COVID-19 et soins critiques

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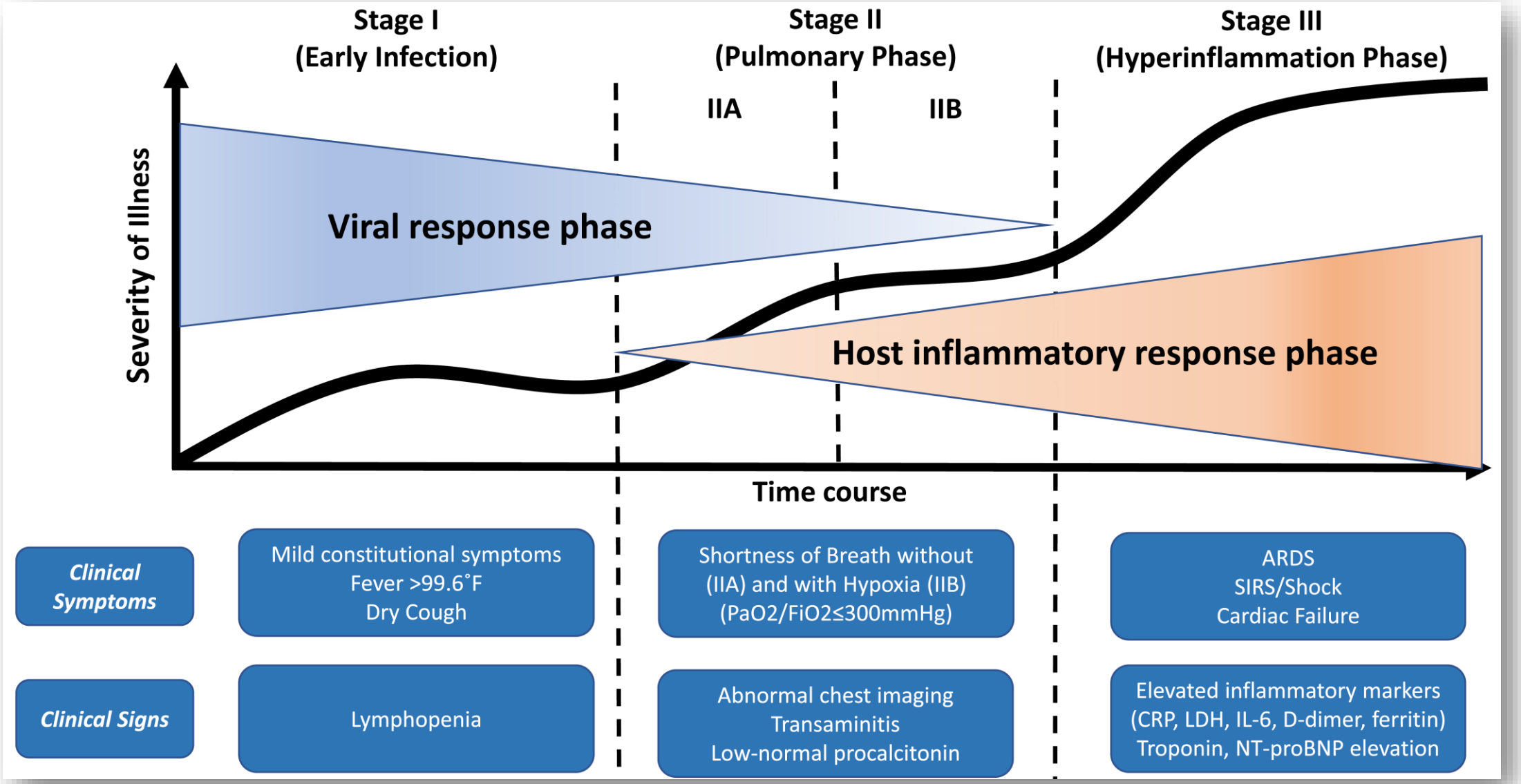
Inserm

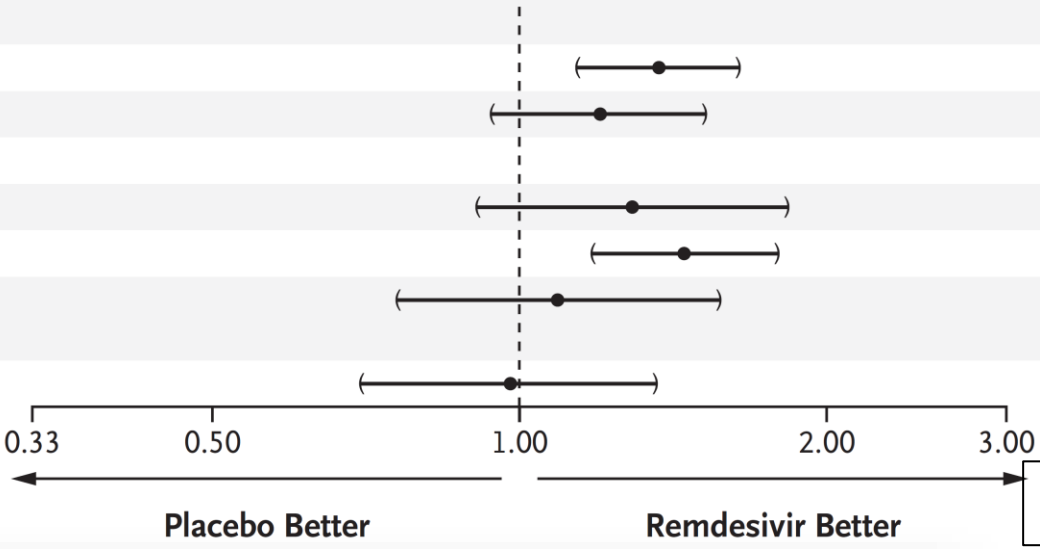
Fenêtre d'opportunité antivirale en réa ?



Siddiqui HK et al. J Heart Lung Transplant. 2020

Remdesivir

Symptoms duration		
≤10 days	676	1.37 (1.14–1.64)
>10 days	383	1.20 (0.94–1.52)
Baseline ordinal score		
4 (not receiving oxygen)	138	1.29 (0.91–1.83)
5 (receiving oxygen)	435	1.45 (1.18–1.79)
6 (receiving high-flow oxygen or noninvasive mechanical ventilation)	193	1.09 (0.76–1.57)
7 (receiving mechanical ventilation or ECMO)	285	0.98 (0.70–1.36)



ACCT 1 et time to recovery

Beigel JH et al. NEJM. 2020

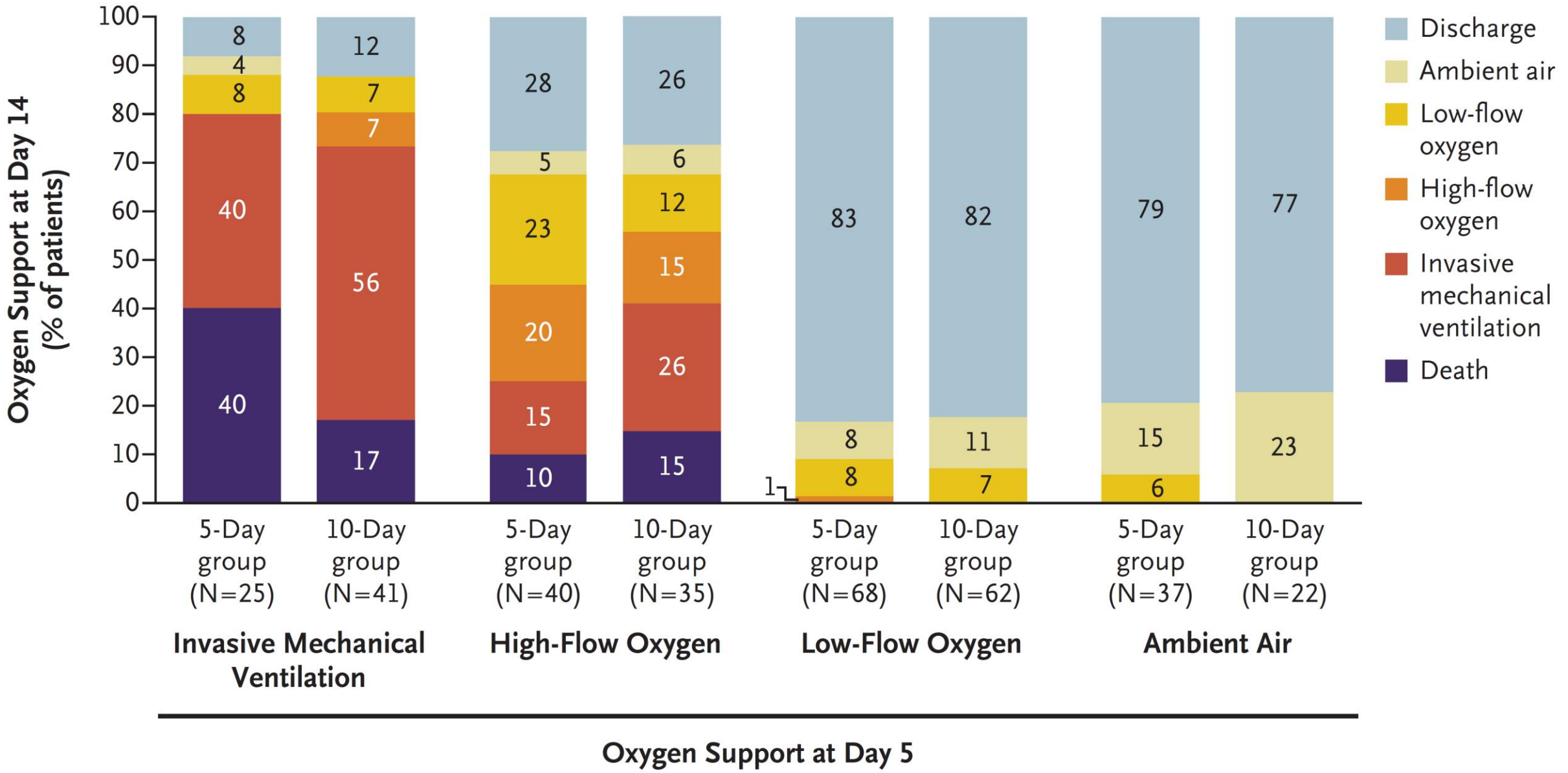
26% patients intubés ou ECMO

Characteristic	5-Day Group (N=200)	10-Day Group (N=197)	Baseline-Adjusted Difference (95% CI)*
Clinical status at day 14 on the 7-point ordinal scale — no. of patients (%)			P=0.14†
1: Death	16 (8)	21 (11)	
2: Hospitalized, receiving invasive mechanical ventilation or ECMO	16 (8)	33 (17)	
3: Hospitalized, receiving noninvasive ventilation or high-flow oxygen	9 (4)	10 (5)	
4: Hospitalized, requiring low-flow supplemental oxygen	19 (10)	14 (7)	
5: Hospitalized, not receiving supplemental oxygen but requiring ongoing medical care	11 (6)	13 (7)	
6: Hospitalized, not requiring supplemental oxygen or ongoing medical care	9 (4)	3 (2)	
7: Not hospitalized	120 (60)	103 (52)	
Time to clinical improvement (median day of 50% cumulative incidence‡)	10	11	0.79 (0.61 to 1.01)

