DEUTSCHES smart meeting

Spontaneous breathing in ARDS :

Feasible ? Dangerous ? Beneficial ?

Alain Mercat

université angers

ReV

the PLAG

CHU ANGERS CENTRE HOSPITALIER UNIVERSITAIRE

Conflicts of interests

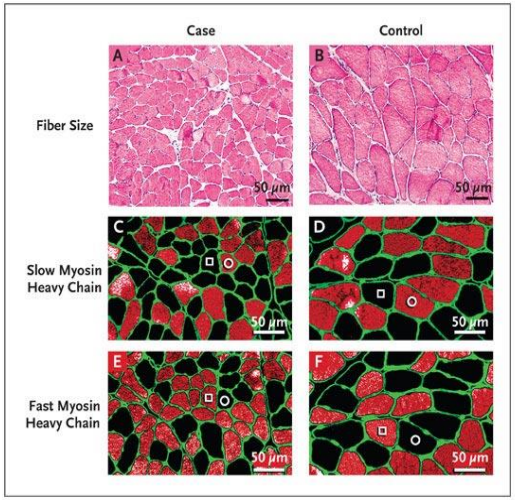
- Fundings for clinical researchs
  - General Electric
  - Fisher-Paykel
- Patent
  - General Electric
- Fees for lectures
  - Covidien
  - Fisher Paykel
  - Alung
  - Dräger Medical
- Fees for consulting
  - Faron Pharmaceuticals
  - Air Liquide Medical Systems

Spontaneous breathing : Expected benefits

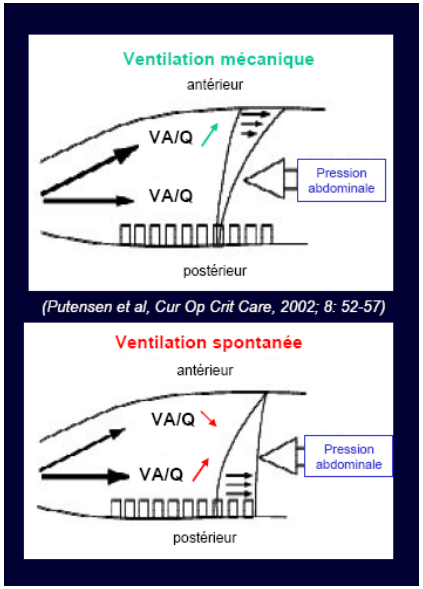
Preserved respiratory muscle function (avoid VIDD)

