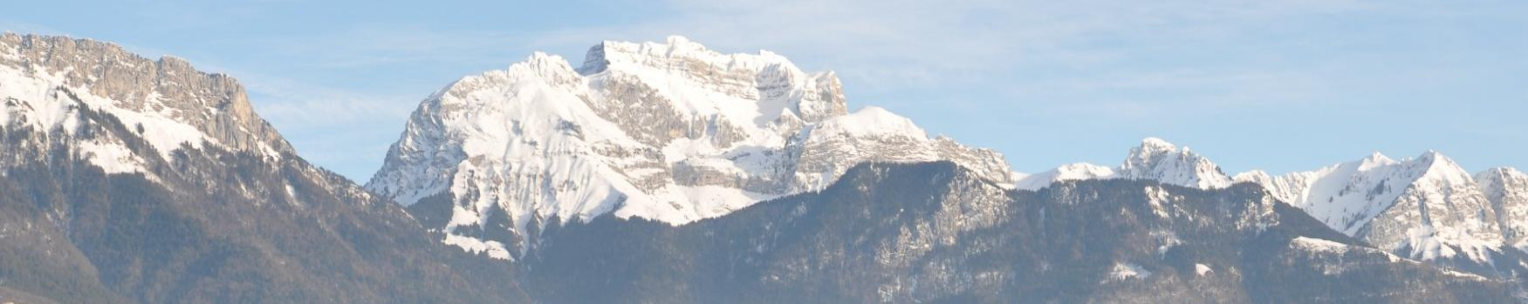




Birds trial

Breathing spontaneously at the early phase of ARDS

Jean-Christophe M Richard

Laurent Brochard

Alain Mercat



Creteil



CONFLICTS OF INTEREST

Air Liquide Medical Systems (part time)

Financial support for research (Genève /Annecy/Angers)

- VYGON (personal fee for lectures)
- COVIDIEN (PAV+) (personal fee for lectures)
- DRAGER (SmartCare)
- GE (FRC)

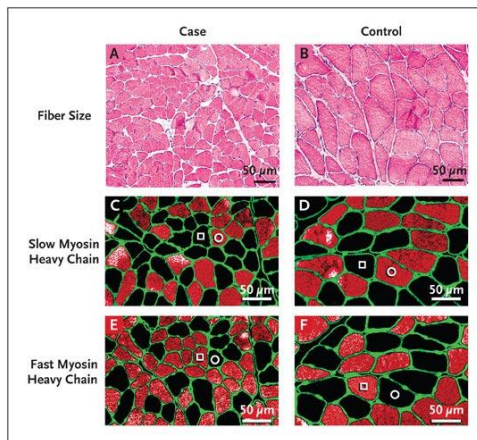
No COI directly related to the BIRDS study

Why is spontaneous breathing desirable?

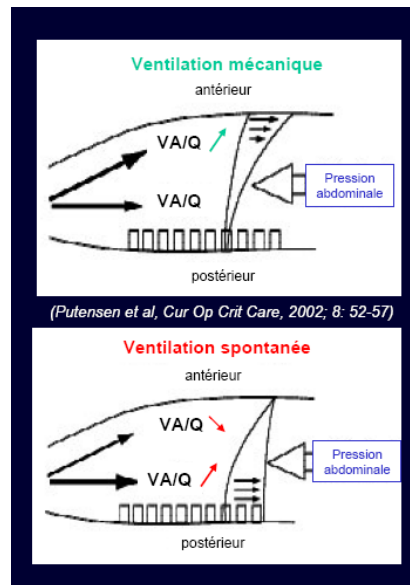
Preserve Respiratory Muscle Function (avoid VIDD)