65% amélioration 2 points Vs 54%

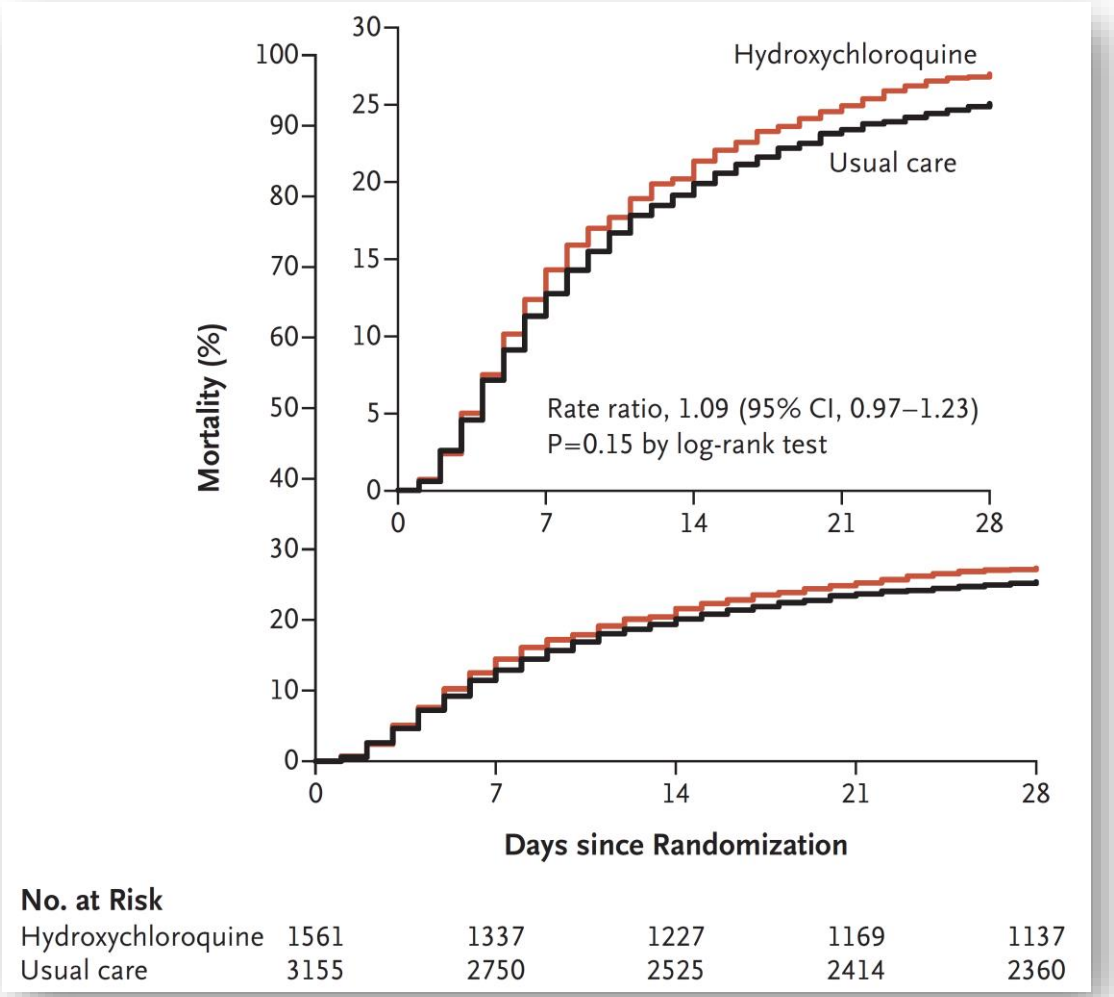
Simple : 5 jours versus 10

Goldman JD et al. NEJM. 2020



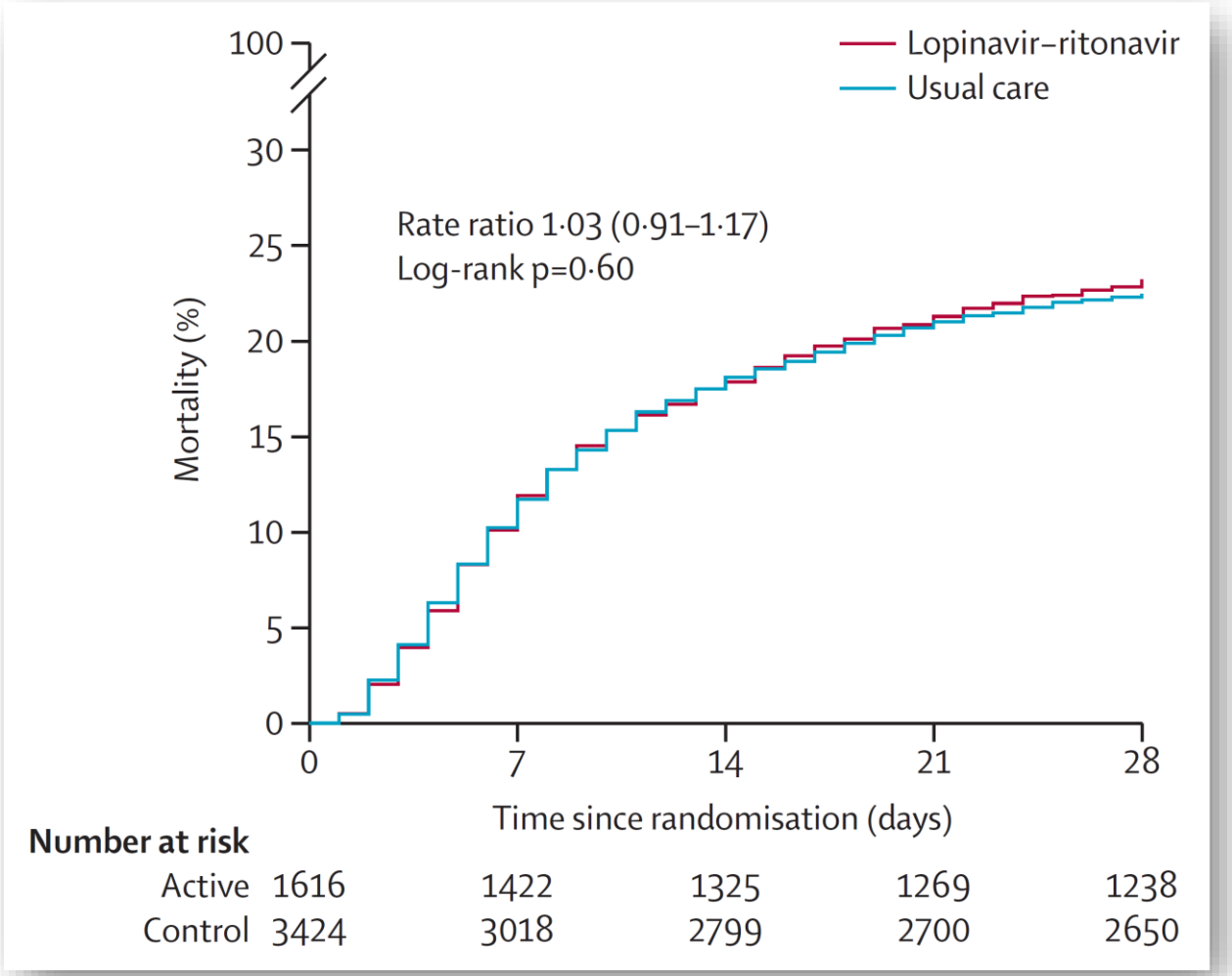
Goldman JD et al. NEJM. 2020

Recovery. Mortalité J28. OH-chloroquine et Lopi/r



Recovery collaborative group. NEJM. 2020

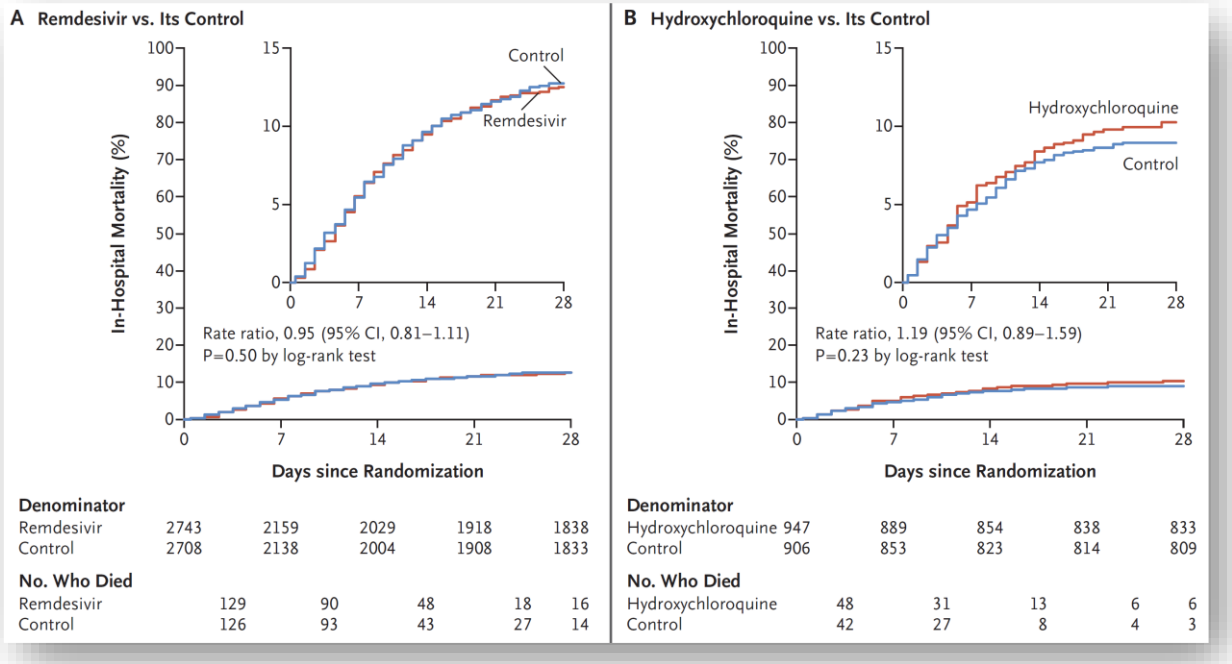
Pas d'o2 : 23%
O2 : 60%
Intubation : 16%

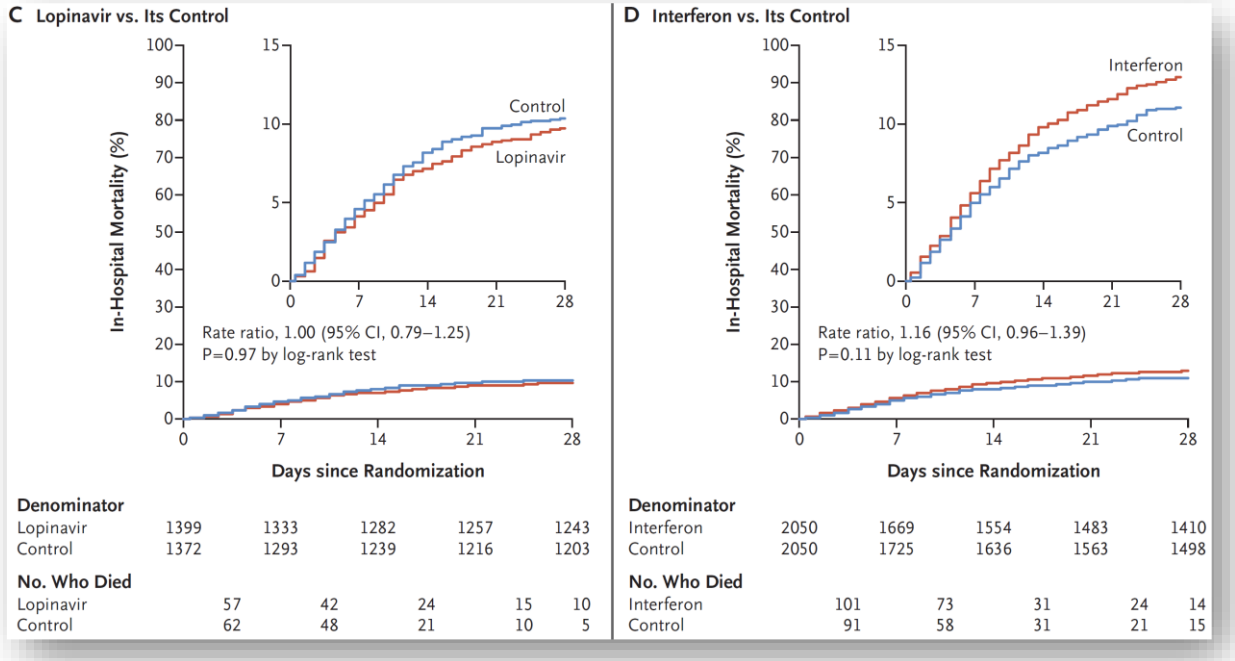


Recovery collaborative group. Lancet. 2020

Pas d'o2 : 26%
O2 : 70%
Intubation : 4%

Remdesivir OH-chloroquine Lopi/rito Interféron





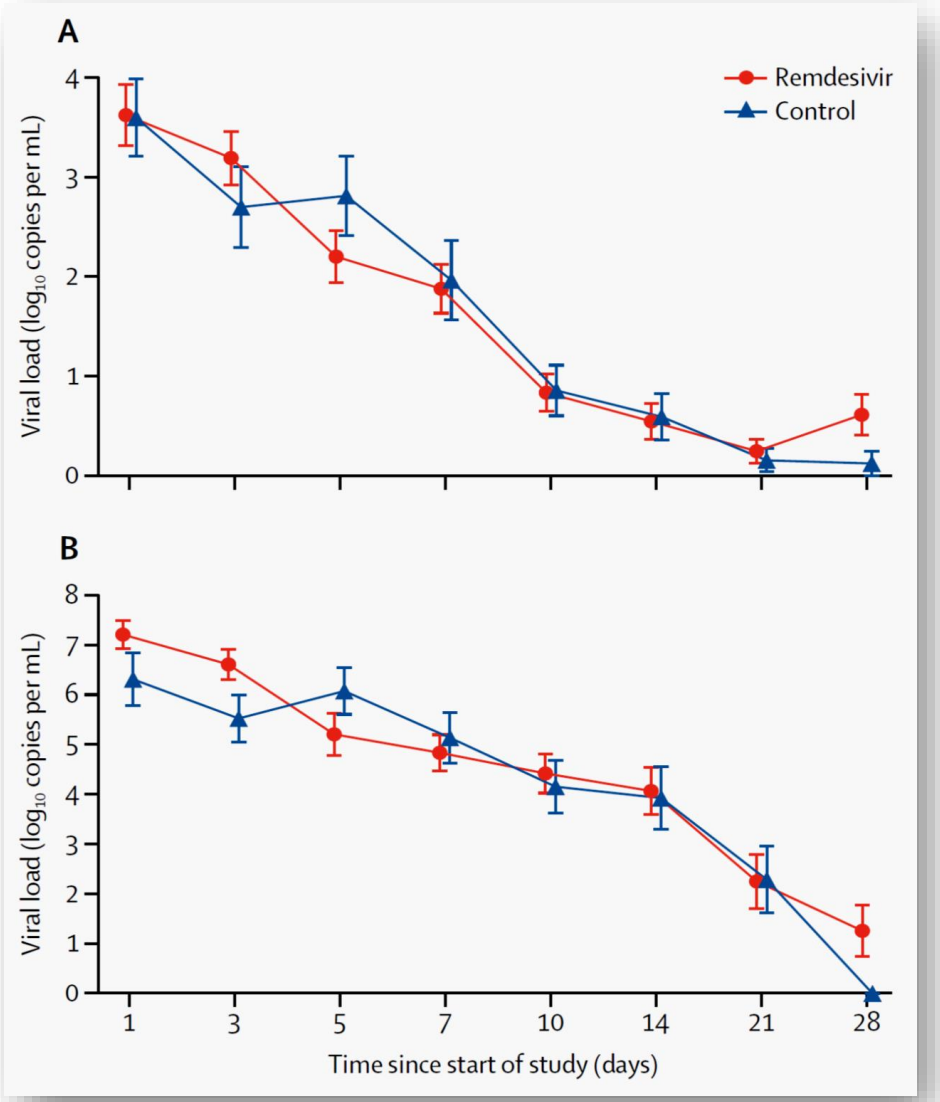
Pas d'o2 : 28%. O2 : 63%. Intubation : 8%

WHO Solidarity Trial Consortium. NEJM 2021

Outcome/analysis	Lopinavir-ritonavir (*N* = 255)	Hydroxychloroquine (*N* = 50)	Combination therapy (*N* = 27)	Control (*N* = 362)
Primary outcome, organ support-free days (OSFDs)				
Median (IQR)	4 (− 1, 15)	0 (− 1, 9)	− 1 (− 1, 7)	6 (− 1, 16)
Adjusted OR—median (95% CrI)	0.73 (0.55, 0.99)	0.57 (0.35, 0.83)	0.41 (0.24, 0.72)	1
Probability of futility, %	99.9	> 99.9	> 99.9	–
Probability of harm compared to control, %	98	99.9	> 99.9	–
Subcomponents of OSFDs				

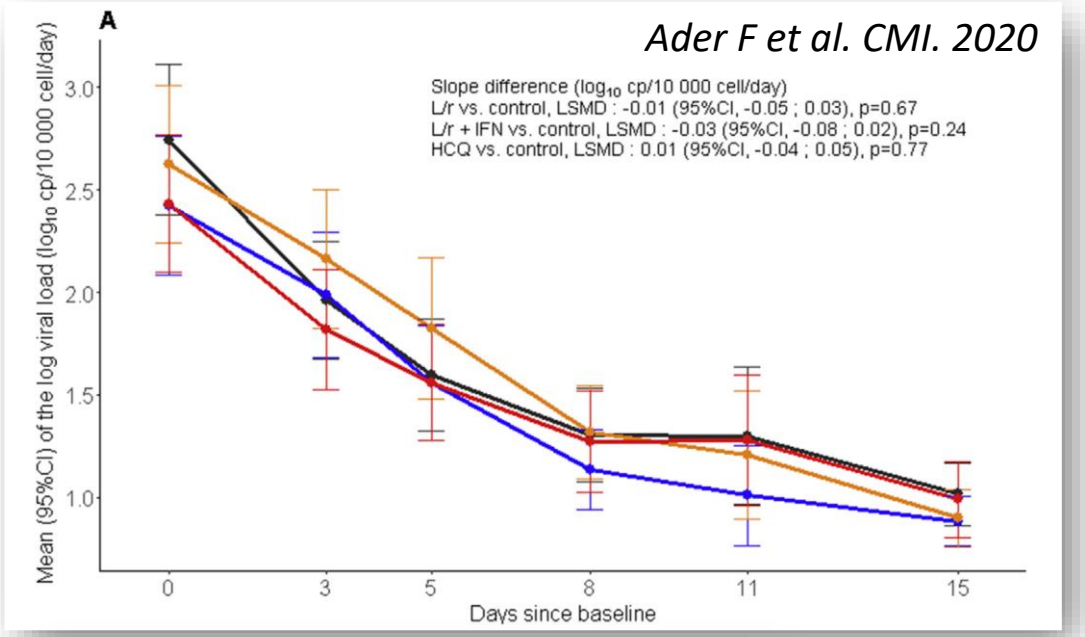
Remap Cap (réa). Arabi YM et al. ICM 2021

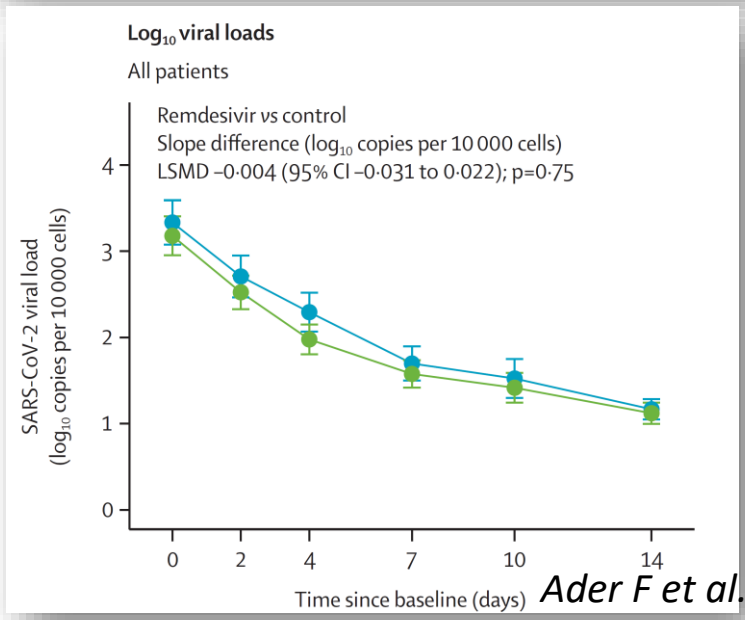
Un manque d'efficacité intrinsèque ou une fenêtre antivirale dépassée ?