Improved distribution of aeration → less VILI, better oxygenation

Reduced need for sedation and reduction of MV duration



Levine S et al. NEJM 2008



Putensen et al. AJRCCM 1999

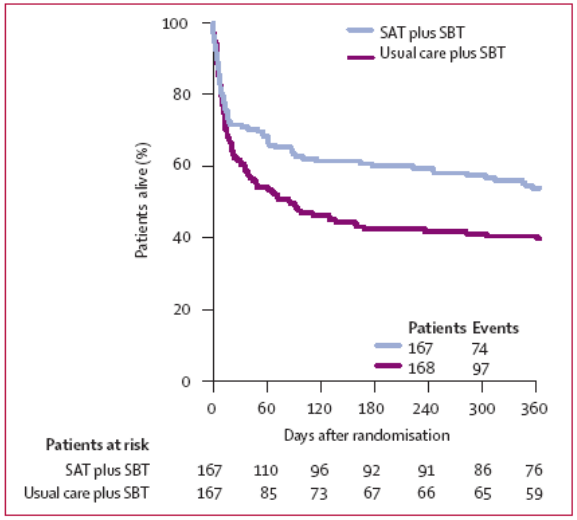
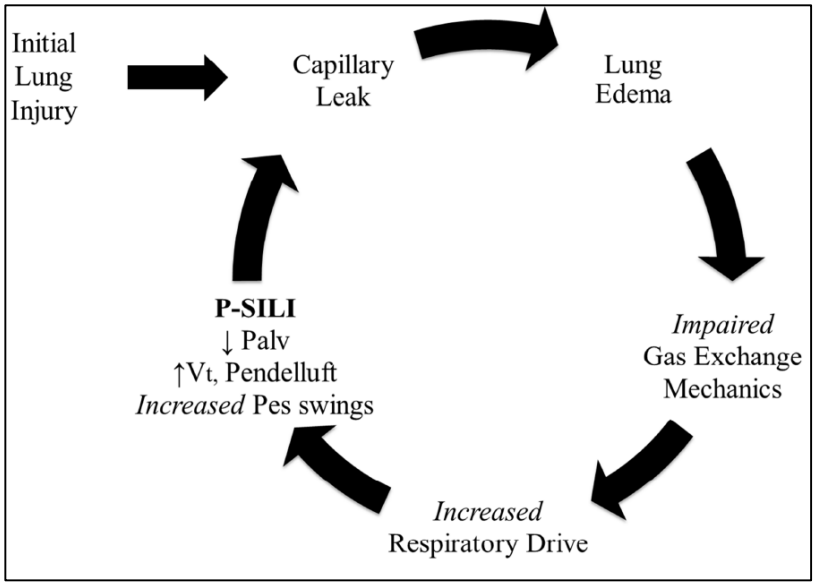


Figure 4: **Survival at 1 year**
Events indicate the number of deaths in each group in the year after enrolment.

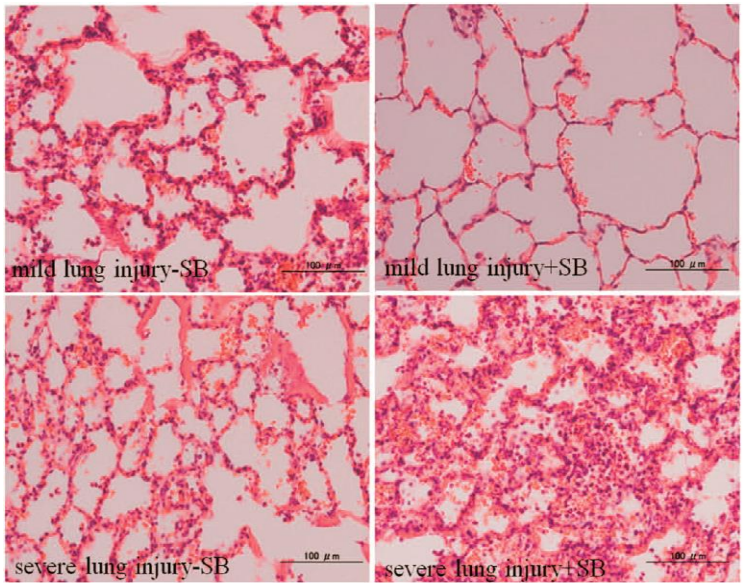
Girard et al. Lancet 2008

Spontaneous breathing : Risks

- Excessive inspiratory efforts (high respiratory drive) →
  - Increased WOB and VO2 / VCO2 of respiratory muscles
  - Severe asynchronies (stacked breaths)
  - High transpulmonary pressure, « pendelluft » → « P-SILI »



Brochard et al. AJRCCM 2017



Yoshida et al. CCM 2013

Birds trial

Breathing spontaneously at the early phase of ARDS

Inclusion criteria:

- ARDS for less than 48 hr with PaO2/FiO2 < 200 mmHg with PEEP > 5

Main objective:

- Impact of a mode allowing spontaneous breathing (PC-IMV / APRV) compared to volume ACV on outcome.