Improve VA/Q and Regional Ventilation

Reduce sedation and days with MV



Levine S et al. N Engl J Med 2008
Jaber et al. Am J Respir Crit Care Med 2013



Putensen et al. Am J Respir Crit Care Med 1999

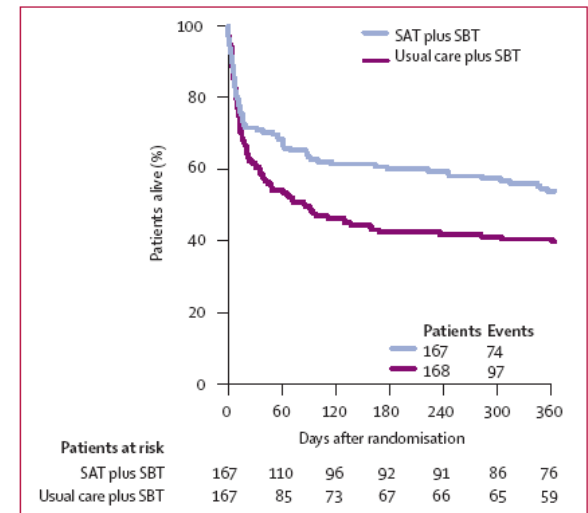


Figure 4: Survival at 1 year
Events indicate the number of deaths in each group in the year after enrolment.

Girard et al. Lancet 2008

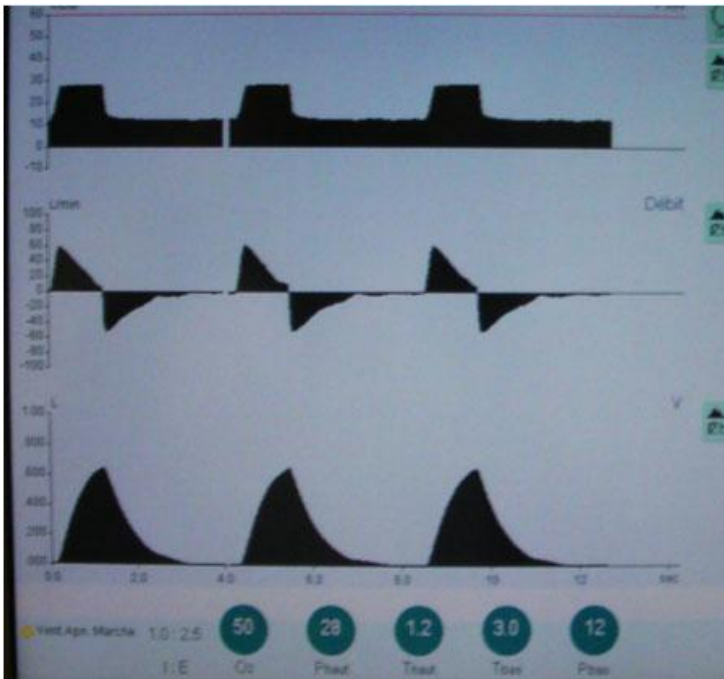


Birds trial



Breathing spontaneously at the early phase of ARDS

PC-IMV / (APRV with conventional I/E ratio)



Paralysed



With SB



Birds trial



Breathing spontaneously at the early phase of ARDS

Inclusion criteria:

ARDS with PF < 200 mmHg with PEEP > 5 cmH₂O

Main objective:

Promoting spontaneous breathing (PC-IMV / APRV) at the early phase of ARDS may reduce hospital mortality.

Secondary objectives:

- may reduce sedation drugs
- may reduce vasoactive drugs
- May reduce days under mechanical ventilation
- May reduce days in the ICU, days with organ dysfunction

Primary endpoint:

Hospital mortality

N = 700 for a 10% absolute hospital mortality reduction (35% to 25%)