Wang Y et al. Lancet. 2020

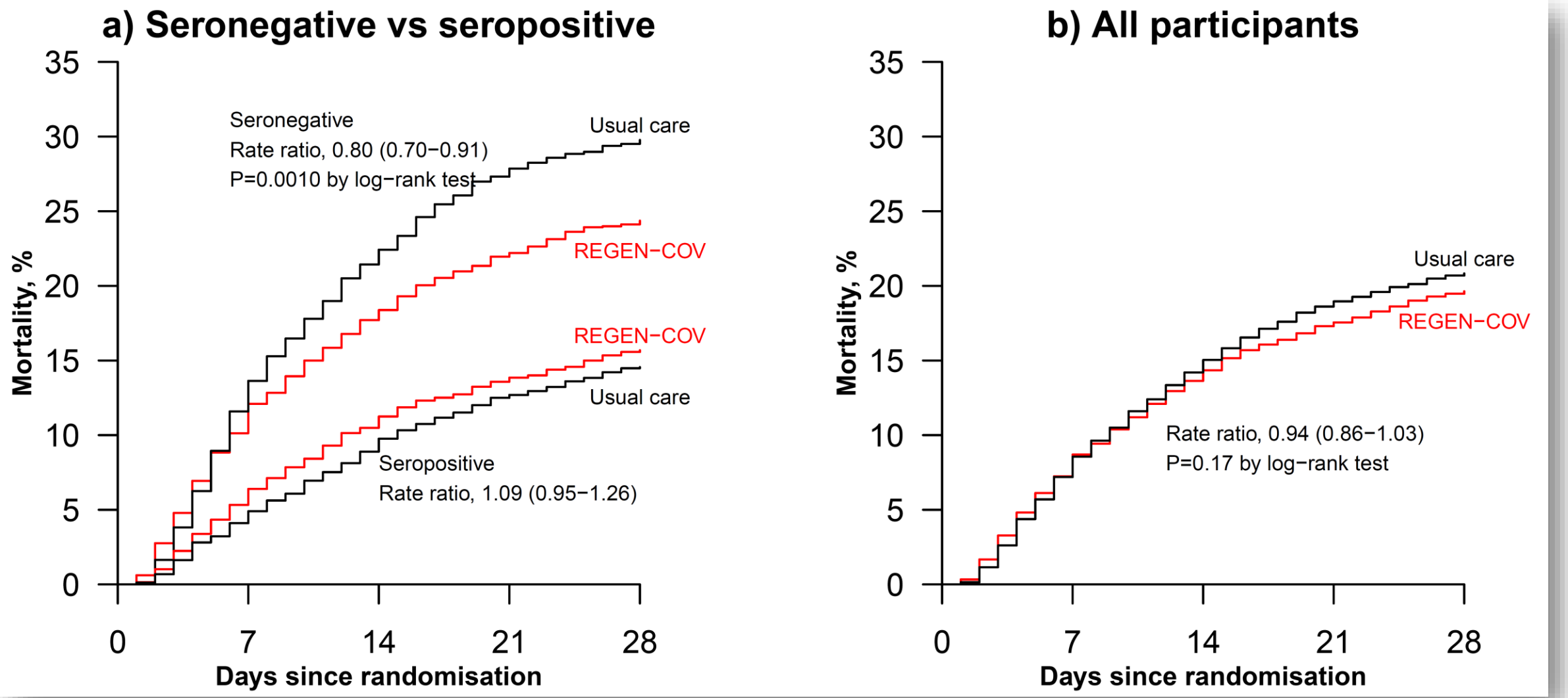
Ader F et al. CMI. 2020





Ader F et al. Lancet Inf Dis. 2021

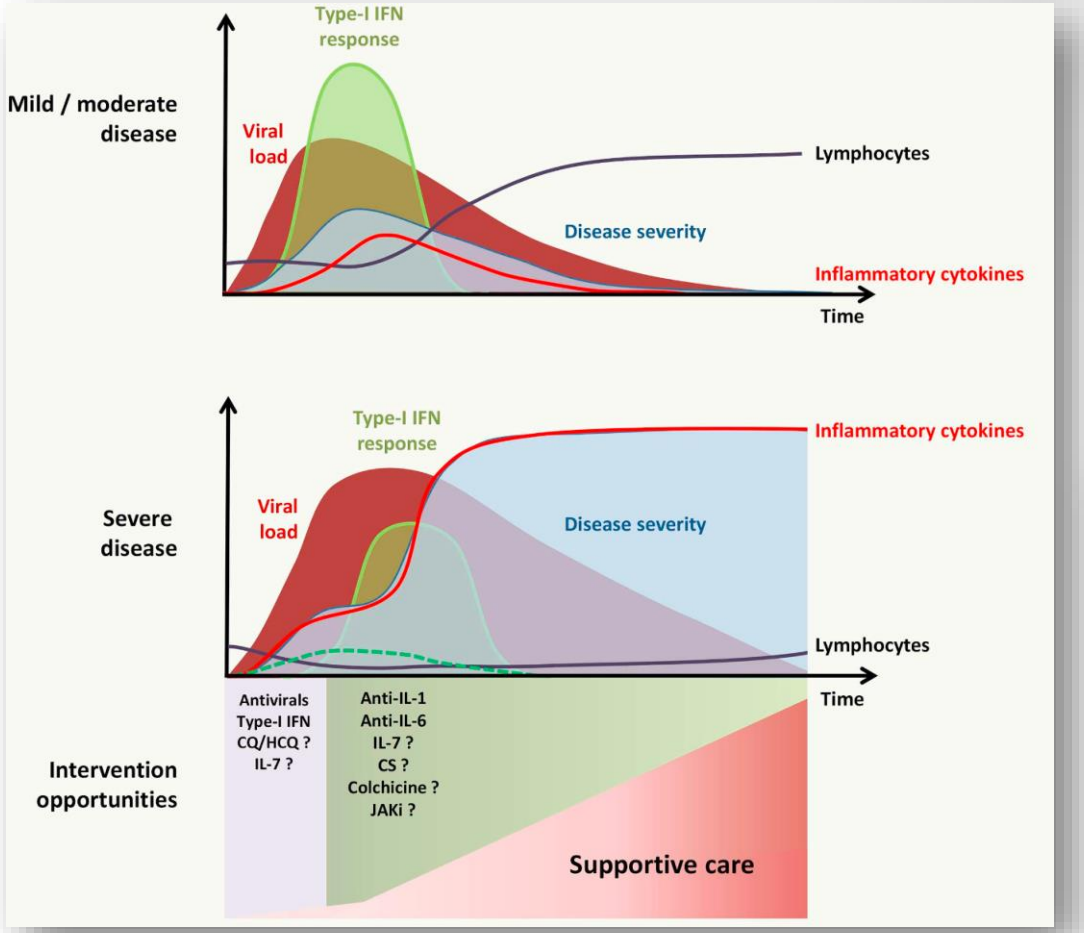
REGEN-COV chez les malades hospitalisés : un intérêt chez les séronégatifs ?



2% de patients intubés ventilés. 60% d'O2

Recovery collaborative group. medRxiv. Non reviewed

COVID-19 grave : une maladie inflammatoire



Jamillou Y et al. Autoimmunity Reviews. 2020

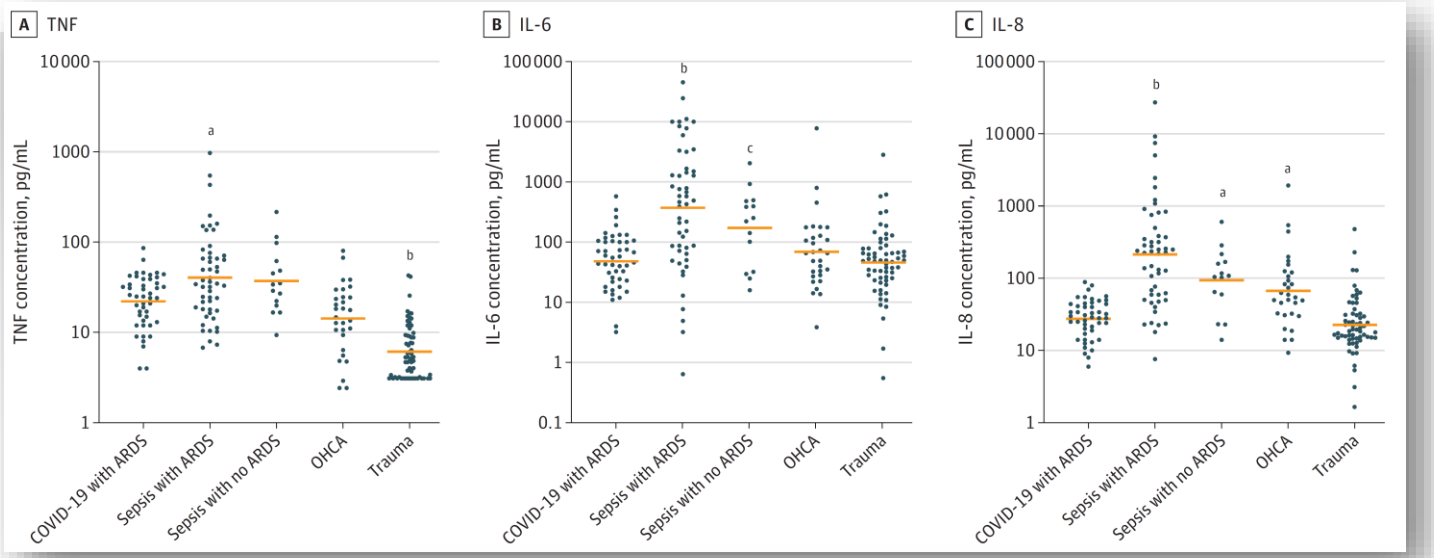


Table. Plasma Levels of Interleukin-6 Reported in COVID-19 Compared With Levels Previously Reported in ARDS[a]

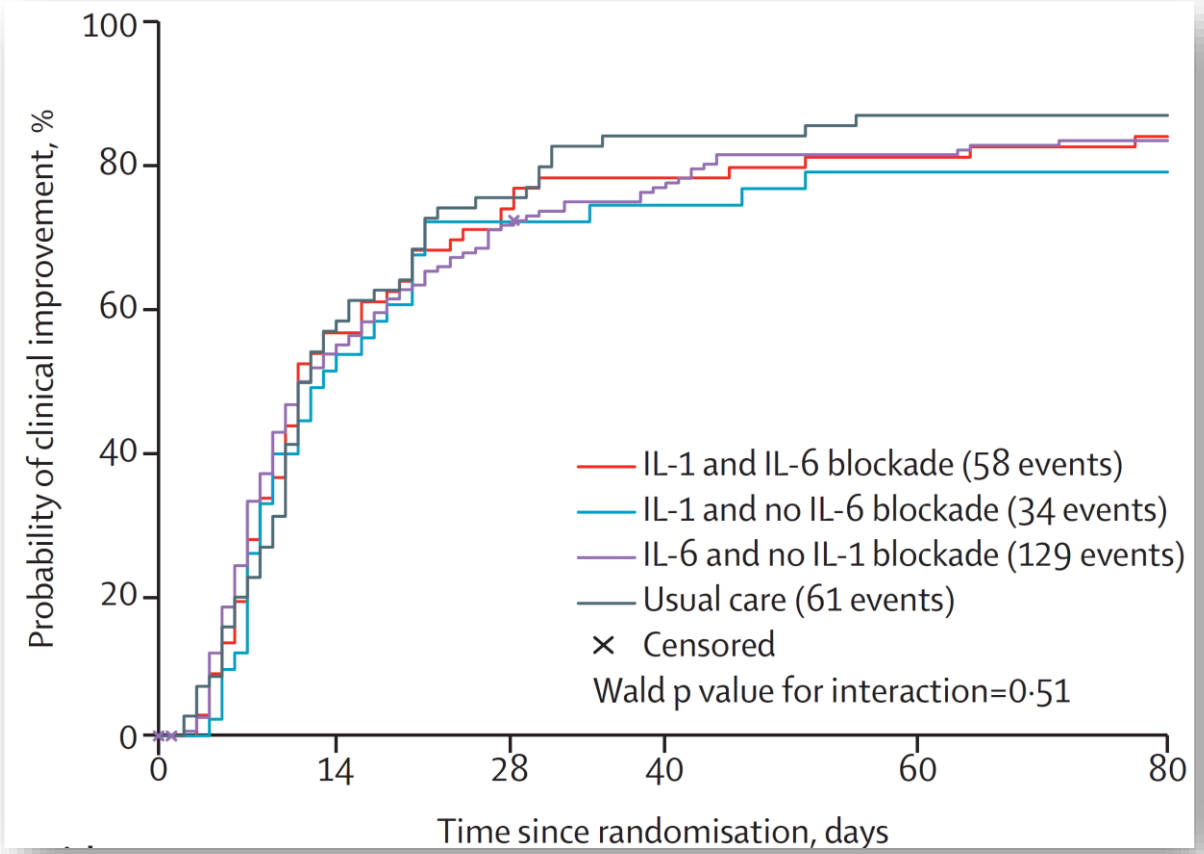
	Total population				Severe disease		
COVID-19	No.	IL-6 levels, pg/mL			No.	IL-6 levels, pg/mL	Measurement platform
Zhou et al[4]	191	7 (5-11)			54[b]	11 (8-14)	CL
Wu et al[1]	123	7 (6-9)			84[c]	7 (6-11)	CL
Mo et al[5]	155	45 (17-96)			85[d]	64 (31-165)	CL
Qin et al[2]	452	21 (6-47)			286[e]	25 (10-55)	CL
Cummings et al[6]	NR	NR			237[f]	26 (11-69)	CL
	Total population		Hypoinflammatory		Hyperinflammatory		
ARDS	No.	IL-6 levels, pg/mL	No.	IL-6 levels, pg/mL	No.	IL-6 levels, pg/mL	Measurement platform
ALVEOLI[7]	521	238 (94-741)[f]	386	154 (67-344)	135	1525 (584-3802)	ELISA
FACTT[8]	884	130 (46-411)[f]	638	86 (34-216)	246	578 (181-2621)	ELISA
SAILS[9]	720	443 (173-1513)[f]	451	282 (115-600)	269	1618 (517-3205)	ELISA

Sinha P et al. JAMA Internal Med. 2020

Pot pourri des RCT tocilizumab réa

Référence	Critères d'inclusion	Méthodo	Critères de jugement principal	Délai médian traitement	Résultats	Remarque
Salvarani C et al. JAMA Int Med. 2020	-200<P/F<300 mmHg -Optiflow et CPAP Venturi possible -fièvre + CRP -Exclusion réa	Randomisé Ouvert Pas de placebo	Aggravation clinique J14 : réa;DC;P/F<150 mmHg	8 j	NS	-cortico anecdotiques
Gupta S et al. JAMA Int Med. 2020	H48 réa	Essai émulé Rétrospectif	-Délai survenue DC -mortalité J28	48h réa	**Significatif**	-15% cortico **-bénéfice :les + sévères et <J3 des symptômes avant réa**
Rosas IO et al. NEJM 2021 (COVACTA)	-Hypoxie P/F<300 (37% de patients ventilés)	Randomisé Double aveugle placebo	Statut clinique échelle ordinale à 7 points J28	10 j	-NS	-<50% de cortico -pas de différence de mortalité à J28 **-bénéfice dans le sous-groupe de patients non ventilés ?**
REMAPCAP NEJM 2021	-H24 réa -Support ventilatoire ou hémodynamique (30% ventilés, 30% O2 haut débit, 40% VNI)	-Randomisé Double aveugle Placebo -bras sari -méthode bayésienne	Nombre de jours sans support à J21	? (J hospit)	**Significatif**	-94% cortico -amélioration mortalité J90 (HR=1,61) **-impact des autres traitements expérimentaux ???**