Primary endpoint:

- Hospital mortality

Secondary endpoints :

- Ventilator free days, organ failure free daysmay reduce sedation drugs
- Need for sedative and for vasoactive drugs
- Incidence of refractory hypoxemia and pneumothorax

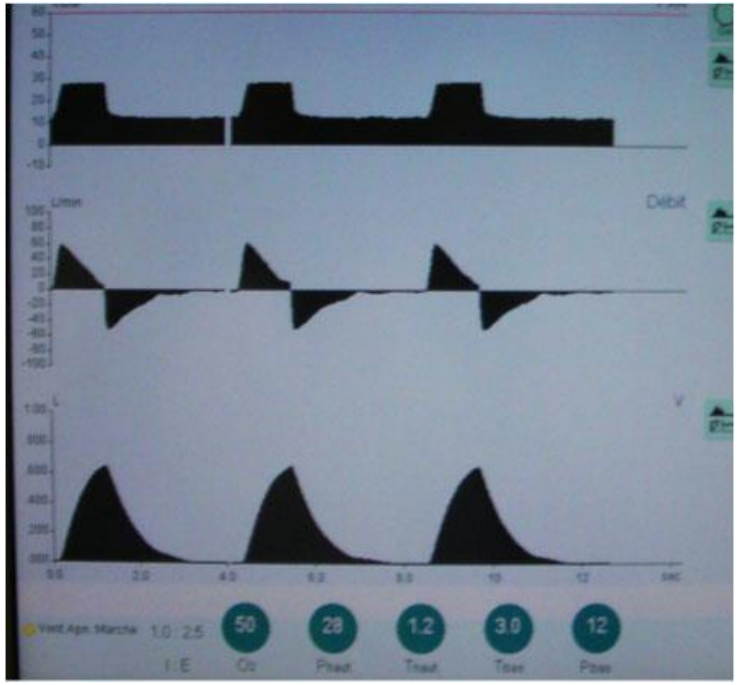
700 patients

- To demonstrate a 10% absolute reduction of mortality (35% to 25%)