Birds trial



Breathing spontaneously at the early phase of ARDS

Vt = 6 ml/kg PBW and PEEP for Pplat = 28 cmH₂O

ACV

PC-IMV / APRV

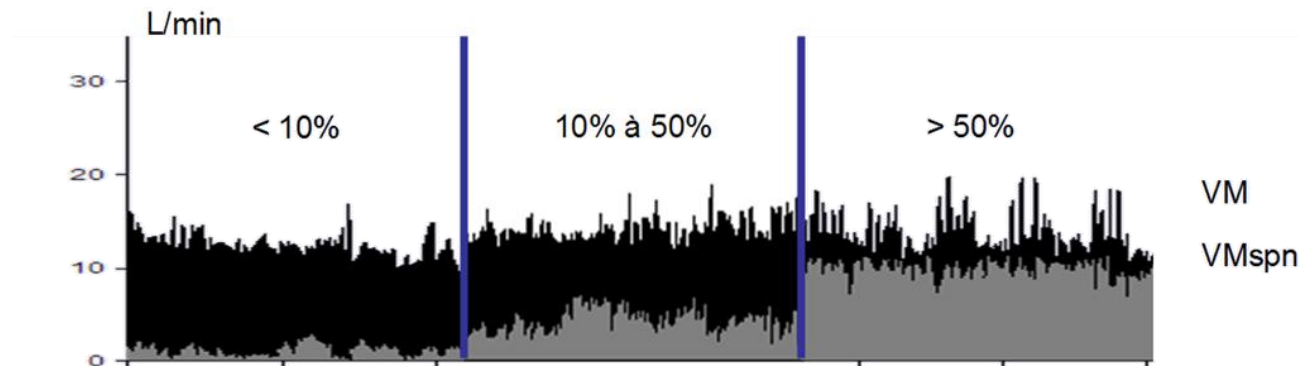