Référence	Critères d'inclusion	Méthodo	Critères de jugement principal	Délai médian traitement	Résultats	Remarque
Recovery NEJM 2021	-hypoxie -CRP>75 (« VNI » 41%; VI : 13%)	Randomisé Double aveugle Placebo	Mortalité J28	9 j	**Significatif** Additif aux cortico	-90 % cortico **-impact des autres traitements expérimentaux ???** -Flowchart ?? -Mortalité bras contrôle élevée



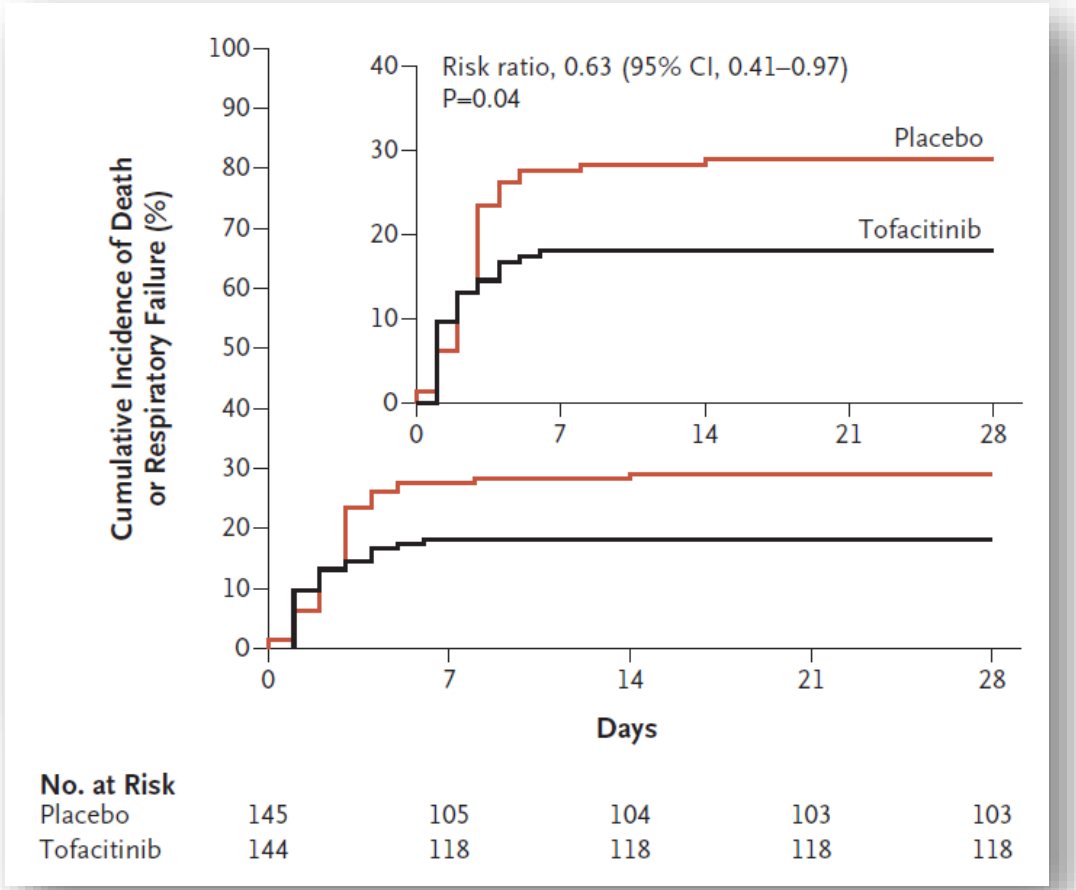
P/F<350 en air ambiant ou <280 sous O2
+infiltrats pulmonaires bilatéraux
+inflammation : ferritine, LDH, D-Dimères, CRP, lymphopénie
-15% ventilation invasive
-35% VNI/O2 haut débit
-45% O2 standard

COV-AID. Declercq J et al. Lancet Respir Med. 2021

Anti-JAK ? Malades immunodéprimés et intubés exclus des études publiées

	Baricitinib group (n=764)	Placebo group (n=761)	Baricitinib vs placebo	
			Point estimate (95% CI)	p value*
Primary outcome				
Progression to high-flow oxygen, non-invasive ventilation, invasive mechanical ventilation (including ECMO), or death, by day 28†				
Population 1‡	27·8%	30·5%	OR 0·85 (0·67 to 1·08)	0·18
Population 2§	28·9%	27·1%	OR 1·12 (0·58 to 2·16)	0·73
Key secondary outcomes				
All-cause mortality	62/764 (8%)	100/761 (13%)	HR 0·57 (0·41 to 0·78)	0·0018

Essai COV BARRIER. Marconi VC et al. Lancet respir med. 2021



Guimaraes PO et al. NEJM. 2021

L'immunomodulation polyvalente tout terrain des formes graves : les corticoïdes

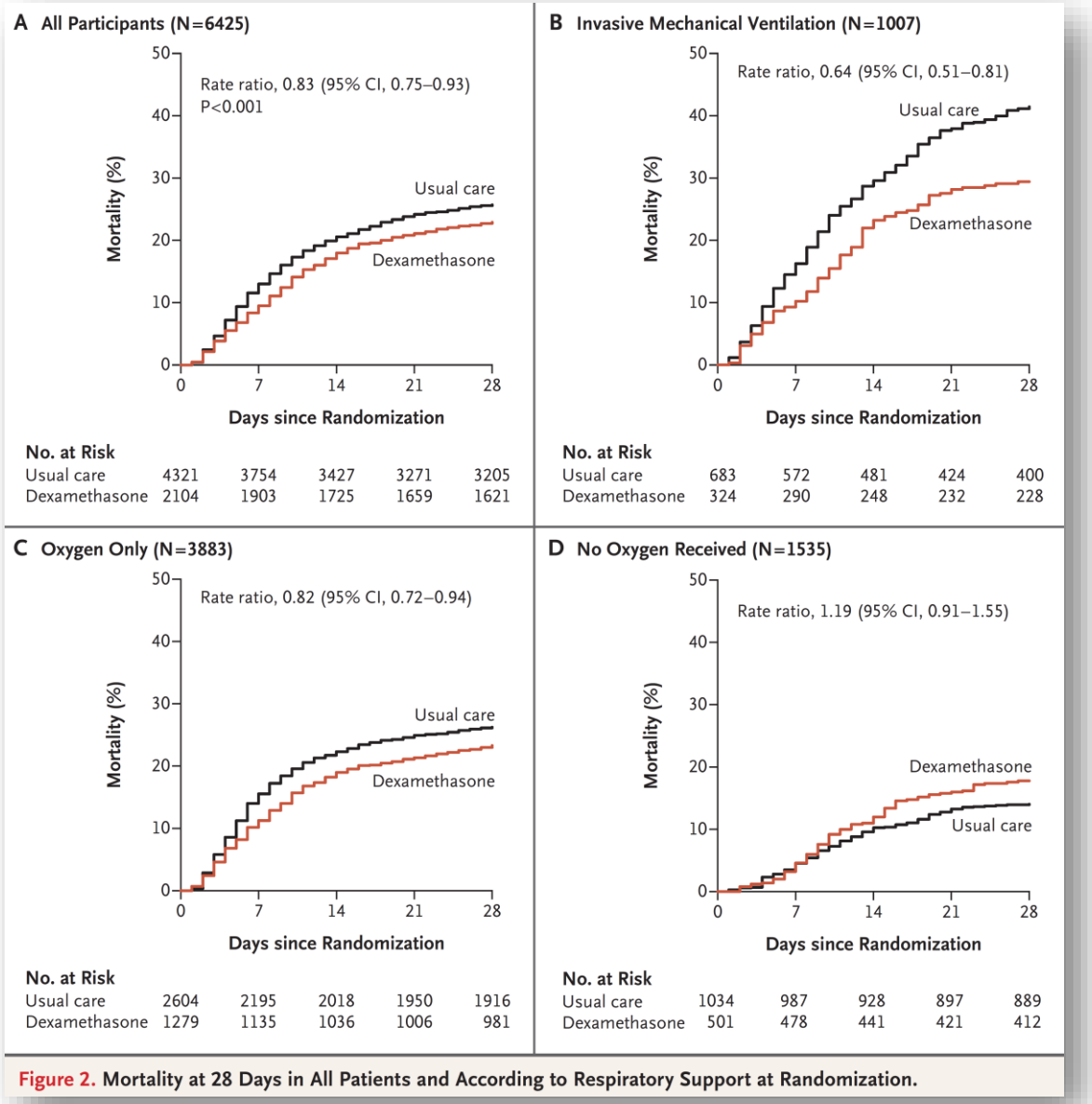


Figure 2. Mortality at 28 Days in All Patients and According to Respiratory Support at Randomization.

- **Bénéfice en termes de mortalité à 28 jours**
- **Bénéfice en termes de recours à la ventilation mécanique**
- **Bénéfice chez les patients sous O2**
- **Rôle sur inflammation systémique et atteinte pulmonaire**

Recovery. NEJM. 2020

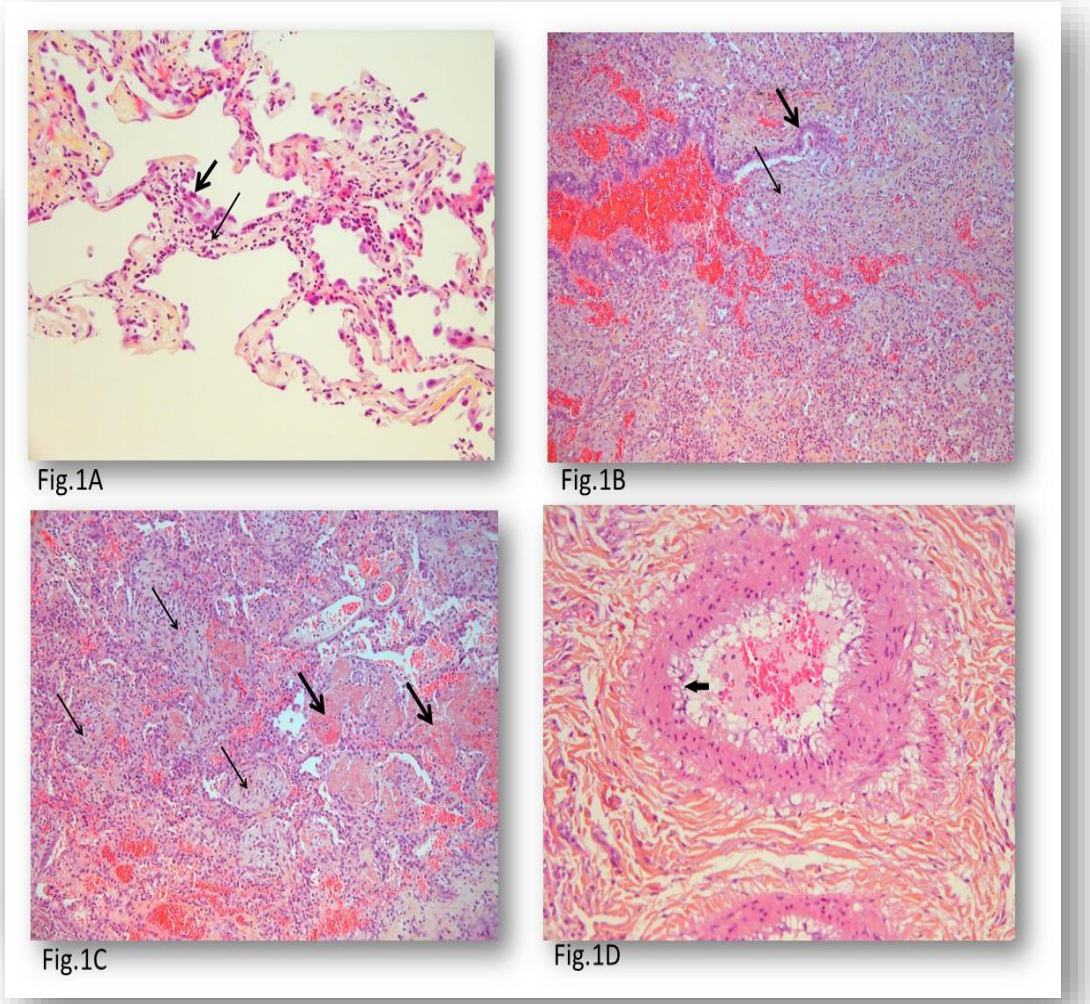
Rochwerg B et al. BMJ. 2021

A mettre en perspective avec « l'ARDS » : quelle est la bonne dose chez les malades les plus sévères ?

Dexa 20mg 5 jours puis 10 mg 5 jours

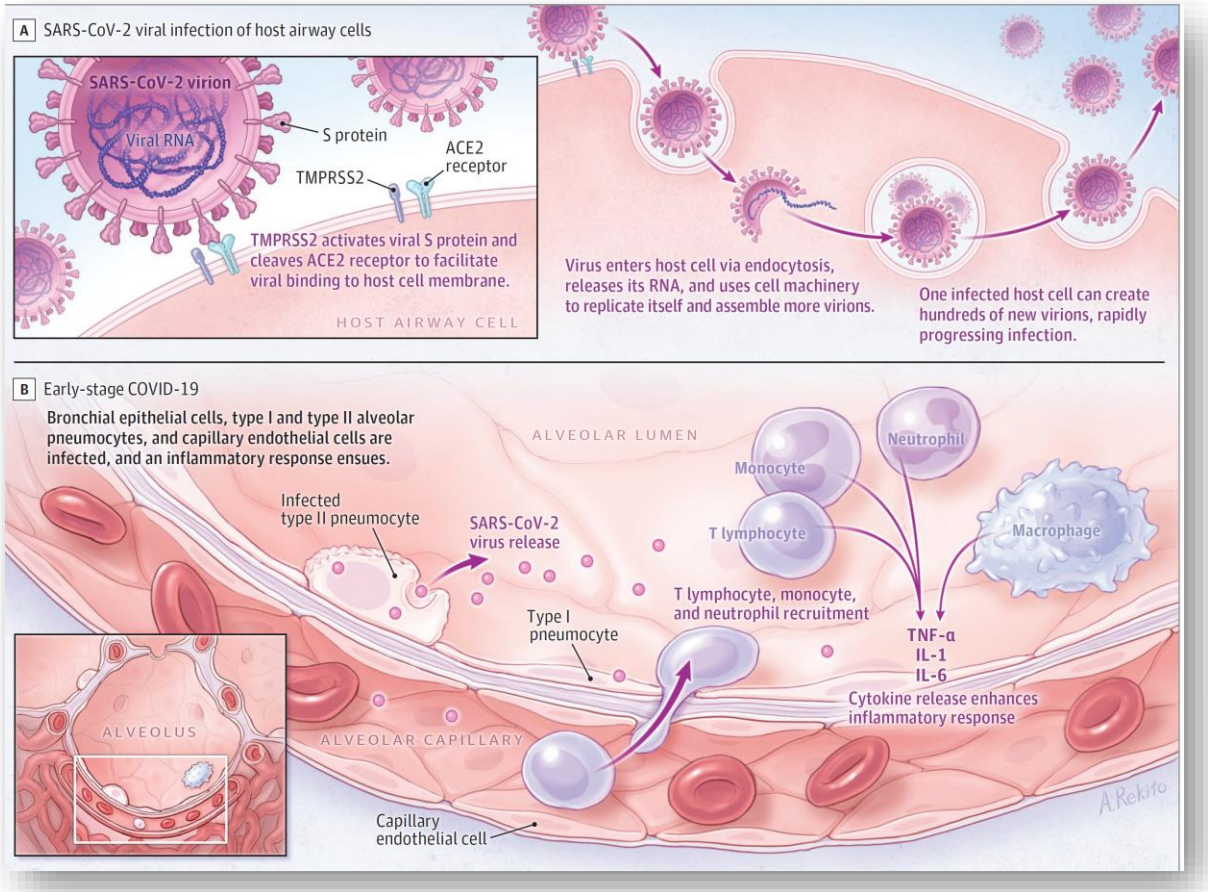
	Dexamethasone group (n=139)	Control group (n=138)	Between-group difference (95% CI)	p value
Ventilator-free days at 28 days	12·3 (9·9)	7·5 (9·0)	4·8 (2·57 to 7·03)	<0·0001
All-cause mortality at day 60	29 (21%)	50 (36%)	−15·3% (−25·9 to −4·9)	0·0047
ICU mortality	26 (19%)	43 (31%)	−12·5% (−22·4 to −2·3)	0·0166
Hospital mortality	33 (24%)	50 (36%)	−12·5% (−22·9 to −1·7)	0·0235
Actual duration of mechanical ventilation in ICU survivors, days	14·2 (13·2)	19·5 (13·2)	−5·3 (−8·4 to −2·2)	0·0009
Actual duration of mechanical ventilation in survivors at day 60, days	14·3 (13·3)	20·2 (14·0)	−5·9 (−9·1 to −2·7)	0·0004
Adverse events and complications*				
Hyperglycaemia in ICU	105 (76%)	97 (70%)	5·2% (−5·2 to 15·6)	0·33
New infections in ICU	33 (24%)	35 (25%)	1·6% (−8·5 to 11·7)	0·75
Barotrauma	14 (10%)	10 (7%)	2·8% (−4·0 to 9·8)	0·41