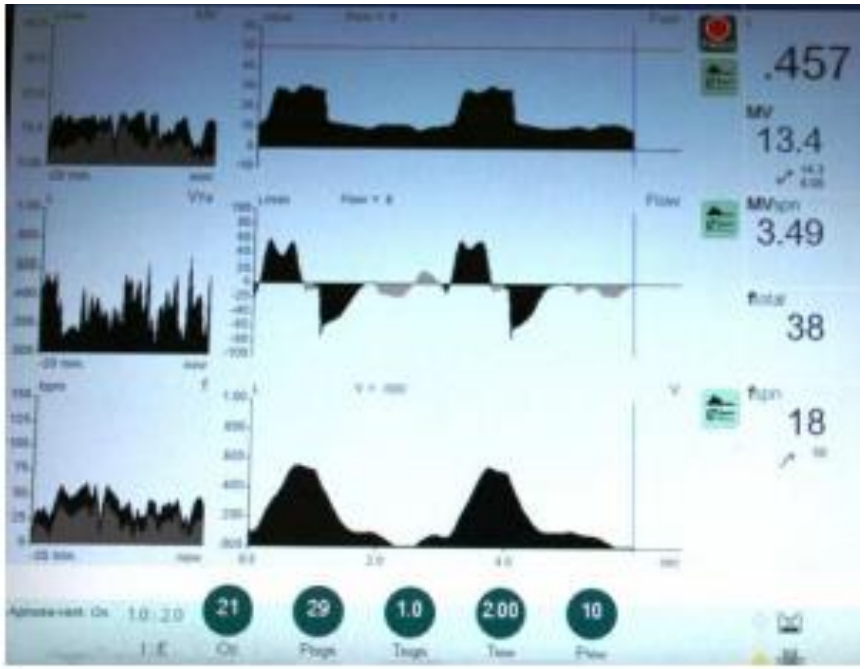
Birds trial

Breathing spontaneously at the early phase of ARDS

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



Paralyzed



With SB

Birds trial

Breathing spontaneously at the early phase of ARDS

Vt = 6 ml/kg PBW and PEEP for Pplat = 28 cmH_2O

ACV

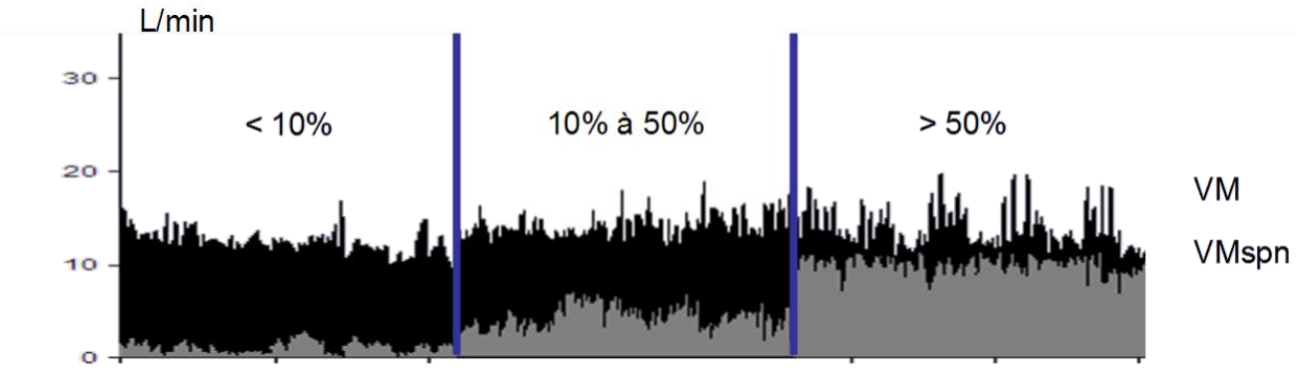
- Vt = 6 ml/kg PBW
- PEEP for Pplat = 28 cmH_2O
- Insp flow. : 50 à 70 L/mn

PC-IMV / APRV

- P_{high} for Vt=6ml/kg PBW
- P_{low} for Pplat = 28 cmH_2O
- T_{high} : 0.8 – 1 sec
- SV : 10% to 50% of Vmin

Same targets for oxygenation and PaCO2

Similar strategies for sedation, weaning of PEEP, and weaning of MV



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

- SV < 10%
  - SV < 10% and RASS < -2 → ↘ Sedation
  - SV < 10% and Sedation OK → pH: alcalosis? If yes ↗ Tlow ↘ RR
- SV > 50%
  - SV > 50% and Sedation OK → pH: acidosis If yes ↘ Tlow ↗ RR If T° > 38° C +/- cooling
  - SV > 50% and RASS > -2 → ↗ Sedation

Birds trial

Breathing spontaneously at the early phase of ARDS

PC-IMV APRV
RASS : -2 or -3
SV : 10 et 50 % VM tot

INCLUSION
(randomisation)