Mode : ACV

- ♦ Vt = 6 ml/kg PBW
- ♦ PEEP for Pplat = 28 cmH₂O
- ♦ Insp flow. : 50 à 70 L/mn

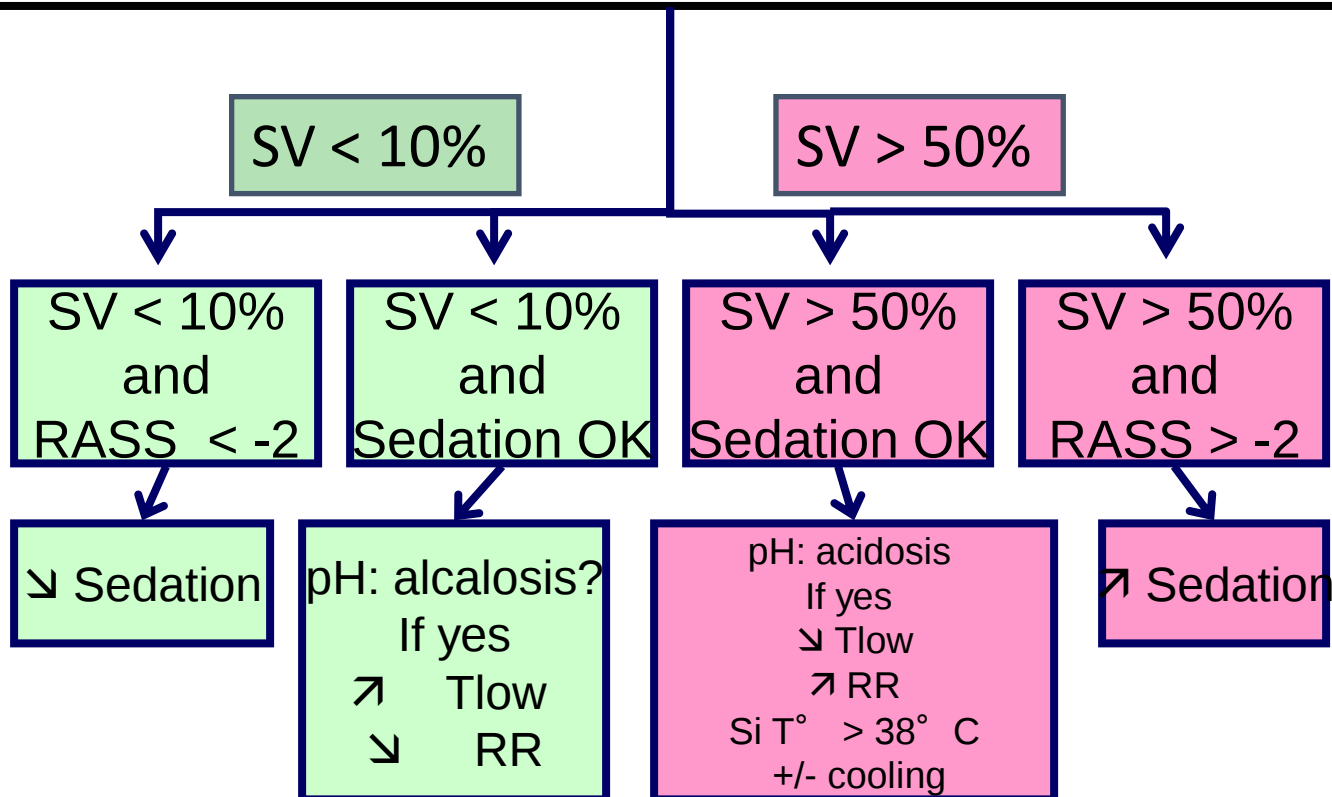
Mode : APRV (PC-IMV)

