Non-treatment (n=129)	Treatment (n=45)	P value	SMD	Non-treatment (n=173)	Treatment (n=178)	P value	SMD
Maternal characteristics								
Multiple births	43 (33.3)	18 (40.0)	0.420	0.14	60 (34.7)	70 (39.3)	0.617	0.09
Cesarean delivery	76 (58.9)	23 (51.1)	0.363	0.16	99 (57.2)	94 (52.8)	0.596	0.09
Premature rupture of membranes >24 h	25 (19.4)	7 (15.6)	0.569	0.10	33 (19.1)	26 (14.6)	0.490	0.12
Chorioamnionitis	34 (26.4)	11 (24.4)	0.801	0.05	49 (28.3)	32 (18.0)	0.131	0.25
Antenatal corticosteroids	100 (77.5)	39 (86.7)	0.188	0.24	136 (78.6)	147 (82.6)	0.631	0.10
Neonatal characteristics								
Male sex	73 (56.6)	19 (42.2)	0.096	0.29	96 (55.5)	86 (48.3)	0.417	0.14
Gestational age, weeks	28.0 (27.1–29.3)	27.4 (26.6–29.0)	0.144	0.23	27.9 (27.0–29.1)	27.6 (26.9–29.0)	0.455	0.08
<28	59 (45.7)	27 (60.0)			83 (48.0)	100 (56.2)		
28–29 [†]	70 (54.3)	18 (40.0)			90 (52.0)	78 (43.8)		
Birth weight, g	1,100 (900–1,300)	1,020 (900–1,150)	0.082	0.33	1,085 (891–1,293)	1,029 (896–1,180)	0.369	0.10
Small for gestational age	6 (4.7)	3 (6.7)	0.893	0.09	9 (5.2)	9 (5.1)	0.994	0.00
Apgar 5 min score	9 (8–9)	9 (8–10)	0.535	0.07	8 (7–9)	8 (7–9)	0.434	0.09
CRIB-II score	8 (6–10)	8 (7–10)	0.210	0.27	8 (6–9)	8 (6–9)	0.679	0.03
≥2 surfactant doses within 3 days of life	18 (14.0)	7 (15.6)	0.792	0.05	23 (13.3)	24 (13.5)	0.977	0.01
Respiratory support at echocardiography			0.037	0.36			0.865	0.03
Noninvasive ventilation	83 (64.3)	21 (46.7)			104 (60.1)	104 (58.4)		
Conventional ventilation, FiO ₂ ≤30%	46 (35.7)	24 (53.3)			69 (39.9)	74 (41.6)		
Conventional ventilation, FiO ₂ >30%	–	–			–	–		
High-Frequency Ventilation, any FiO ₂	–	–			–	–		
Inotropes at echocardiography	–	–	–	–	–	–	–	–

Data are presented as n (%) or median (IQR). [†], higher values represent greater illness severity. CRIB-II, clinical risk index for babies II; FiO₂, fraction of inspired oxygen; IPTW, inverse probability of treatment weighting; IQR, interquartile range; SMD, standardized mean difference.

Table S3 Maternal and neonatal baseline characteristics in the observational (unweighted) and emulated trial (IPTW-weighted) cohorts among the intolerant subgroup