H0 **H1-H3** **NMBA stopped H24**

ACV

PC-IMV / APRV

ACV

PC-IMV / APRV

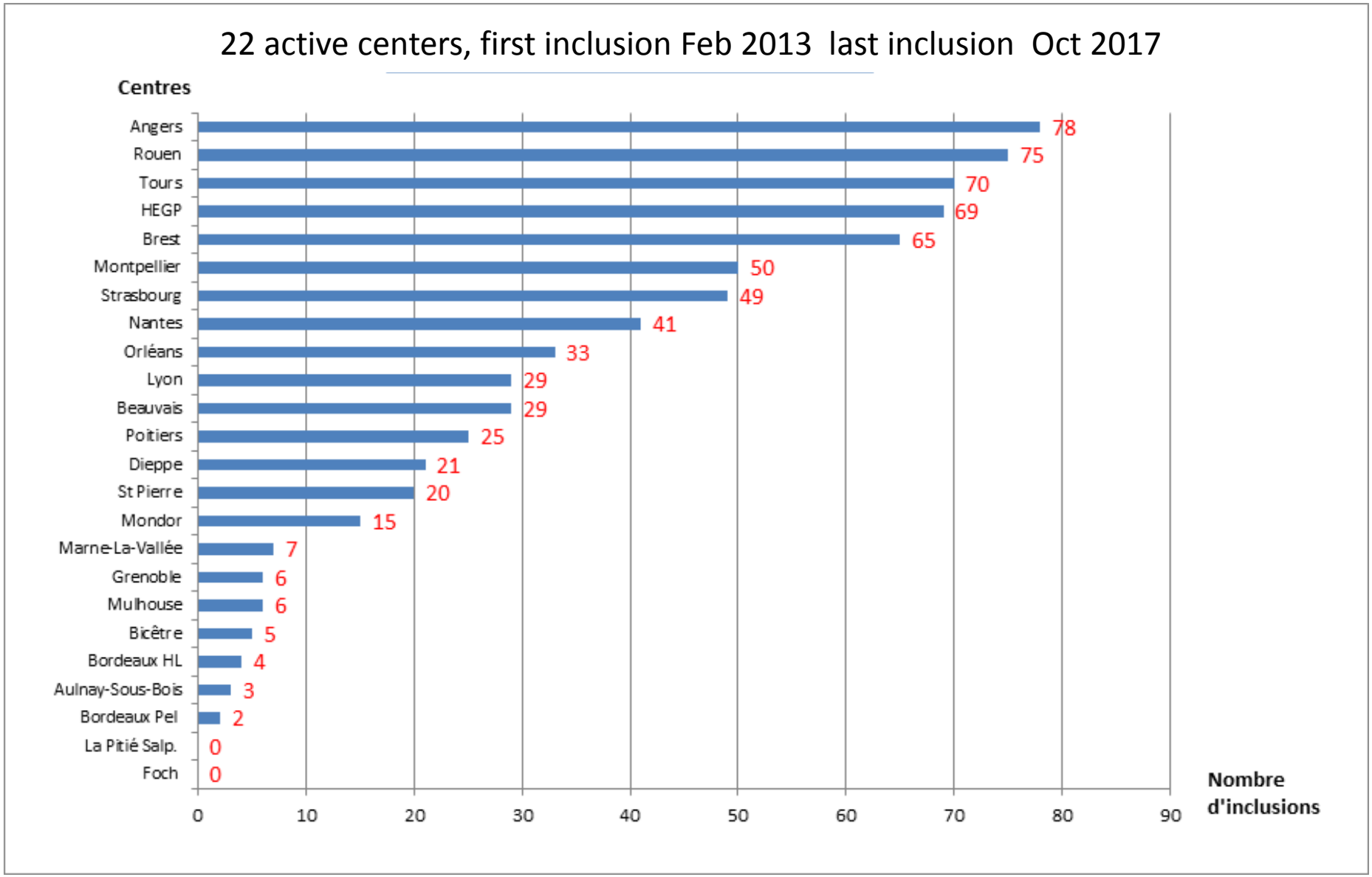
ACV

NMBA Paralysis / RASS: - 5

ACV
RASS : -2 et -3
Absence of severe asynchronies

PEEP weaning attempt/day after day 3 if PaO/FiO2 > 150
Pressure Support and moderate PEEP (with RASS 0 to -2) after weaning from high PEEP
SBT daily after weaning from high PEEP, and from vasoactive and sedative drugs
Prone Position recommended if PaO2/FiO2 < 150
ECMO if refractory hypoxemia