- ♦ Phigh for Pplat = 28 cmH₂O
- ♦ PEEP for Vt=6ml/kg PBW
- ♦ Thigh : 1s
- ♦ **SV 10% to 50% of Vmin**

Similar management of PEEP and ventilation weaning



PC-IMV / APRV: Spontaneous Ventilation = 10 à 50 % of VM tot





Birds trial

Breathing spontaneously at the early phase of ARDS

INCLUSION
(randomisation)

PC_IMV APRV
RASS : -2 et -3
10 et 50 % VM tot

H0

H1-H3

NMBA stopped H24

bilan

ACV

bilan

PC-IMV / APRV

ACV

PC-IMV / APRV

VAC

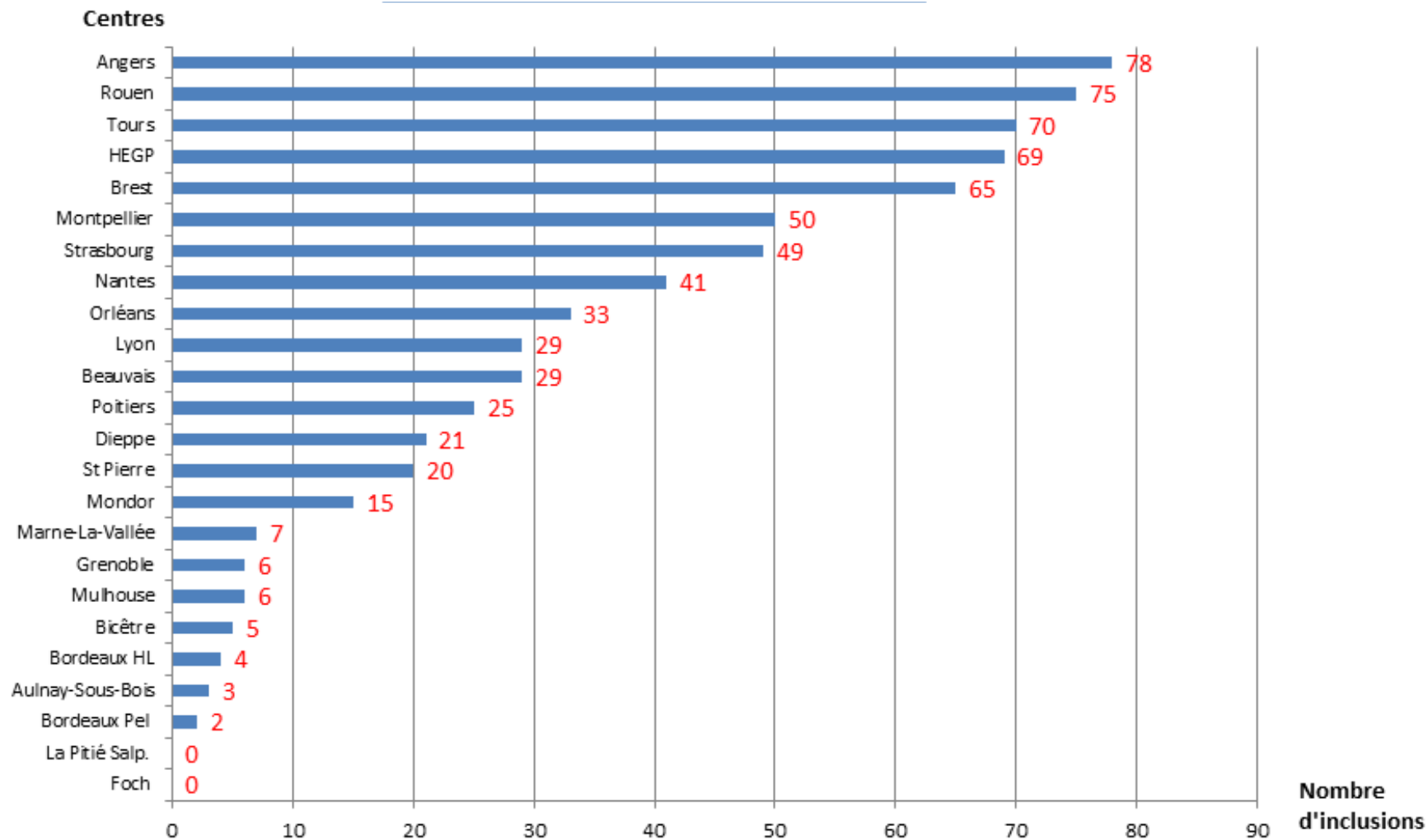
NMBA Paralysis / RASS: - 5

ACV
RASS : -2 et -3
Adapted to asynchrony

PEEP weaning attempt/day after day 3
SBT / day when PEEP < after day 3
Prone Position when PF < 150 mmHg
ECMO if refractory hypoxemia under DV
NO if refractory hypoxemia under DV