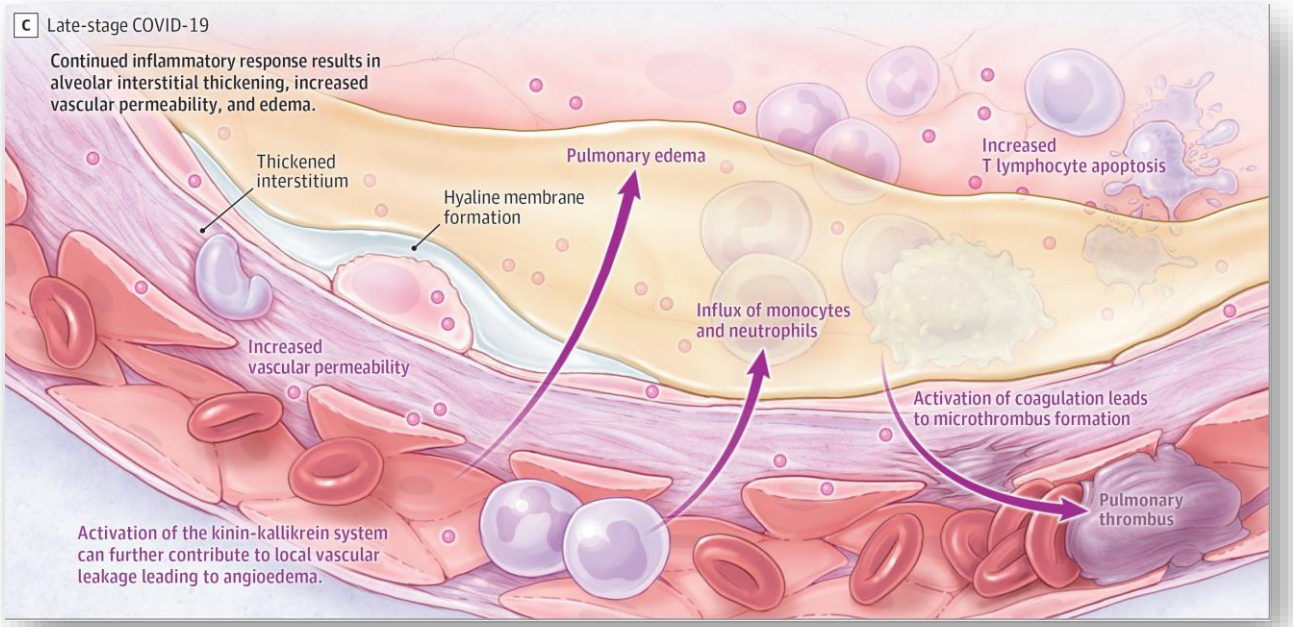
Villar J et al. Lancet Respir Med. 2020



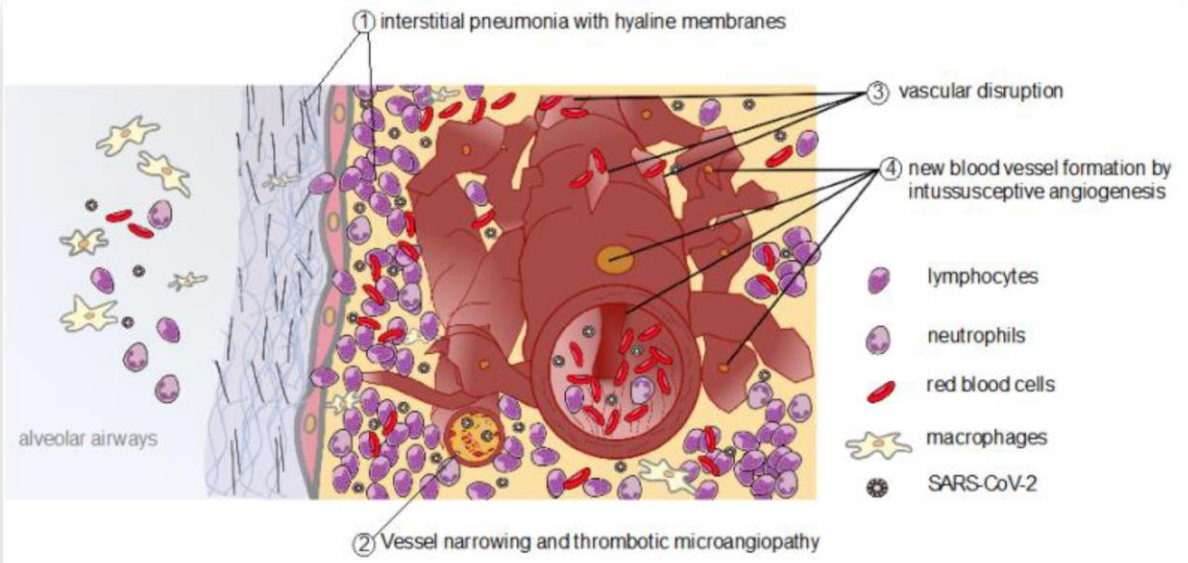
Copin MC et al. ICM. 2020

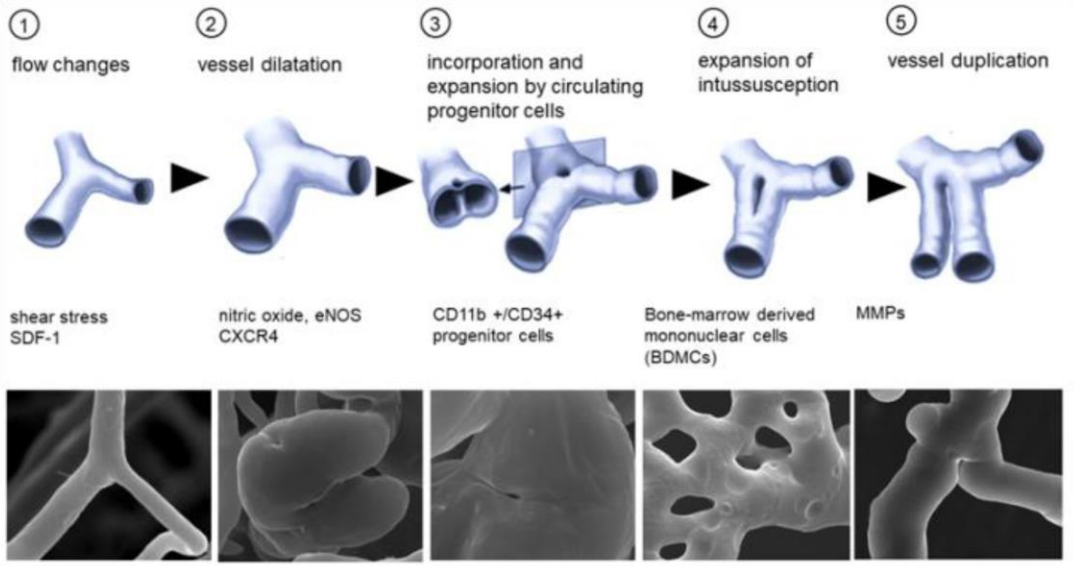
L'atteinte pulmonaire associe atteinte épithéliale (ARDS) et endothéliale. Inflammation « compartimentalisée »