Participating centers and inclusions



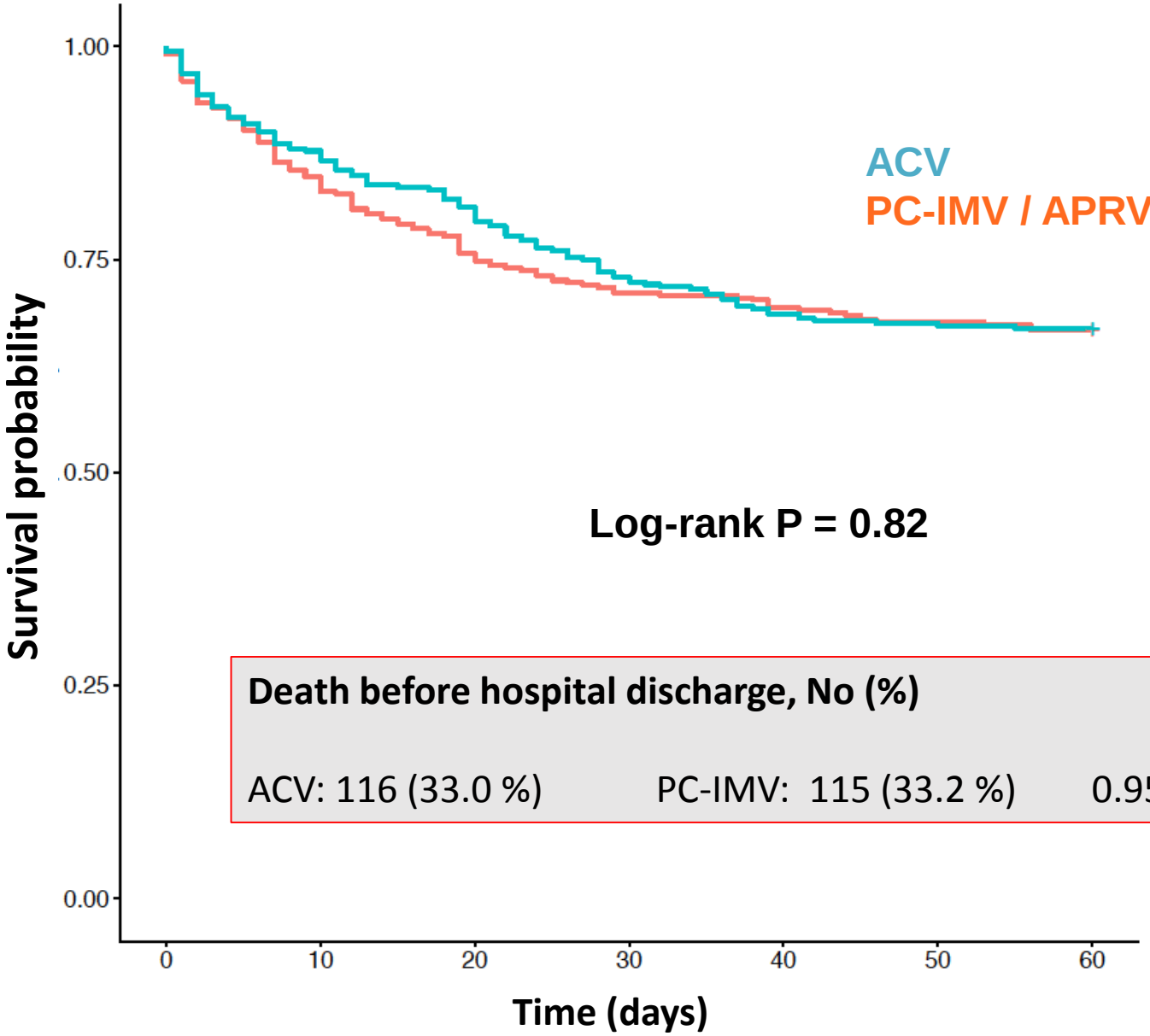
Baseline Characteristics

	ACV (n = 351)	PC-IMV / APRV (n = 346)
Age, mean (SD), y	62 (15)	62 (14)
Female sex, No (%)	100 (29)	116 (34)
SAPS II, mean (SD)	48 (16)	50 (16)
Receiving vasoactive drugs, No (%)	226 (65)	230 (67)
Time since onset of ARDS, mean (SD), h	17 (17)	17 (14)
Cause of lung injury, No (%)		
Pneumonia	248 (70.7)	227 (65.6)
Aspiration	49 (14)	54 (15.6)
Intra-abdominale sepsis	9 (2.6)	10 (2.9)
Other sepsis	10 (2.8)	9 (2.6)
Acute pancreatitis	9 (2.6)	18 (5.1)
Other	25 (7.1)	28 (8.1)