Participating centers and inclusions

22 active centers, first inclusion Feb 2013 last inclusion Oct 2017



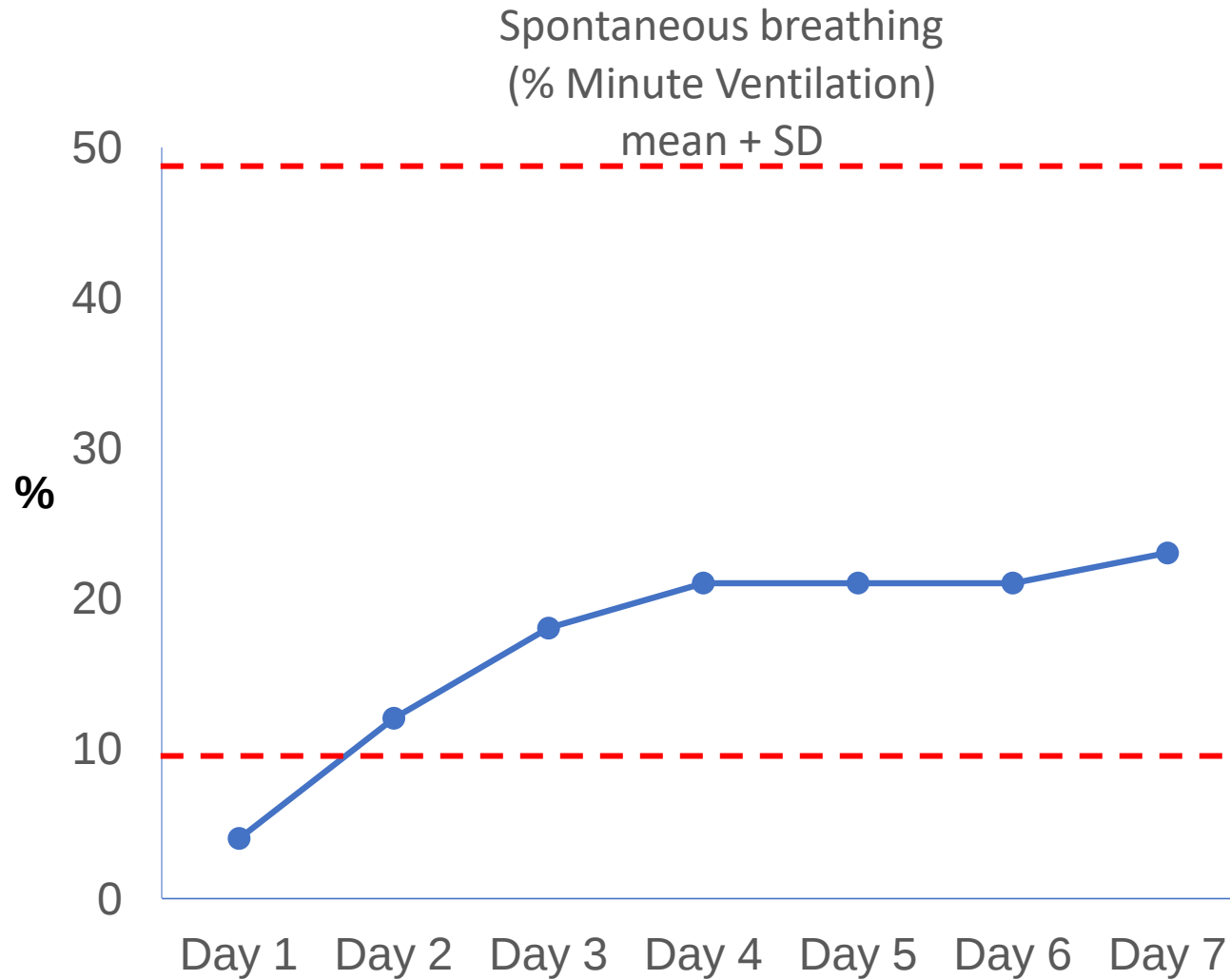
Baseline Characteristics

	ACV (n = 351)	PC-IMV / APRV (n = 346)
Age, mean (SD), y	62.4 ± 14.6	62 ± 14.4
Female sex, No (%)	100 (28.5)	116 (33.5)
SAPS II, mean (SD)	48.4 (15.3)	49.8 (15.5)
Receiving vasoactive drugs, No (%)	226 (64.6)	230 (66.5)
Time since onset of ARDS, mean (SD), h	17.1 (16.6)	17.2 (13.9)
Cause of lung injury, No (%)		
Pneumonia	248 (71.7)	227 (65.6)
Aspiration	49 (14)	54 (15.4)
Intra-abdominale sepsis	9 (2.6)	10 (2.9)
Other sepsis	10 (2.9)	9 (2.6)
Acute pancreatitis	9 (2.6)	18 (5.2)
Other	25 (7.1)	28 (8)