Characteristic	Observational cohort (unweighted)				Emulated trial cohort (IPTW-weighted)			
	Non-treatment (n=45)	Treatment (n=20)	P value	SMD	Non-treatment (n=66)	Treatment (n=61)	P value	SMD
Maternal characteristics								
Multiple births	19 (40.0)	7 (35.0)	0.702	0.10	27 (40.9)	23 (37.7)	0.828	0.06
Cesarean delivery	27 (60.0)	12 (60.0)	1.000	0.00	38 (57.6)	40 (65.6)	0.497	0.16
Premature rupture of membranes >24 h	5 (11.1)	3 (15.0)	0.975	0.16	7 (10.6)	13 (21.3)	0.325	0.29
Chorioamnionitis	8 (17.8)	10 (50.0)	0.007	0.72	12 (18.2)	27 (44.3)	0.043	0.59
Antenatal corticosteroids	36 (80.0)	16 (80.0)	1.000	0.00	54 (81.8)	44 (72.1)	0.391	0.23
Neonatal characteristics								
Male sex	20 (44.4)	12 (60.0)	0.247	0.32	27 (40.9)	36 (59.0)	0.229	0.37
Gestational age, weeks, median (IQR)	27.7 (26.3-28.7)	28.1 (26.9-28.9)	0.493	0.16	27.7 (26.1-28.7)	28.1 (26.7-28.8)	0.362	0.16
<28	25 (55.6)	9 (45.0)			36 (54.5)	26 (42.6)		
28–29 ^a	20 (44.4)	11 (55.0)			30 (45.5)	35 (57.4)		
Birth weight, g, median (IQR)	977 (850-1140)	1015 (895-1210)	0.221	0.30	962 (807-1109)	1035 (894-1198)	0.198	0.23
Small for gestational age	2 (4.4)	1 (5.0)	1.000	0.03	3 (4.5)	4 (6.6)	0.839	0.09
Apgar 5 min score, median (IQR)	8 (8-9)	8 (7-9)	0.365	0.16	8 (7-9)	8 (7-8)	0.540	0.11
CRIB-II score, median (IQR) [†]	9 (7-11)	8.5 (7.5-11)	0.926	0.05	8 (6-11)	8 (6-10)	0.580	0.10
≥2 surfactant doses within 3 days of life	18 (40.0)	5 (25.0)	0.243	0.32	24 (36.4)	17 (27.9)	0.525	0.18
Respiratory support at echocardiography			0.561	0.27			0.808	0.08
Noninvasive ventilation	–	–			–	–		
Conventional ventilation, FiO ₂ ≤30%	8 (17.8)	2 (10.0)			11 (16.7)	6 (9.8)		
Conventional ventilation, FiO ₂ >30%	16 (35.6)	6 (30.0)			22 (33.3)	22 (36.1)		
High-Frequency Ventilation, any FiO ₂	21 (46.7)	12 (60.0)			33 (50.0)	33 (54.1)		
Inotropes at echocardiography	21 (46.7)	7 (35.0)	0.381	0.24	28 (42.4)	26 (42.6)	0.984	0.00

Data are presented as n (%) or median (IQR). [†], higher values represent greater illness severity. FiO₂, fraction of inspired oxygen; IPTW, inverse probability of treatment weighting; SMD, standardized mean difference; IQR, interquartile range; CRIB-II, clinical risk index for babies II.

Table S4 Sensitivity analysis: comparison of outcomes using univariable and multivariable generalized linear mixed-effects models in the observational cohort, overall and by tolerant and intolerant subgroups

Outcomes	Non-treatment	Treatment	Univariable analysis		Multivariable analysis [†]	
			OR (95% CI)	P value	OR (95% CI)	P value
Overall cohort	n=174	n=65				
Death	24 (13.8)	5 (7.7)	0.52 (0.18–1.53)	0.234	0.45 (0.15–1.39)	0.165
IVH ≥ grade 3	16 (9.2)	5 (7.7)	0.85 (0.29–2.52)	0.767	0.76 (0.25–2.35)	0.636
NEC ≥ stage II	11 (6.3)	4 (6.2)	0.97 (0.30–3.19)	0.962	0.99 (0.30–3.31)	0.986
BPD ≥ grade 2 [‡]	41/151 (27.2)	25/60 (41.7)	2.54 (1.20–5.36)	0.015	2.08 (0.93–4.63)	0.074
Death/BPD	64 (36.8)	30 (46.2)	1.53 (0.81–2.86)	0.187	1.35 (0.68–2.69)	0.394
Death/IVH/NEC/BPD	73 (42.0)	34 (52.3)	1.65 (0.88–3.06)	0.116	1.49 (0.77–2.92)	0.238
Tolerant subgroup	n=129	n=45				
Death	10 (7.8)	4 (8.9)	1.16 (0.34–3.94)	0.810	1.05 (0.29–3.81)	0.937
IVH ≥ grade 3	5 (3.9)	3 (6.7)	1.83 (0.40–8.36)	0.434	1.59 (0.33–7.74)	0.561
NEC ≥ stage II	8 (6.2)	3 (6.7)	1.08 (0.27–4.31)	0.912	1.00 (0.25–4.04)	0.999
BPD ≥ grade 2 [‡]	36/120 (30.0)	17/41 (41.5)	2.55 (1.06–6.17)	0.038	2.00 (0.79–5.09)	0.144
Death/BPD	45 (34.9)	21 (46.7)	2.30 (1.03–5.14)	0.043	1.91 (0.82–4.45)	0.135
Death/IVH/NEC/BPD	49 (38.0)	23 (51.1)	2.38 (1.08–5.25)	0.032	1.99 (0.87–4.56)	0.102
Intolerant subgroup	n=45	n=20				
Death	14 (31.1)	1 (5.0)	0.12 (0.01–1.07)	0.057	0.05 (0.01–0.70)	0.027
IVH ≥ grade 3	11 (24.4)	2 (10.0)	0.34 (0.07–1.79)	0.199	0.32 (0.06–1.75)	0.186
NEC ≥ stage II	3 (6.7)	1 (5.0)	0.74 (0.07–7.98)	0.798	0.81 (0.07–9.26)	0.866
BPD ≥ grade 2 [‡]	5/31 (16.1)	8/19 (42.1)	3.61 (0.39–33.19)	0.248	5.85 (0.42–81.35)	0.182
Death/BPD	19 (42.2)	9 (45.0)	0.69 (0.17–2.92)	0.612	0.68 (0.13–3.69)	0.652
Death/IVH/NEC/BPD	24 (53.3)	11 (55.0)	0.93 (0.26–3.33)	0.910	1.12 (0.28–4.51)	0.869