Respiratory measures on 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	27.8 (5.4)	27.8 (5.4)
PEEP, cmH_2O	10.5 (3.9)	10.5 (4.1)
Plateau pressure, cmH_2O	24.0 (4.8)	23.3 (4.6)
Driving pressure, cmH_2O	13.4 (4.2)	12.6 (3.8)
Compliance ml/cmH_2O	33.4 (11.8)	34.0 (10.6)
PaO_2/FIO_2 (mmHg)	133 (44)	137 (43)
$PaCO_2$ (mmHg)	45 (11)	44 (11)

Primary endpoint



Death before hospital discharge, No (%)

ACV: 116 (33.0 %)	PC-IMV: 115 (33.2 %)	0.958

Main secondary endpoints

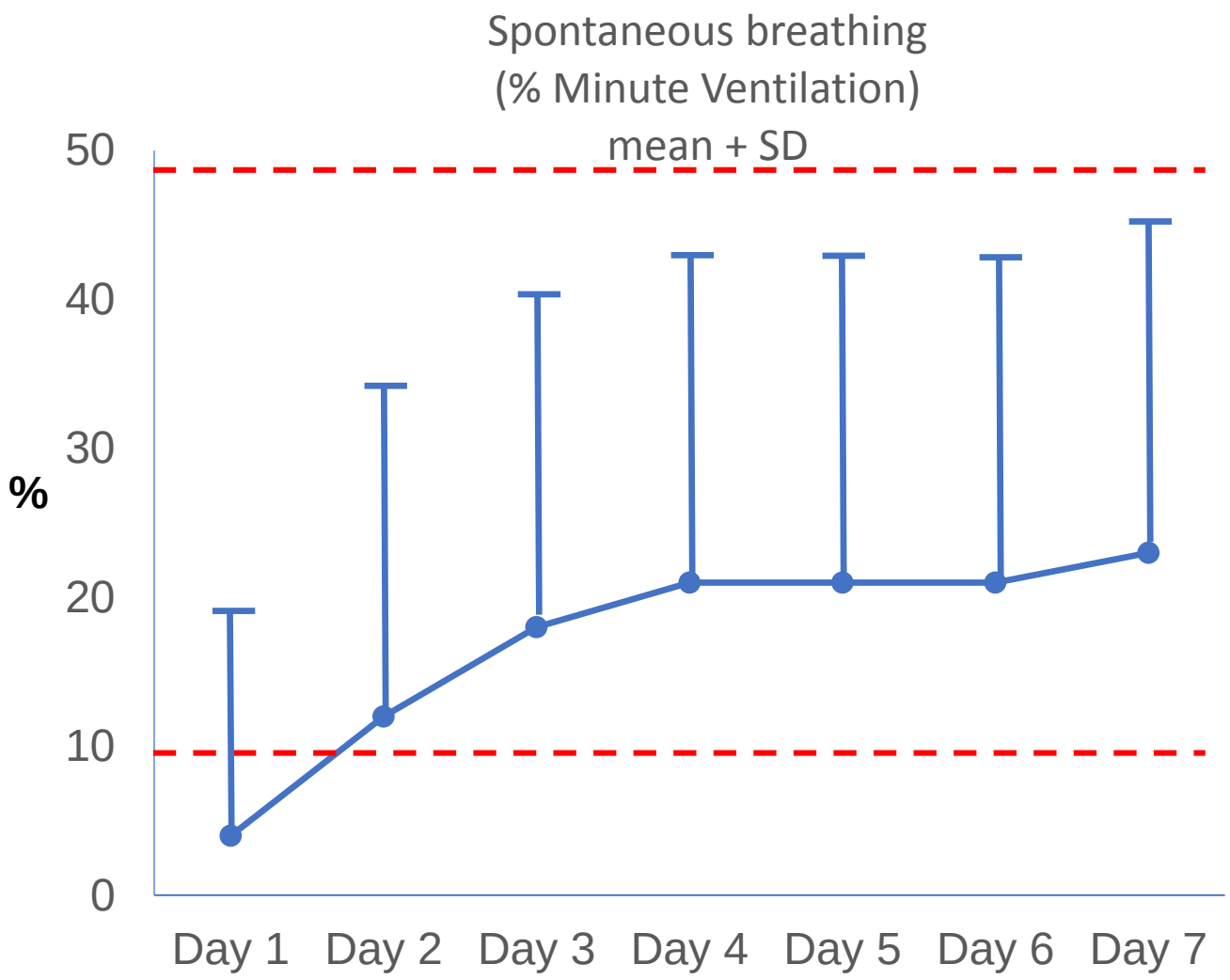
	ACV	PC-IMV /APRV	p
Death in the first 28 d, No (%)	93 (26.5)	100 (28.9)	0.589
Ventilator free days at day 28, mean (SD)	10.0 (9.7)	9.8 (10.0)	0.451
Organ failure free days at day 28, mean (SD)	11.4 (10.1)	11.2 (10.4)	0.422
Refractory hypoxemia* from inclusion to day 7, No (%)	34 (9.7)	25 (7.2)	0.243
Pneumothorax from inclusion to day 28, No (%)	17 (4.8)	17 (4.9)	0.974