Respiratory measures at inclusion

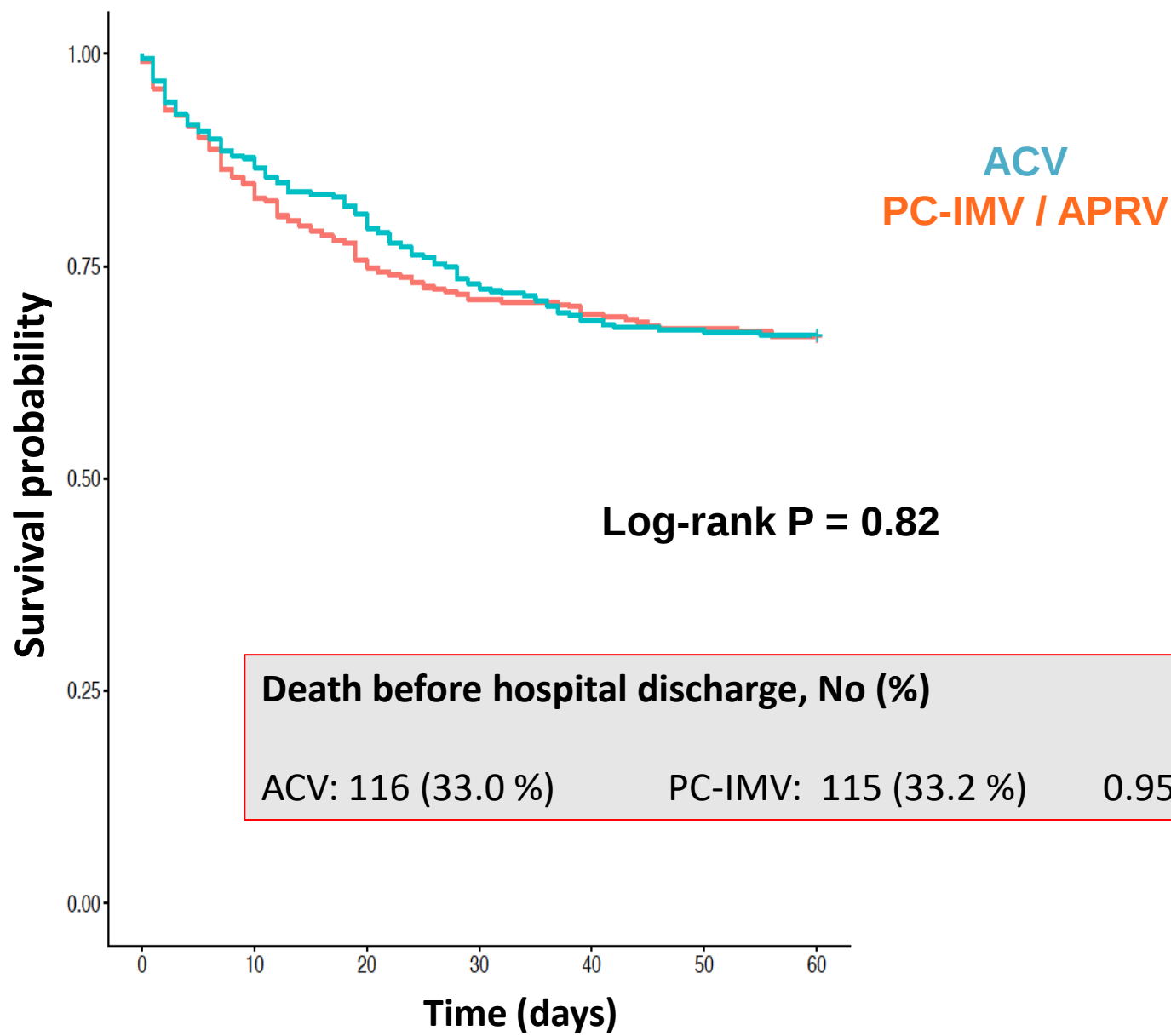
	ACV (n = 351)	PC_IMV / APRV (n = 346)
Respiratory measures, mean (SD)		
VT, ml/kg PBW	6.4 (1.0)	6.4 (0.8)
RR, cycles/min	27.6 (5.0)	27.8 (5.4)
PEEP, cmH ₂ O	10.5 (3.9)	10.5 (4.1)
Plateau pressure, cmH ₂ O	24.0 (4.8)	23.3 (4.6)
Driving pressure, cmH ₂ O	13.4 (4.2)	12.6 (3.8)
Compliance ml/cmH ₂ O	35.8 (21.5)	37.5 (29.3)
PaO ₂ /FIO ₂ (mmHg)	133 (44)	137 (43)
PaCO ₂ (mmHg)	45 (11)	44 (11)