Data are presented as n (%) or n/N (%). [†], generalized linear mixed-effects model with a random intercept for study center, additionally adjusted for sex, gestational age, birth weight, CRIB-II score; [‡], among infants alive at 36 weeks of postmenstrual age, or discharge to home, if earlier. BPD, bronchopulmonary dysplasia; CI, confidence interval; IPTW, inverse probability of treatment weighting; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; OR, odds ratio.

Table S5 Sensitivity analysis: maternal and neonatal baseline characteristics in the observational (unweighted) and emulated trial (IPTW-weighted) cohorts after exclusion of two untreated infants who died within 2 days following echocardiographic assessment

Characteristic	Observational cohort (unweighted)				Emulated trial cohort (IPTW-weighted)			
	Non-treatment (n=172)	Treatment (n=65)	P value	SMD	Non-treatment (n=237)	Treatment (n=238)	P value	SMD
Maternal characteristics								
Multiple births	60 (34.9)	25 (38.5)	0.608	0.07	86 (36.3)	92 (38.7)	0.776	0.04
Cesarean delivery	102 (59.3)	35 (53.8)	0.448	0.11	136 (57.4)	134 (56.3)	0.864	0.03
Premature rupture of membranes >24 h	30 (17.4)	10 (15.4)	0.706	0.06	40 (16.9)	39 (16.4)	0.900	0.02
Chorioamnionitis	40 (23.3)	21 (32.3)	0.155	0.20	59 (24.9)	57 (23.9)	0.846	0.03
Antenatal corticosteroids	134 (77.9)	55 (84.6)	0.252	0.17	188 (79.3)	189 (79.4)	0.998	0.00
Neonatal characteristics								
Male sex	91 (52.9)	31 (47.7)	0.474	0.10	122 (51.5)	120 (50.4)	0.897	0.02
Gestational age, weeks	28.0 (27.0–29.1)	27.7 (26.7–29.0)	0.287	0.14	27.9 (26.8–29.0)	27.7 (26.9–29.0)	0.865	0.02
<28	82 (47.7)	36 (55.4)			117 (49.4)	125 (52.5)		
28–29 ^a	90 (52.3)	29 (44.6)			120 (50.6)	113 (47.5)		
Birth weight, g	1,065 (890–1,280)	1,020 (900–1,180)	0.349	0.17	1,030 (873–1239)	1,035 (898–1,197)	0.904	0.02
Small for gestational age	8 (4.7)	4 (6.2)	0.890	0.07	12 (5.1)	12 (5.0)	0.969	0.00
Apgar 5 min score	9 (8–9)	8 (8–9)	0.886	0.03	8 (7–9)	8 (7–9)	0.644	0.07
CRIB-II score [†]	8 (6–10)	8 (7–10)	0.210	0.21	8 (6–9)	8 (6–9)	0.906	0.02
≥2 surfactant doses within 3 days of life	34 (19.8)	12 (18.5)	0.821	0.03	45 (19.0)	39 (16.4)	0.647	0.06
Respiratory support at echocardiography			0.144	0.33			1.000	0.00
Noninvasive ventilation	83 (48.3)	21 (32.3)			104 (43.9)	105 (44.1)		
Conventional ventilation, FiO ₂ ≤30%	54 (31.4)	26 (40.0)			80 (33.8)	80 (33.6)		
Conventional ventilation, FiO ₂ >30%	15 (8.7)	6 (9.2)			21 (8.9)	21 (8.8)		
High-Frequency Ventilation, any FiO ₂	20 (11.6)	12 (18.5)			32 (13.5)	32 (13.4)		
Inotropes at echocardiography	20 (11.6)	7 (10.8)	0.853	0.03	27 (11.4)	25 (10.5)	0.870	0.02

Data are presented as n (%) or median (IQR). [†], higher values represent greater illness severity. CRIB-II, clinical risk index for babies II; FiO₂, fraction of inspired oxygen; IPTW, inverse probability of treatment weighting; IQR, interquartile range; SMD, standardized mean difference.