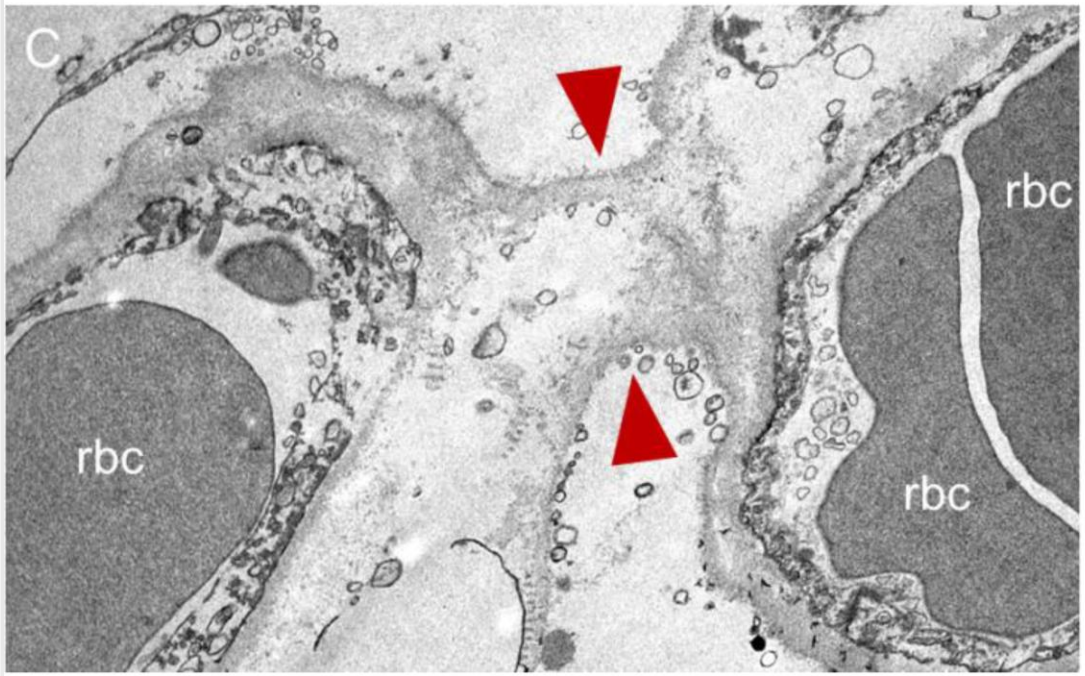


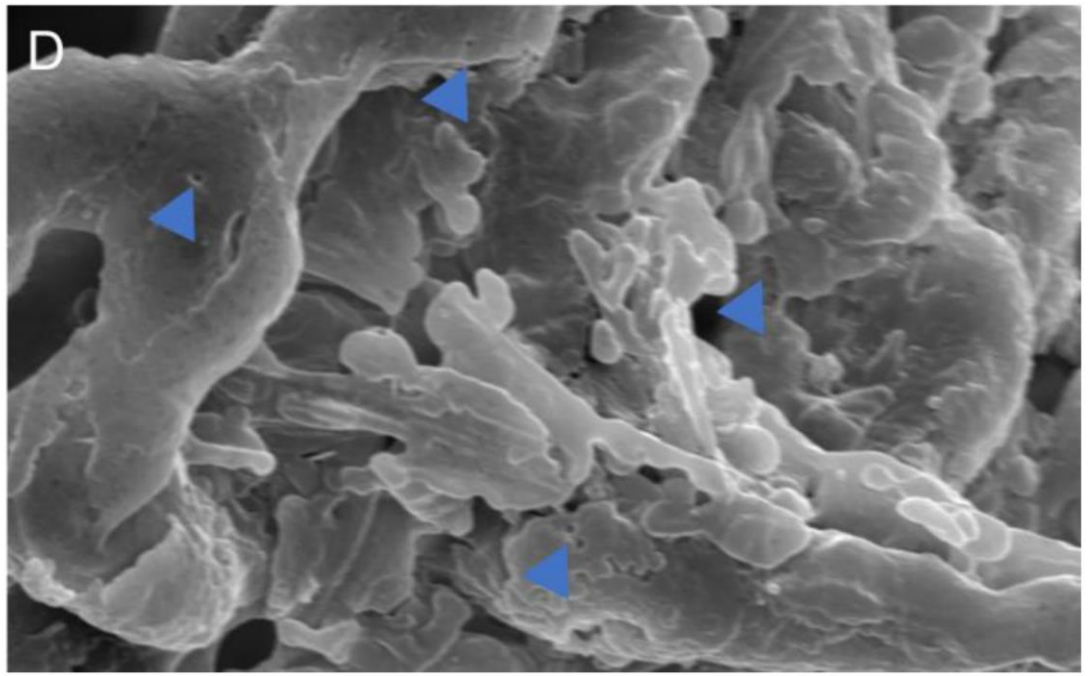


Wiersinga WJ et al. JAMA. 2020

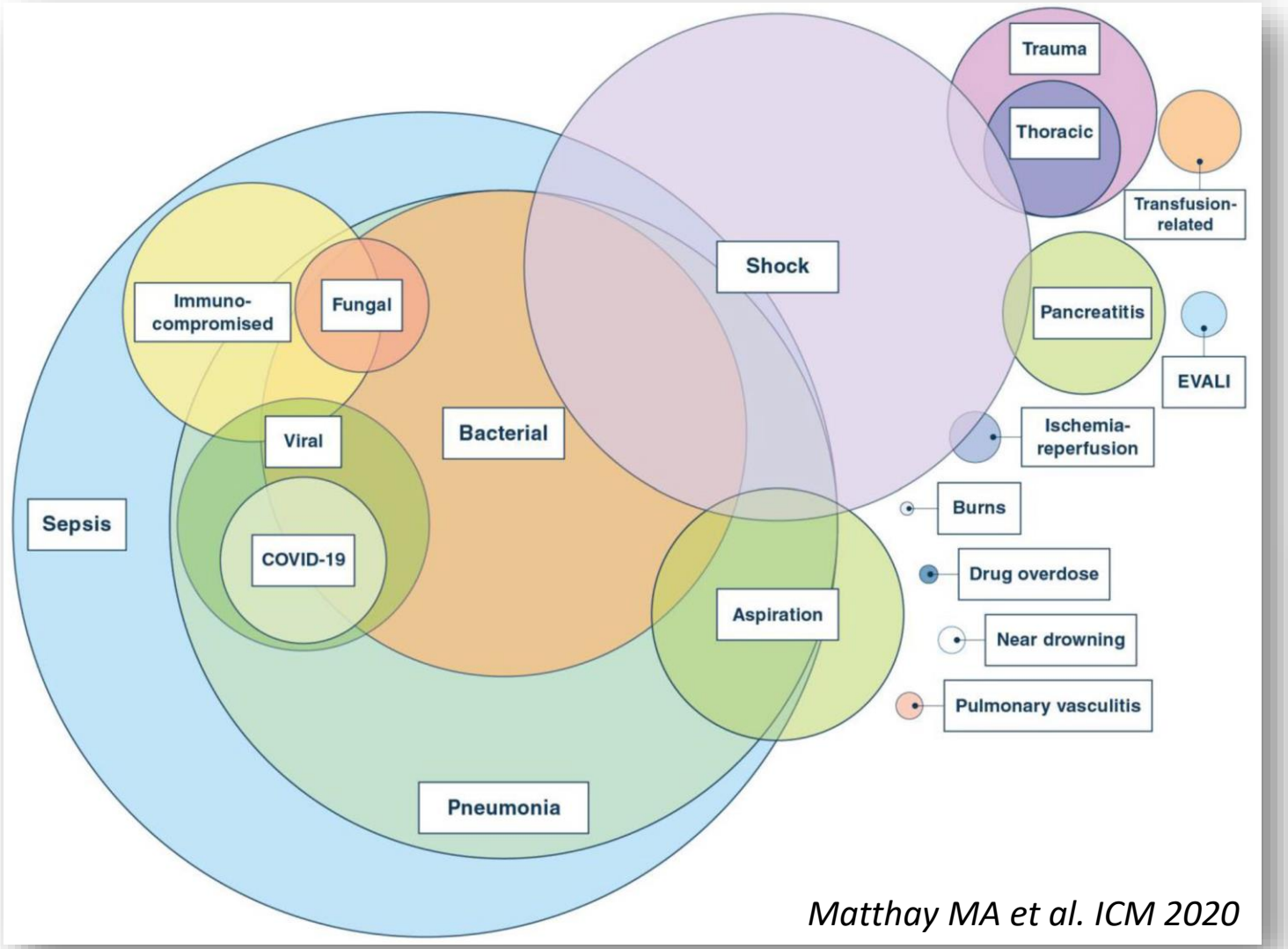




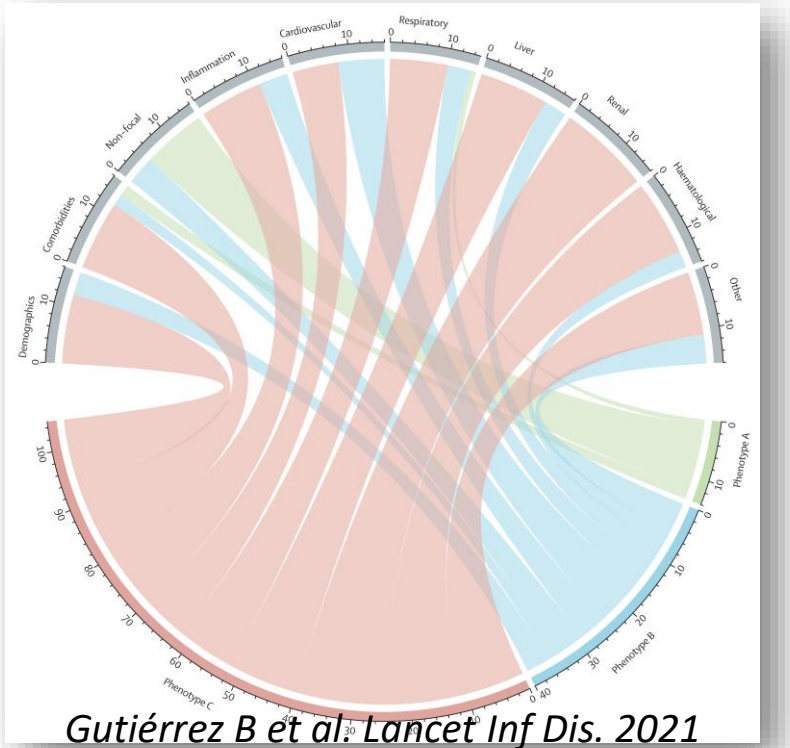




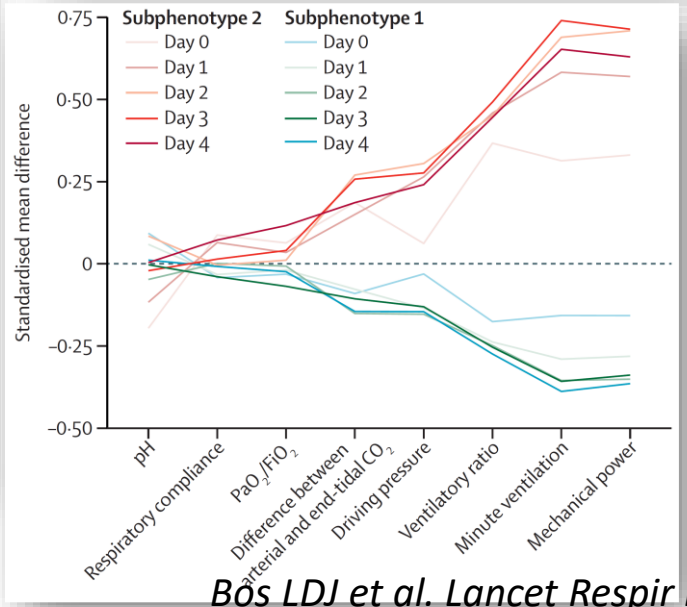
Ackerman RJ et al. ERJ. 2002



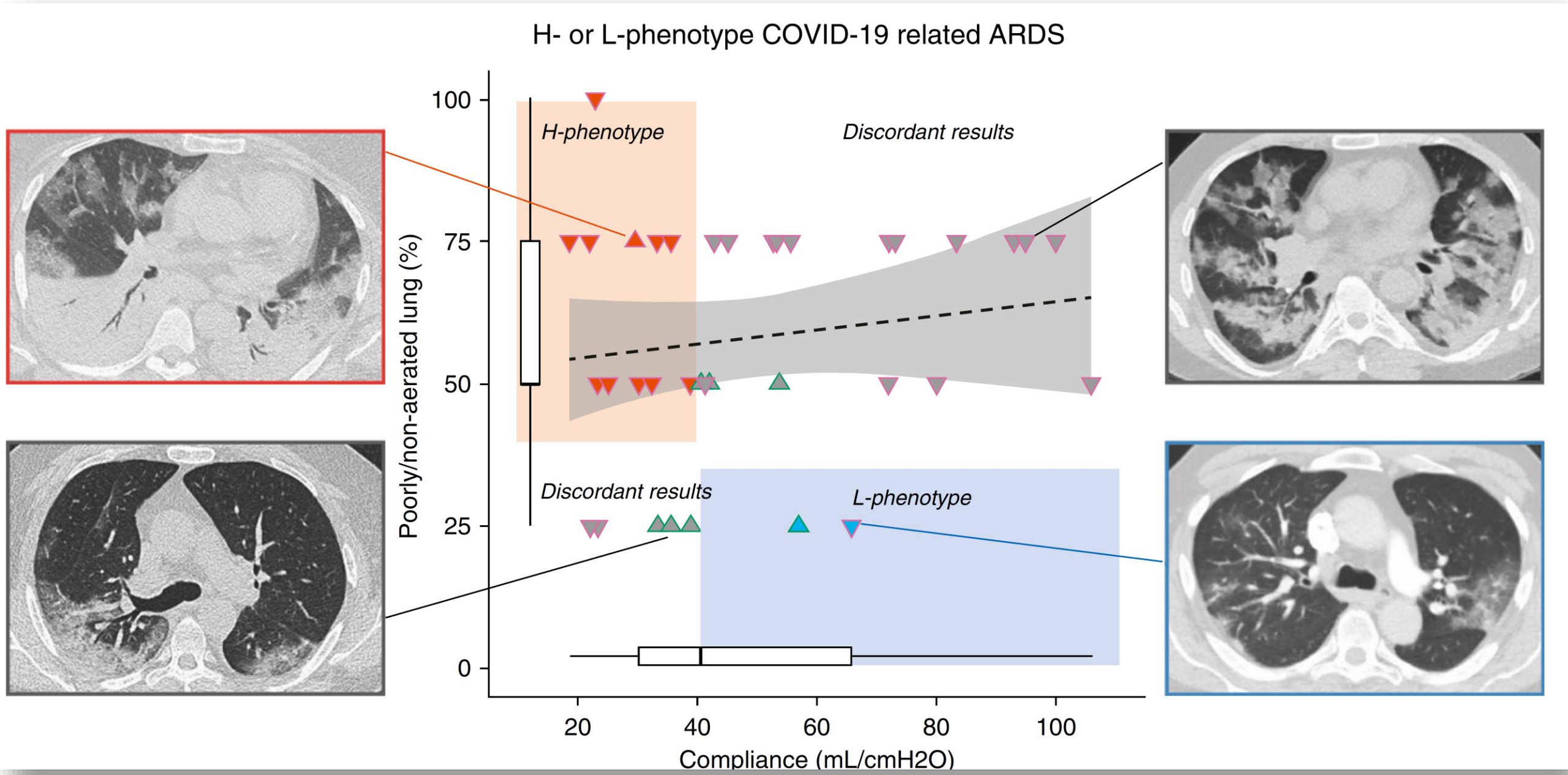
Matthay MA et al. ICM 2020



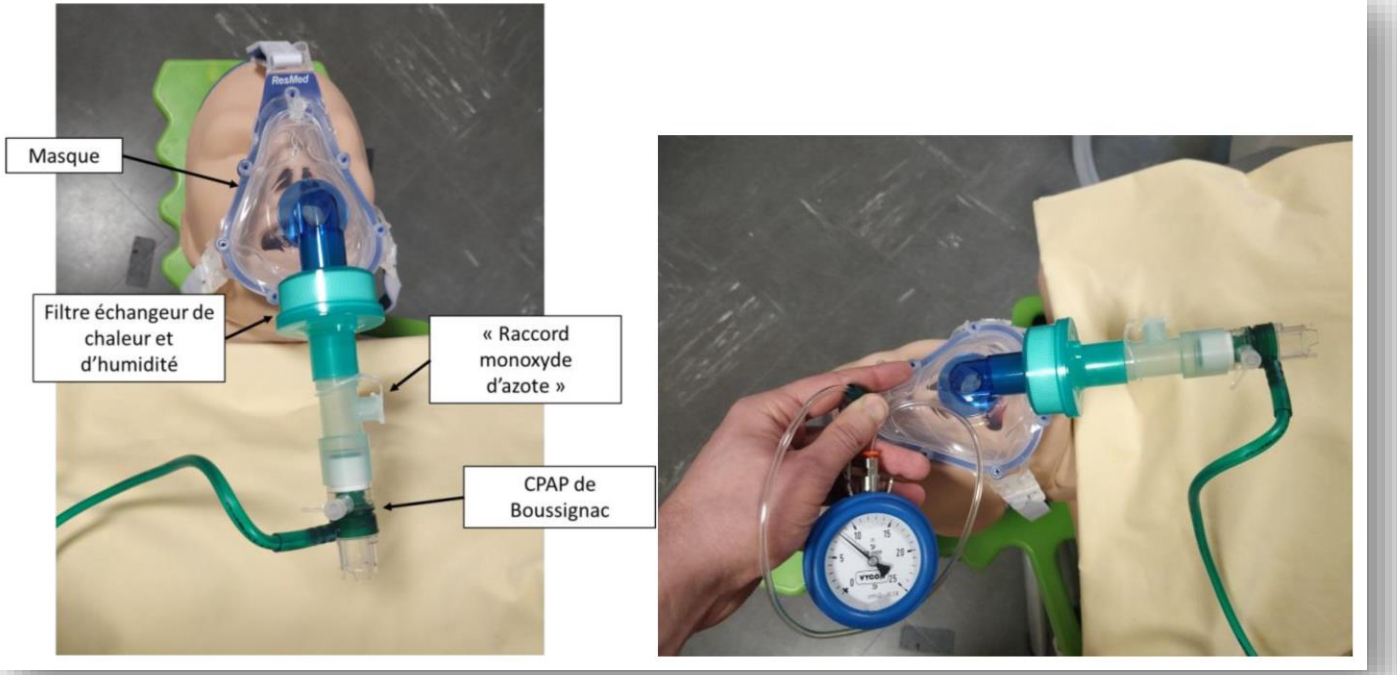
Gutiérrez B et al. Lancet Inf Dis. 2021



Bos LDJ et al. Lancet Respir Med. 2021



Lieuwe DJ et al. AJRCCM. 2020



Mekontso Dessap A, Carteaux G, Demoule A

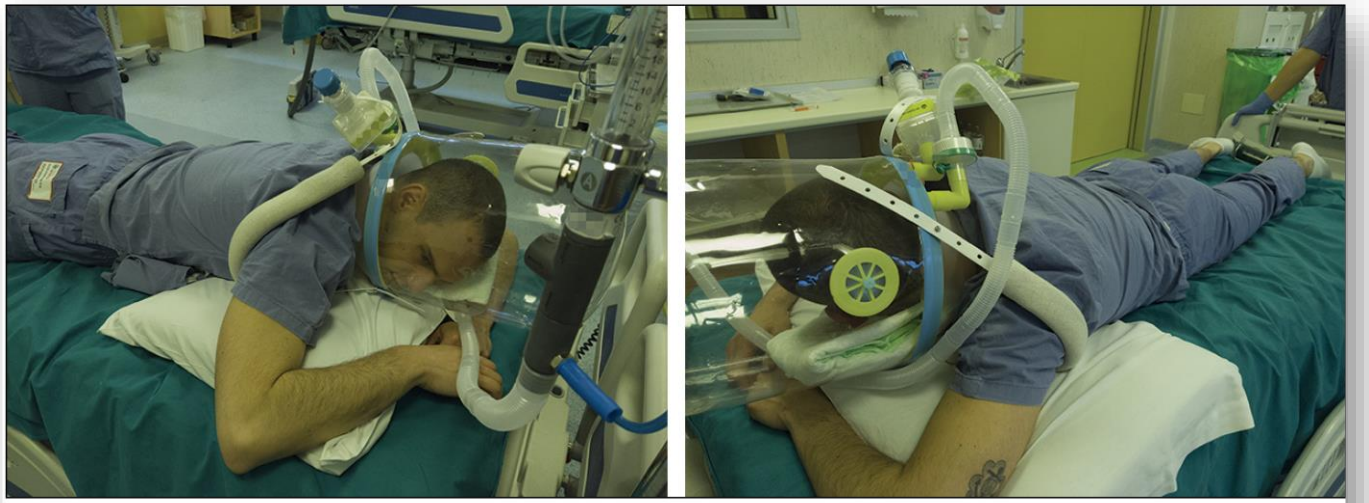
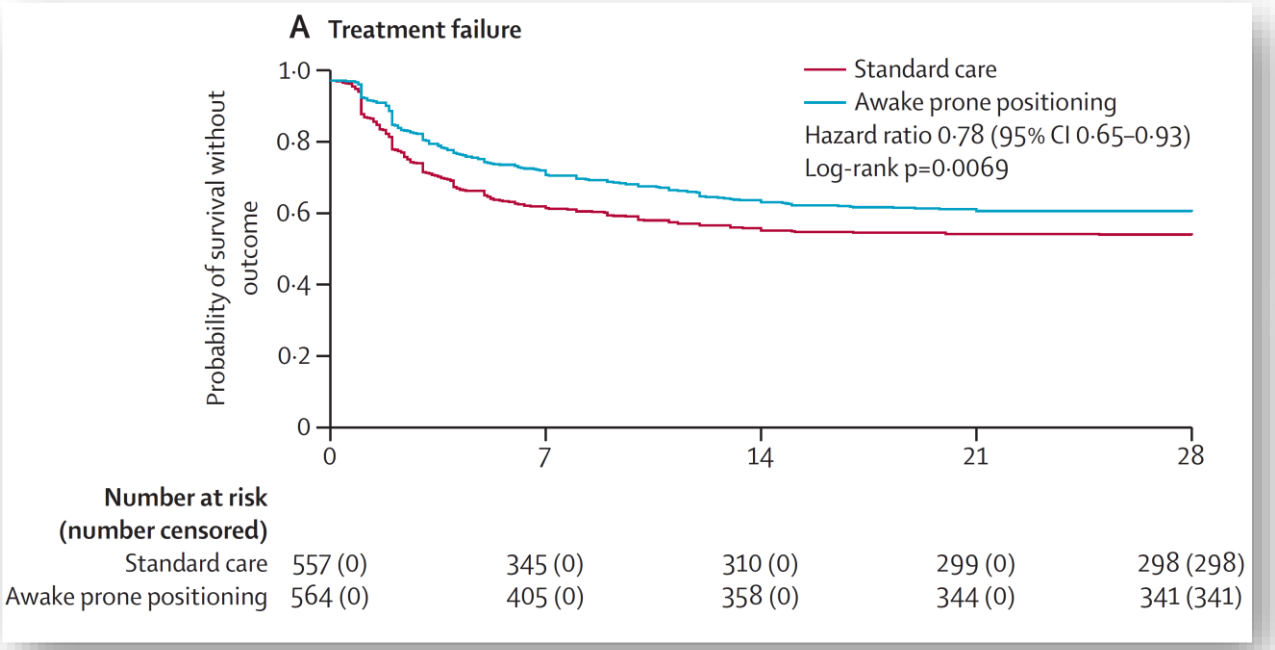