Spontaneous breathing (PC-IMV /APRV)





Primary endpoints





Secondary endpoints

	ACV	PC-IMV /APRV	p
Death in the first 28 d, No (%)	93 (26.5)	98 (28.3)	0.589
Ventilator free days at day 28, median (IQR)	17 (10-21)	18 (12-22)	0.451
Organ failure free days at day 28, median (IQR)	18 (10-23)	19 (10-23)	0.422

Cointerventions (by day alive)

From inclusion to day 7	ACV	PC-IMV	P
Fluid loading, mean (SD), ml/day	532 (1578)	459 (1212)	0.493
Epinephrine or norepinephrine, mean (SD), mg/day	51 ± 242	39 ± 113	0.385
Midazolam, mean (SD), mg/day	141 (155)	107 (106)	0.001
Morphine equivalent*, mean (SD), mg/day	332 (359)	277 (367)	0.046
Cisatracurium, mean (SD), mg/day	130 (241)	90 (190)	0.014

* : 1 mg morphine = 10 µg fentanyl = 1 µg sufentanyl

Complications and Adjunctive Therapies

From inclusion to day 7	ACV	PC-IMV / APRV	p value
Pneumothorax, No (%)	10 (2.8)	10 (2.9)	0.974
Refractory hypoxemia*, No (%)	34 (9.7)	25 (7.2)	0.243
Adjunctive therapies, No (%)			
Prone position	132 (37.6)	99 (28.6)	0.012
Recruitment maneuver	18 (5.1)	15 (4.3)	0.622
Inhaled NO	33 (9.4)	35 (10.1)	0.751
ECMO	9 (2.6)	7 (2)	0.633
Any	141 (41.9)	117 (33.8)	0.028

* : $\text{PaO}_2 < 55 \text{ mmHg}$ or $\text{SaO}_2 < 88 \%$ for more than 30 min despite an $\text{FiO}_2 \geq 80 \%$



Birds trial

Breathing spontaneously at the early phase of ARDS

Conclusions

- ✦ Promoting spontaneous breathing (SB) using a non synchronized mode (PC-IMV / APRV) did not improve outcome of moderate and severe ARDS patients compared to conventional ACV
- ✦ SB based on PC-IMV /APRV is feasible and safe
- ✦ Targeting SB between 10% and 50% of minute ventilation permit to significantly reduce sedation and the need for paralysis.
- ✦ Additional analysis are underway regarding other secondary outcomes.

Respiratory variables

	Day 1		Day 3		Day 5	
	ACV	BIPAP-APRV	ACV	BIPAP-APRV	ACV	BIPAP-APRV
Minute ventilation, L/min	11.3 (2.7)	11.2 (2.7)	11.6 (2.7)	11.5 ± (3.0)	11.8 (2.8)	12.4 (2.9)
VT machine, ml/kg PBW	6.1 (0.6)	6.3 (0.9)	6.6 (1.3)	6.8 (1.5)	6.8 (1.3)	7.3 (1.8)
PEEP or Plow, cmH ₂ O	13.9 (3.1)	13.4 (3.3)	11.0 (4.5)	11.7 (4.3)	9.0 (4.2)	10.4 (4.3)
Plateau pressure, cmH ₂ O	26.2 (3.1)	26.5 (3.4)	24.0 (4.8)	24.6 (4.7)	23 (5.5)	24.1 (4.7)
Driving pressure, cmH ₂ O	12.2 (3.4)	13.2 (3.5)	12.1 (4.0)	12.9 (4.1)	12.9 (4.7)	13.7 (3.5)
PaO ₂ /FIO ₂ , mmHg	200 (77)	216 (120)	206 (76)	218 (94)	192 (72)	196 (72)
PaCO ₂ , mmHg	45 (9)	44 (10)	43 (11)	43 (12)	42.3 ± 11	41.7 ± 10