Table S6 Sensitivity analysis: comparison of outcomes after exclusion of two untreated infants who died within 2 days following echocardiographic assessment, overall and by tolerant and intolerant subgroups

Outcomes	Observational cohort (unweighted)				Emulated trial cohort (IPTW-weighted)			
	Non-treatment	Treatment	χ^2	P value	Non-treatment	Treatment	RR (95% CI)	P value
Overall	n=172	n=65			n=237	n=238	†	
Death	22 (12.8)	5 (7.7)	1.215	0.270	31 (13.1)	17 (7.1)	0.54 (0.28–1.06)	0.075
IVH \geq grade 3	16 (9.3)	5 (7.7)	0.151	0.697	23 (9.7)	14 (5.9)	0.57 (0.22–1.47)	0.249
NEC \geq stage II	11 (6.4)	4 (6.2)	0.000	1.000	15 (6.3)	13 (5.5)	0.86 (0.37–1.97)	0.722
BPD \geq grade 2 [‡]	41/151 (27.2)	25/60 (41.7)	4.208	0.040	58/207 (28.0)	80/221 (36.2)	1.30 (0.81–2.09)	0.283
Death/BPD	62 (36.0)	30 (46.2)	2.029	0.154	87 (36.7)	97 (40.8)	1.11 (0.71–1.73)	0.649
Death/IVH/NEC/BPD	71 (41.3)	34 (52.3)	2.325	0.127	100 (42.2)	108 (45.4)	1.08 (0.78–1.51)	0.635
Tolerant subgroup	n=129	n=45			n=173	n=179	§	
Death	10 (7.8)	4 (8.9)	0.000	1.000	13 (7.5)	13 (7.3)	0.98 (0.23–4.15)	0.981
IVH \geq grade 3	5 (3.9)	3 (6.7)	0.127	0.722	7 (4.0)	9 (5.0)	1.16 (0.38–3.55)	0.790
NEC \geq stage II	8 (6.2)	3 (6.7)	0.000	1.000	10 (5.8)	10 (5.6)	0.94 (0.25–3.59)	0.928
BPD \geq grade 2 [‡]	36/120 (30.0)	17/41 (41.5)	1.819	0.178	50/161 (31.1)	60/166 (36.1)	1.16 (0.71–1.92)	0.552
Death/BPD	45 (34.9)	21 (46.7)	1.967	0.161	62 (35.8)	73 (40.8)	1.18 (0.80–1.73)	0.395
Death/IVH/NEC/BPD	49 (38.0)	23 (51.1)	2.370	0.124	67 (38.7)	79 (44.1)	1.18 (0.85–1.64)	0.310
Intolerant subgroup	n=43	n=20			n=64	n=59	¶	
Death	12 (27.9)	1 (5.0)	3.087	0.079	18 (28.1)	4 (6.8)	0.18 (0.06–0.55)	0.003
IVH \geq grade 3	11 (25.6)	2 (10.0)	1.184	0.277	16 (25.0)	5 (8.5)	0.29 (0.10–0.83)	0.021
NEC \geq stage II	3 (7.0)	1 (5.0)	–	1.000	5 (7.8)	3 (5.1)	0.77 (0.20–3.03)	0.711
BPD \geq grade 2 [‡]	5/31 (16.1)	8/19 (42.1)	2.892	0.089	8/46 (12.5)	20/55 (36.4)	2.24 (0.71–7.01)	0.168
Death/BPD	17 (39.5)	9 (45.0)	0.168	0.682	25 (39.1)	24 (40.7)	1.14 (0.55–2.37)	0.723
Death/IVH/NEC/BPD	22 (51.2)	11 (55.0)	0.081	0.777	33 (51.6)	29 (49.2)	1.04 (0.74–1.46)	0.811