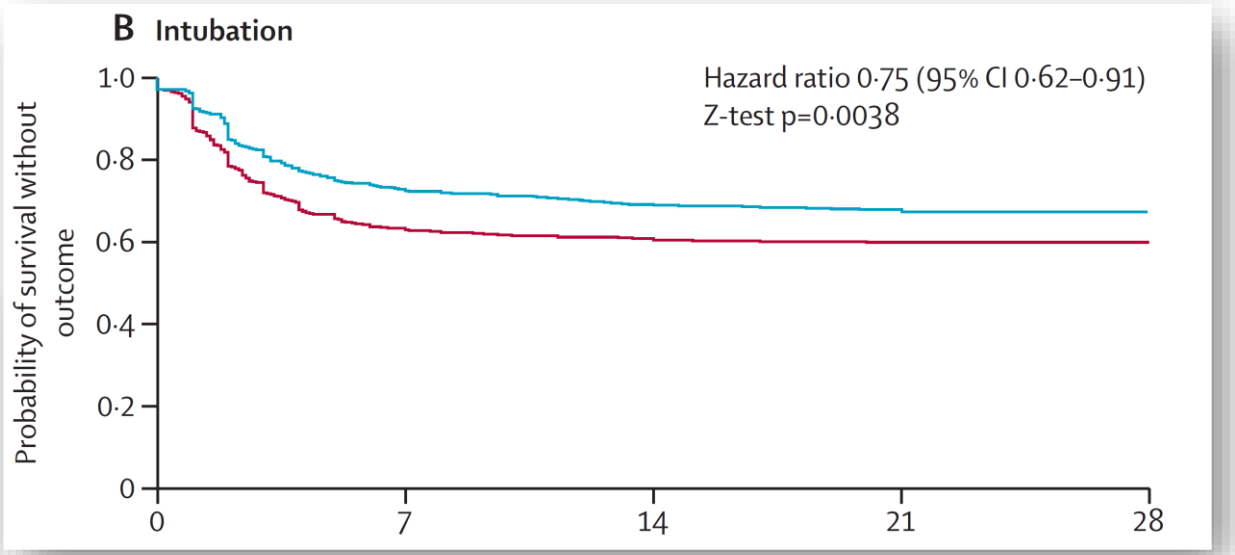
Figure 1: **Prone positioning with a helmet interface to enable continuous positive airway pressure**
Example demonstrated by volunteer.

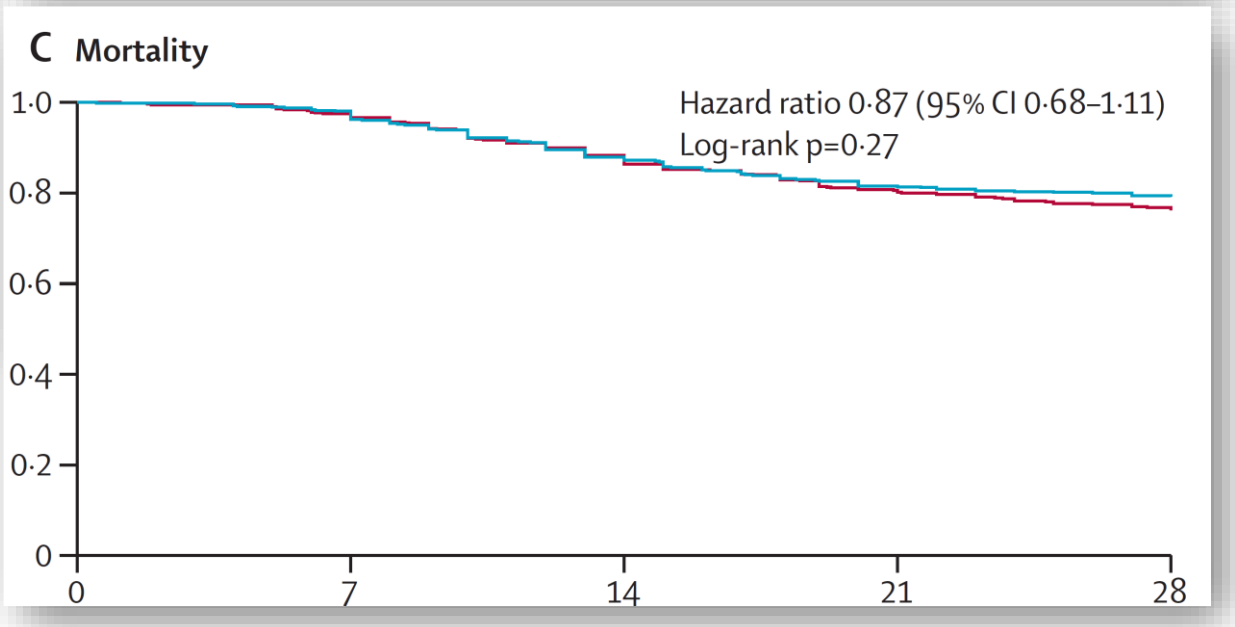
Coppo A et al. Lancet Respir Med. 2020

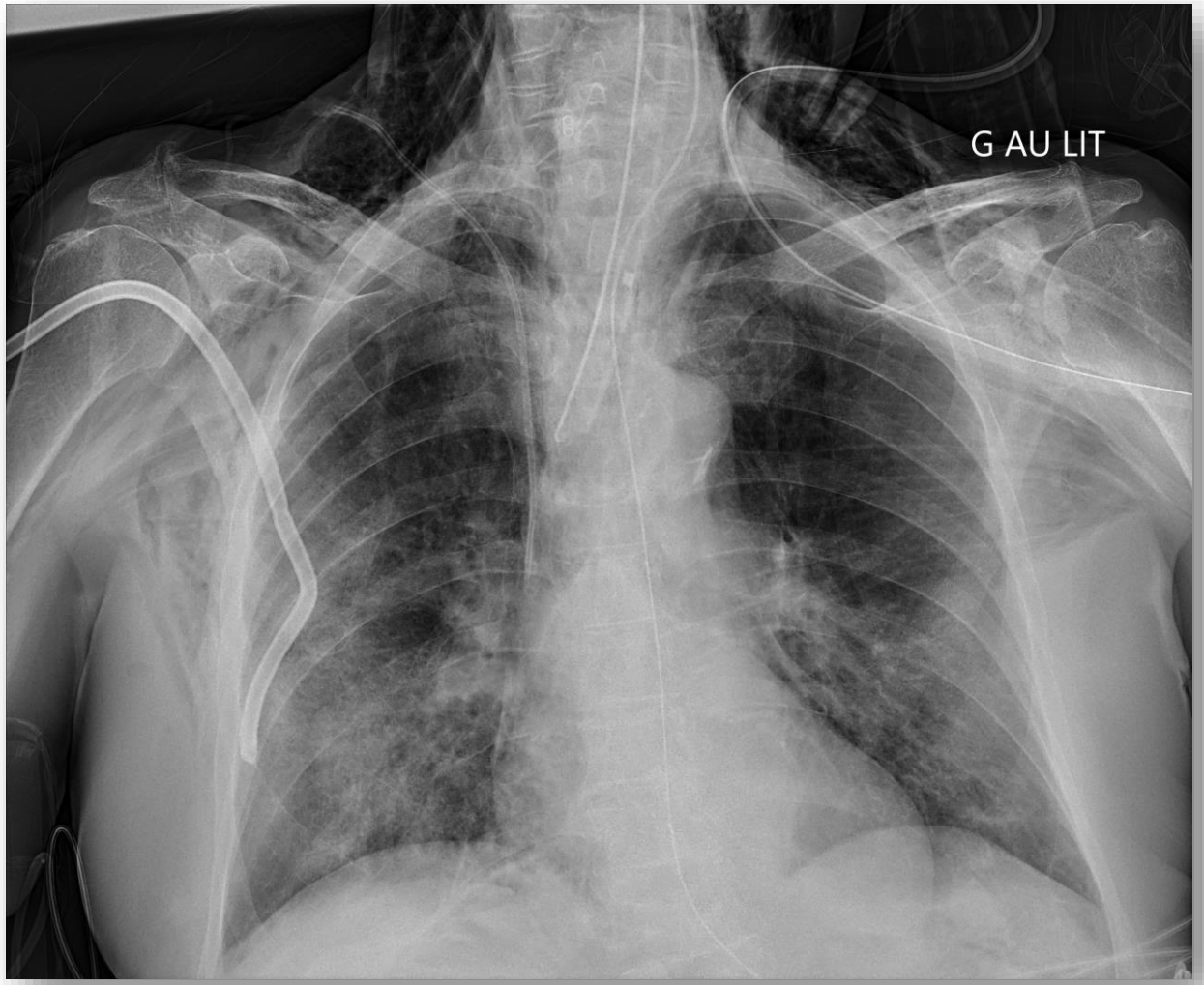
Décubitus ventral chez les patients conscients non intubés