* : PaO_2 < 55 mmHg or SaO_2 < 88 % for more than 30 min despite an FiO_2 ≥ 80 %

Respiratory variables

	Day 1		Day 3	
	ACV	PC-IMV APRV	ACV	PC-IMV APRV
Minute ventilation, L/min	11.3 (2.7)	11.2 (2.7)	11.7 (2.7)	11.5 (2.9)
VT machine, ml/kg PBW	6.1 (0.6)	6.3 (0.9)	6.3 (0.8)	6.7 (1.4)
PEEP or Plow, cmH_2O	13.9 (3.1)	13.4 (3.3)	11.6 (4.4)	11.7 (4.3)
Plateau pressure, cmH_2O	26.2 (3.1)	26.6 (3.2)	24.0 (4.8)	24.6 (4.7)
Driving pressure, cmH_2O	12.2 (3.3)	13.2 (3.4)	12.2 (3.9)	13.0 (3.9)
PaO_2/FIO_2, mmHg	200 (77)	215 (119)	205 (76)	216 (95)
$PaCO_2$, mmHg	45 (9)	44 (10)	43 (10)	44 (12)

Spontaneous breathing activity (PC-IMV /APRV)



Cointerventions

From inclusion to day 7	ACV	PC-IMV / APRV	P
Fluid loading, mean (SD), L	1.8 (2.4)	1.6 (2.1)	0.493
Epinephrine or norepinephrine, mean (SD), mg	116 (185)	122 (209)	0.385
Midazolam, mean (SD), mg	773 (859)	575 (543)	0.001
Morphine equivalent*, mean (SD), mg	1870 (2013)	1501 (1709)	0.046
Cisatracurium, mean (SD), mg	623 (952)	419 (505)	0.014

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

Adjunctive Therapies

From inclusion to day 7	ACV	PC-IMV / APRV	p value
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

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 patients with moderate or severe ARDS compared to conventional ACV
- SB based on PC-IMV / APRV is feasible and safe
- Targeting a SB above 10% of minute ventilation permit to significantly reduce sedation and the need for paralysis.
- Additional analysis are underway regarding the feasibility and impact of this strategy according to the severity of ARDS.