Data are presented as n (%) or n/N (%). †, weighted log-binomial regression with cluster-robust standard errors by study center, estimating marginal risk ratios without additional covariate adjustment after IPTW; ‡, among infants alive at 36 weeks of postmenstrual age, or discharge to home, if earlier; §, weighted Poisson regression (employed after weighted log-binomial regression failed to converge), with cluster-robust standard errors by study center, and additionally adjusted for sex, gestational age, birth weight, CRIB-II score, premature rupture of membranes >24 h, chorioamnionitis, and antenatal corticosteroids; ¶, weighted Poisson regression (employed after weighted log-binomial regression failed to converge), with cluster-robust standard errors by study center, and additionally adjusted for sex, gestational age, birth weight, CRIB-II score, cesarean delivery, premature rupture of membranes >24 h, chorioamnionitis, antenatal corticosteroids, and surfactant doses within 3 days of life. BPD, bronchopulmonary dysplasia; CI, confidence interval; IPTW, inverse probability of treatment weighting; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; RR, risk ratio.

Table S7 Sensitivity analysis: maternal and neonatal baseline characteristics in the observational (unweighted) and emulated trial (IPTW-weighted) cohorts using a 1-day grace period

Characteristic	Observational cohort (unweighted)				Emulated trial cohort (IPTW-weighted)			
	Non-treatment (n=190)	Treatment (n=49)	P value	SMD	Non-treatment (n=239)	Treatment (n=240)	P value	SMD
Maternal characteristics								
Multiple births	65 (34.2)	21 (42.9)	0.261	0.18	87 (36.4)	97 (40.4)	0.636	0.08
Cesarean delivery	110 (57.9)	28 (57.1)	0.924	0.02	137 (57.3)	132 (55.0)	0.783	0.05
Premature rupture of membranes >24 h	32 (16.8)	8 (16.3)	0.931	0.01	40 (16.7)	41 (17.1)	0.980	0.00
Chorioamnionitis	50 (26.3)	13 (26.5)	0.976	0.00	63 (26.4)	58 (24.2)	0.776	0.05
Antenatal corticosteroids	149 (78.4)	42 (85.7)	0.256	0.19	191 (79.9)	186 (77.5)	0.745	0.07
Neonatal characteristics								
Male sex	101 (53.2)	23 (46.9)	0.437	0.12	124 (51.9)	123 (51.3)	0.933	0.01
Gestational age, weeks	28.0 (26.9–29.0)	27.7 (26.6–29.1)	0.511	0.10	27.8 (26.8–28.9)	27.7 (26.8–28.9)	0.709	0.06
<28	94 (49.5)	26 (53.1)			122 (51.0)	125 (52.1)		
28–29 ^a	96 (50.5)	23 (46.9)			117 (49.0)	115 (47.9)		
Birth weight, g	1,050 (890–1,250)	1,000 (890–1,200)	0.293	0.19	1,028 (878–1,234)	1034 (894–1,208)	0.871	0.03
Small for gestational age	8 (4.2)	4 (8.2)	0.446	0.16	11 (4.6)	13 (5.4)	0.804	0.04
Apgar 5 min score	8.5 (8–9)	8 (8–9)	0.908	0.03	8 (7–9)	8 (7–9)	0.685	0.07
CRIB-II score [†]	8 (6–10)	8 (8–10)	0.251	0.21	8 (6–10)	8 (6–9)	0.834	0.04
≥2 surfactant doses within 3 days of life	40 (21.1)	8 (16.3)	0.462	0.12	48 (20.1)	38 (15.8)	0.515	0.10
Respiratory support at echocardiography			0.338	0.28			0.997	0.01
Noninvasive ventilation	88 (46.3)	16 (32.7)			104 (43.5)	103 (42.9)		
Conventional ventilation, FiO ₂ ≤30%	59 (31.1)	21 (42.9)			80 (33.5)	78 (32.5)		
Conventional ventilation, FiO ₂ >30%	17 (8.9)	5 (10.2)			22 (9.2)	25 (10.4)		
High-Frequency Ventilation, any FiO ₂	26 (13.7)	7 (14.3)			33 (13.8)	34 (14.2)		
Inotropes at echocardiography	24 (12.6)	4 (8.2)	0.465	0.15	28 (11.7)	25 (10.4)	0.839	0.04

Data are presented as n (%) or median (IQR). [†], higher values represent greater illness severity. CRIB-II, clinical risk index for babies II; FiO₂, fraction of inspired oxygen; IPTW, inverse probability of treatment weighting; IQR, interquartile range; SMD, standardized mean difference.

Table S8 Sensitivity analysis: comparison of outcomes using a 1-day grace period, overall and by tolerant and intolerant subgroups

Outcomes	Observational cohort (unweighted)				Emulated trial cohort (IPTW-weighted)			
	Non-treatment	Treatment	χ^2	P value	Non-treatment	Treatment	RR (95% CI)	P value
Overall	n=190	=49			n=239	n=240	†	
Death	25 (13.2)	4 (8.2)	0.912	0.340	32 (13.4)	16 (6.7)	0.49 (0.25–0.96)	0.038
IVH \geq grade 3	17 (8.9)	4 (8.2)	0.000	1.000	21 (8.8)	12 (5.0)	0.57 (0.22–1.51)	0.258
NEC \geq stage II	12 (6.3)	3 (6.1)	0.000	1.000	15 (6.3)	16 (6.7)	1.08 (0.32–3.64)	0.905
BPD \geq grade 2 [‡]	45/166 (27.1)	21/45 (46.7)	6.300	0.012	57/208 (27.4)	78/224 (34.8)	1.28 (0.69–2.36)	0.438
Death/BPD	69 (36.2)	25 (51.0)	3.530	0.060	88 (36.8)	94 (39.2)	1.07 (0.60–1.91)	0.819
Death/IVH/NEC/BPD	78 (41.1)	29 (59.2)	5.179	0.023	99 (41.4)	114 (47.5)	1.15 (0.76–1.72)	0.509
Tolerant subgroup	n=139	n=35			n=174	n=174	§	
Death	11 (7.9)	3 (8.6)	0.000	1.000	14 (8.0)	12 (6.9)	0.83 (0.22–3.15)	0.784
IVH \geq grade 3	6 (4.3)	2 (5.7)	0.000	1.000	7 (4.0)	6 (3.4)	0.80 (0.26–2.45)	0.690
NEC \geq stage II	9 (6.5)	2 (5.7)	0.000	1.000	11 (6.3)	7 (4.0)	0.65 (0.18–2.39)	0.515
BPD \geq grade 2 [‡]	39/129 (30.2)	14/32 (43.8)	2.122	0.145	49/161 (30.4)	53/162 (32.7)	1.13 (0.68–1.89)	0.635
Death/BPD	49 (35.3)	17 (48.6)	2.107	0.147	62 (35.6)	65 (37.4)	1.12 (0.74–1.70)	0.601
Death/IVH/NEC/BPD	53 (38.1)	19 (54.3)	3.009	0.083	67 (38.5)	72 (41.4)	1.14 (0.79–1.67)	0.483
Intolerant subgroup	n=51	n=14			n=65	n=66	¶	
Death	14 (27.5)	1 (7.1)	1.536	0.215	18 (27.7)	4 (6.1)	0.16 (0.06–0.46)	0.001
IVH \geq grade 3	11 (21.6)	2 (14.3)	0.051	0.821	14 (21.5)	6 (9.1)	0.46 (0.09–2.33)	0.348
NEC \geq stage II	3 (5.9)	1 (7.1)	–	1.000	4 (6.2)	9 (13.6)	1.10 (0.22–5.39)	0.906
BPD \geq grade 2 [‡]	6/37 (16.2)	7/13 (53.8)	5.259	0.022	8/47 (17.0)	25/62 (40.3)	2.12 (0.81–5.57)	0.127
Death/BPD	20 (39.2)	8 (57.1)	1.440	0.230	26 (40.0)	29 (43.9)	1.22 (0.62–2.38)	0.569
Death/IVH/NEC/BPD	25 (49.0)	10 (71.4)	2.220	0.136	32 (48.5)	42 (63.6)	1.31 (0.83–2.07)	0.241

Data are presented as n (%) or n/N (%). †, weighted log-binomial regression with cluster-robust standard errors by study center, estimating marginal risk ratios without additional covariate adjustment after IPTW; ‡, among infants alive at 36 weeks of postmenstrual age, or discharge to home, if earlier; §, weighted Poisson regression (employed after weighted log-binomial regression failed to converge), with cluster-robust standard errors by study center, and additionally adjusted for sex, gestational age, birth weight, CRIB-II score, premature rupture of membranes >24 h, chorioamnionitis, and antenatal corticosteroids; ¶, weighted Poisson regression (employed after weighted log-binomial regression failed to converge), with cluster-robust standard errors by study center, and additionally adjusted for sex, gestational age, birth weight, CRIB-II score, cesarean delivery, premature rupture of membranes >24 h, chorioamnionitis, antenatal corticosteroids, and surfactant doses within 3 days of life. BPD, bronchopulmonary dysplasia; CI, confidence interval; IPTW, inverse probability of treatment weighting; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; RR, risk ratio.