Ehrmann S et al. Lancet Respir Med. 2021



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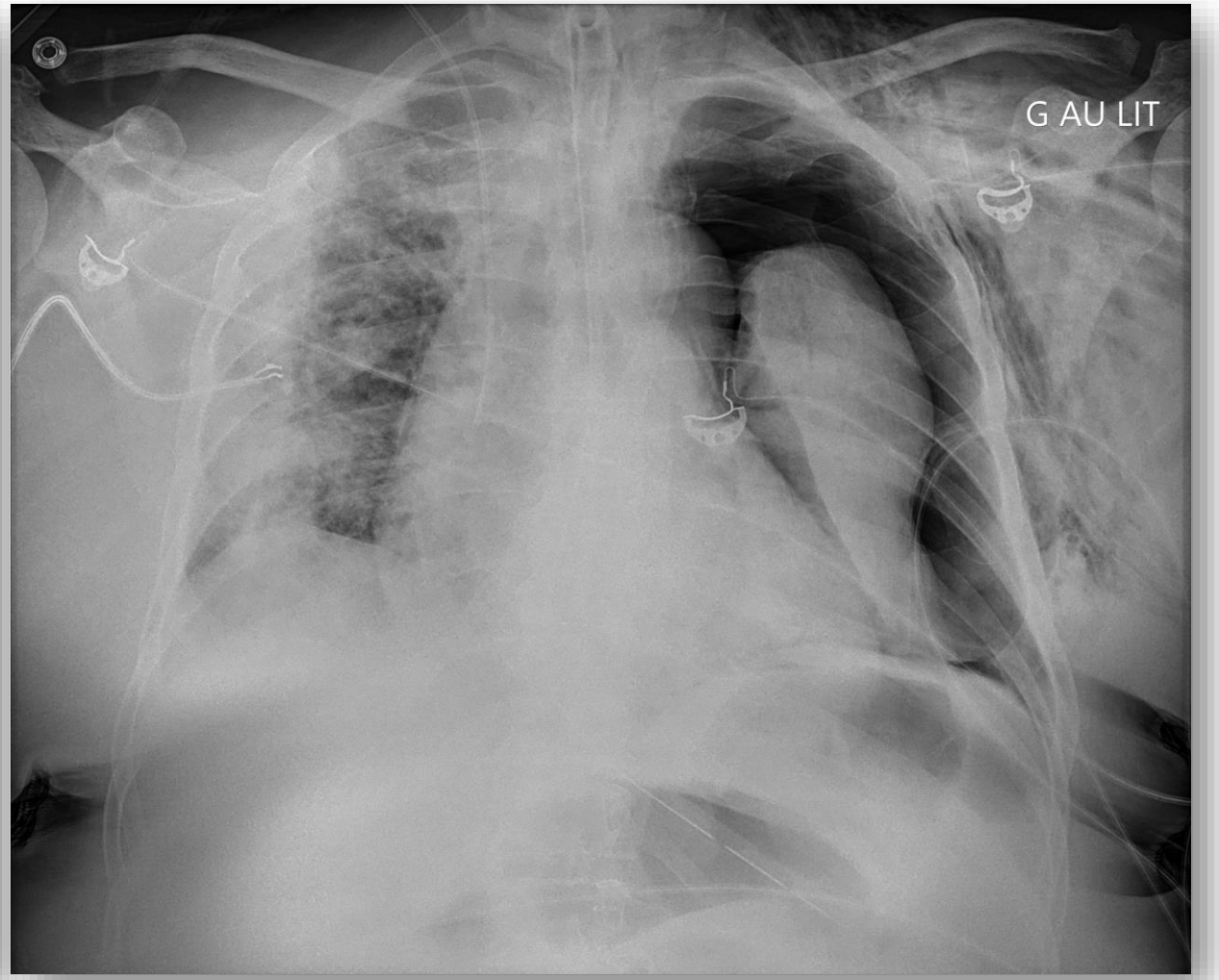
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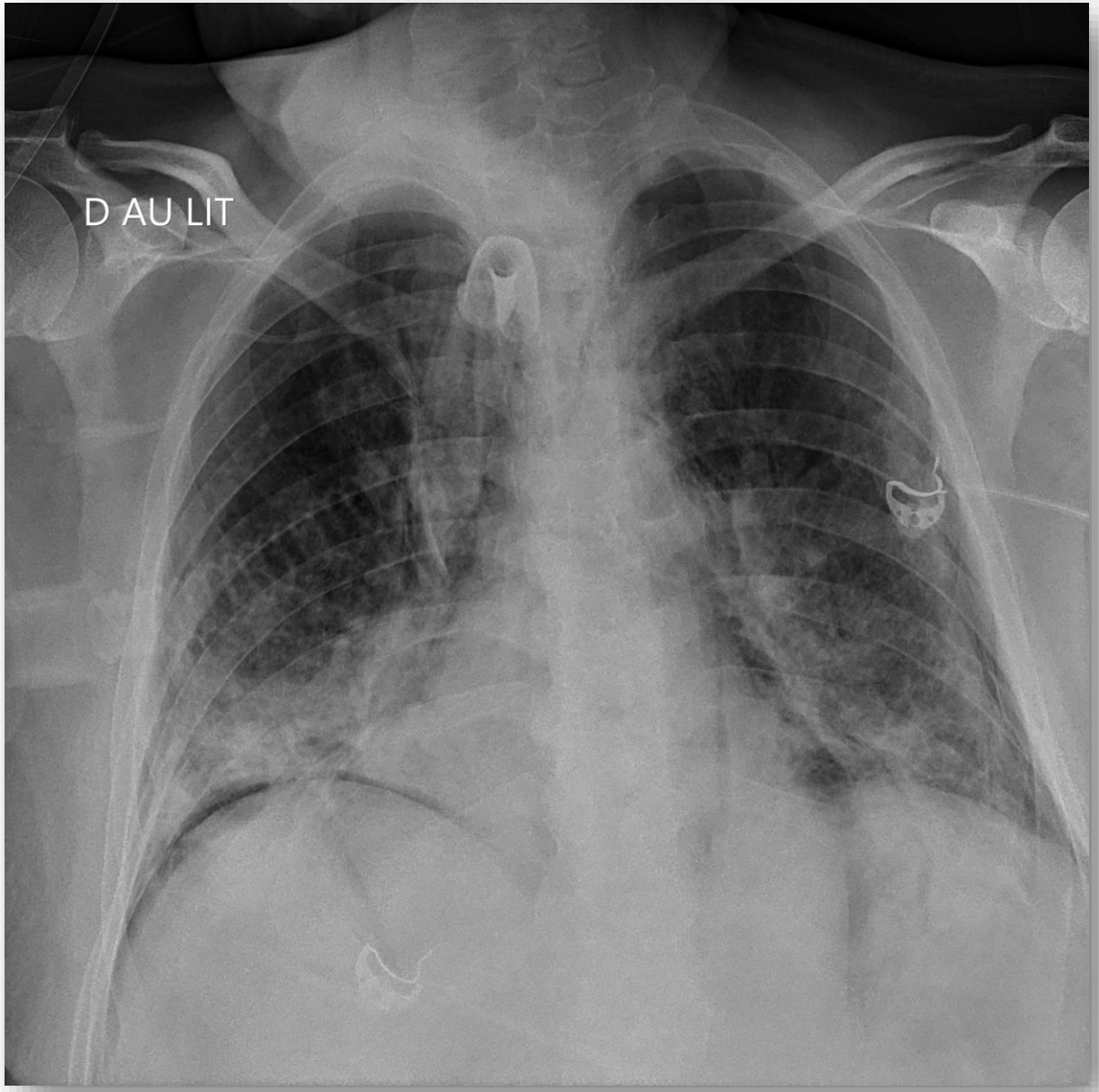
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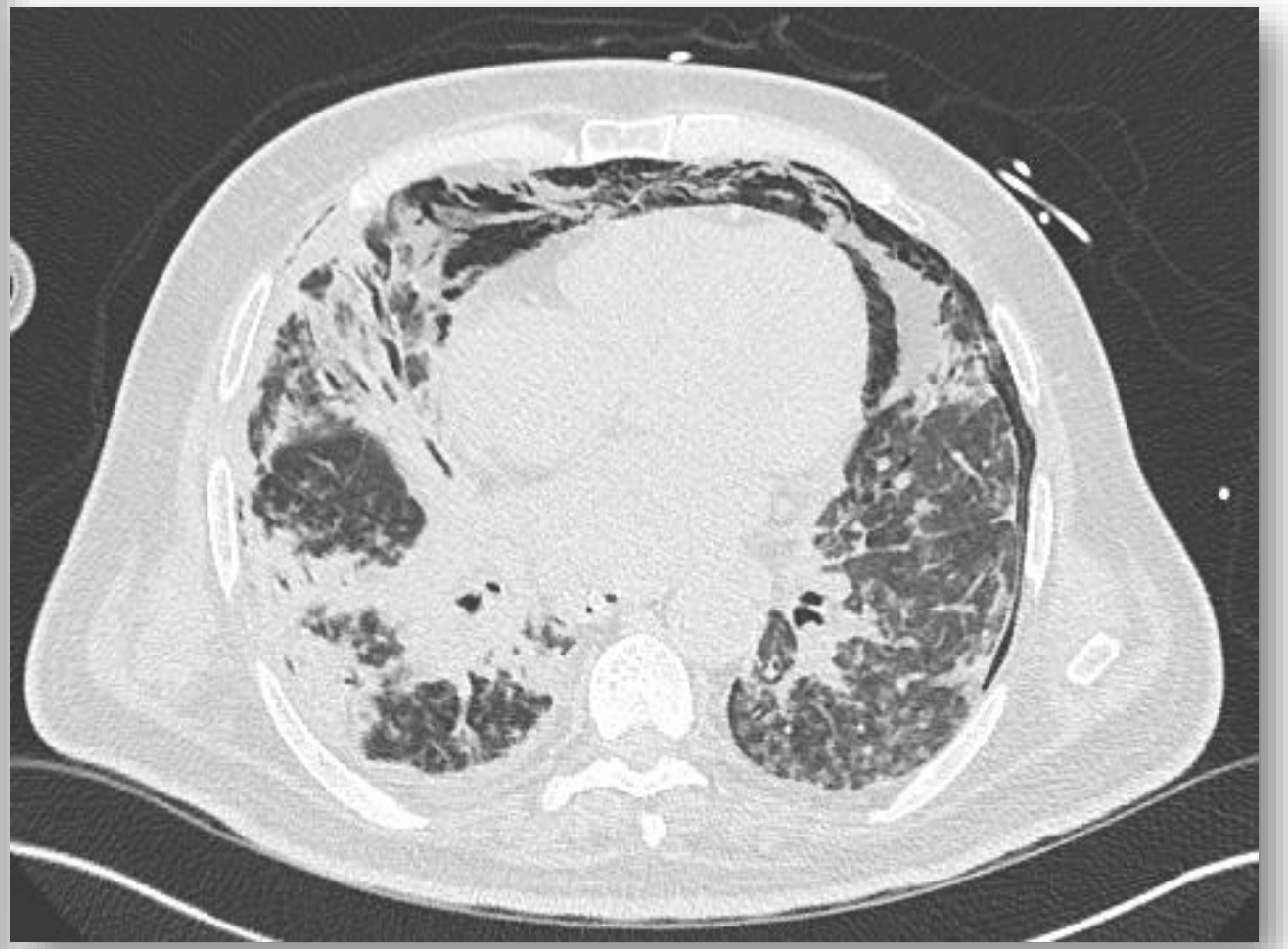
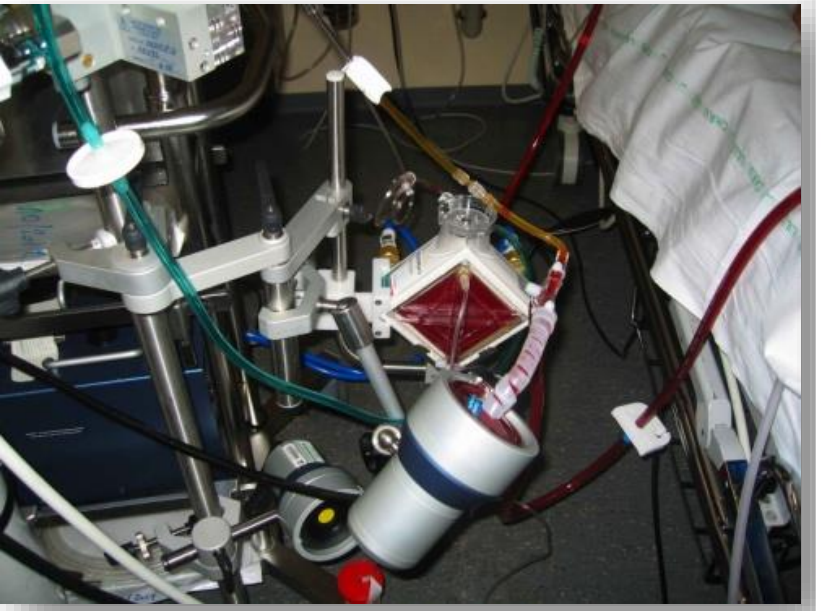
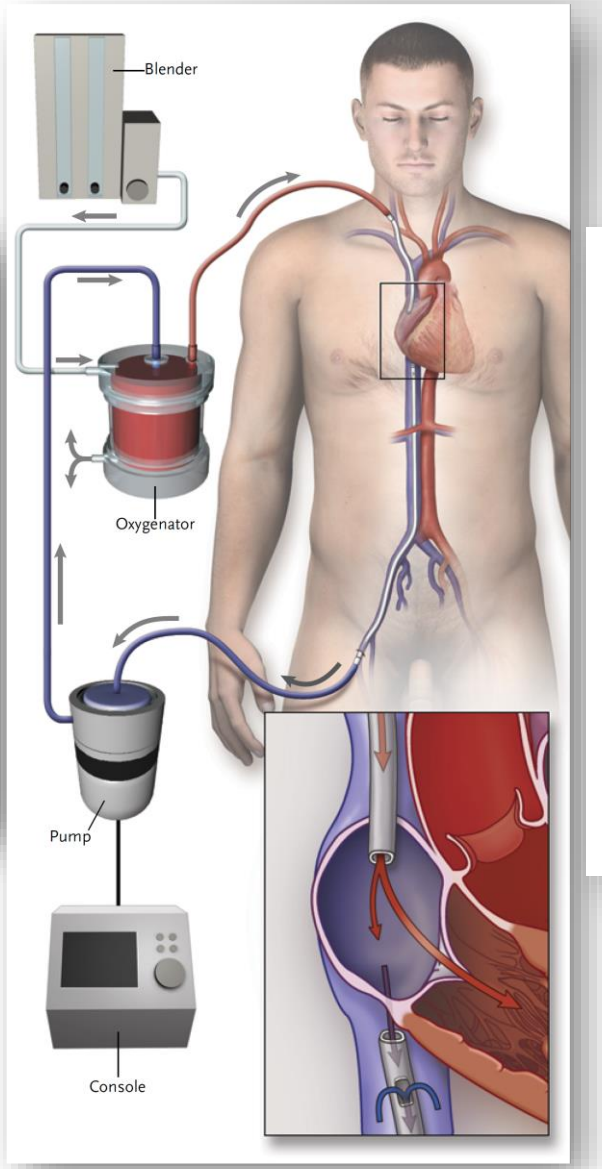
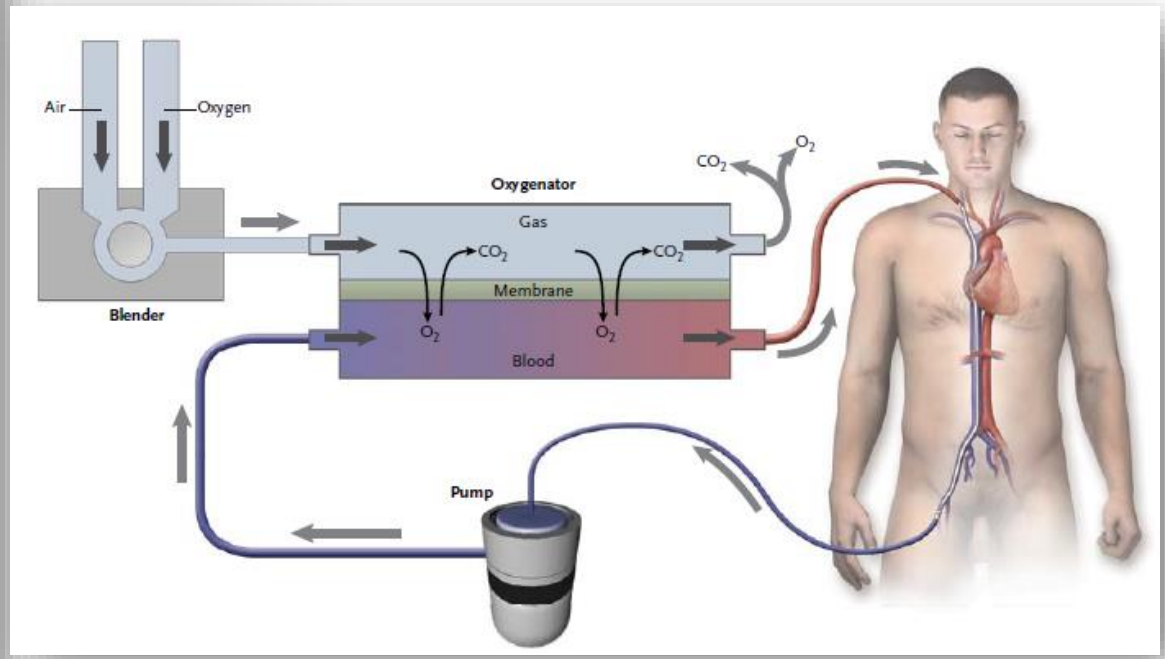


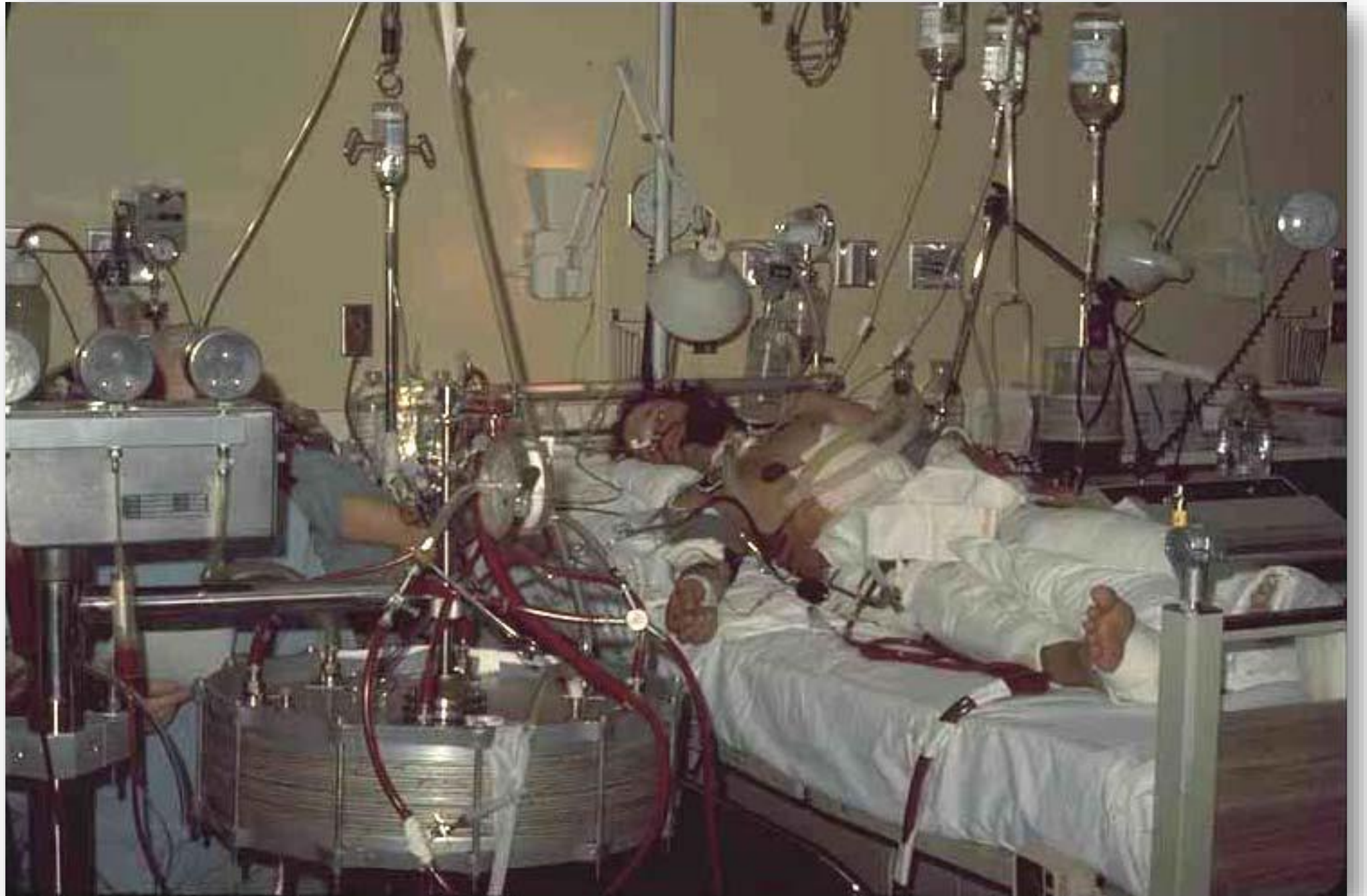
L'ECMO ou oxygénation extra-corporelle







Brodie D. NEJM. 2011



Hill JD et al. NEJM. 1972


SECHRIST
POLE DE REANIMATION
COMMUN STRUCTURE
MAQUET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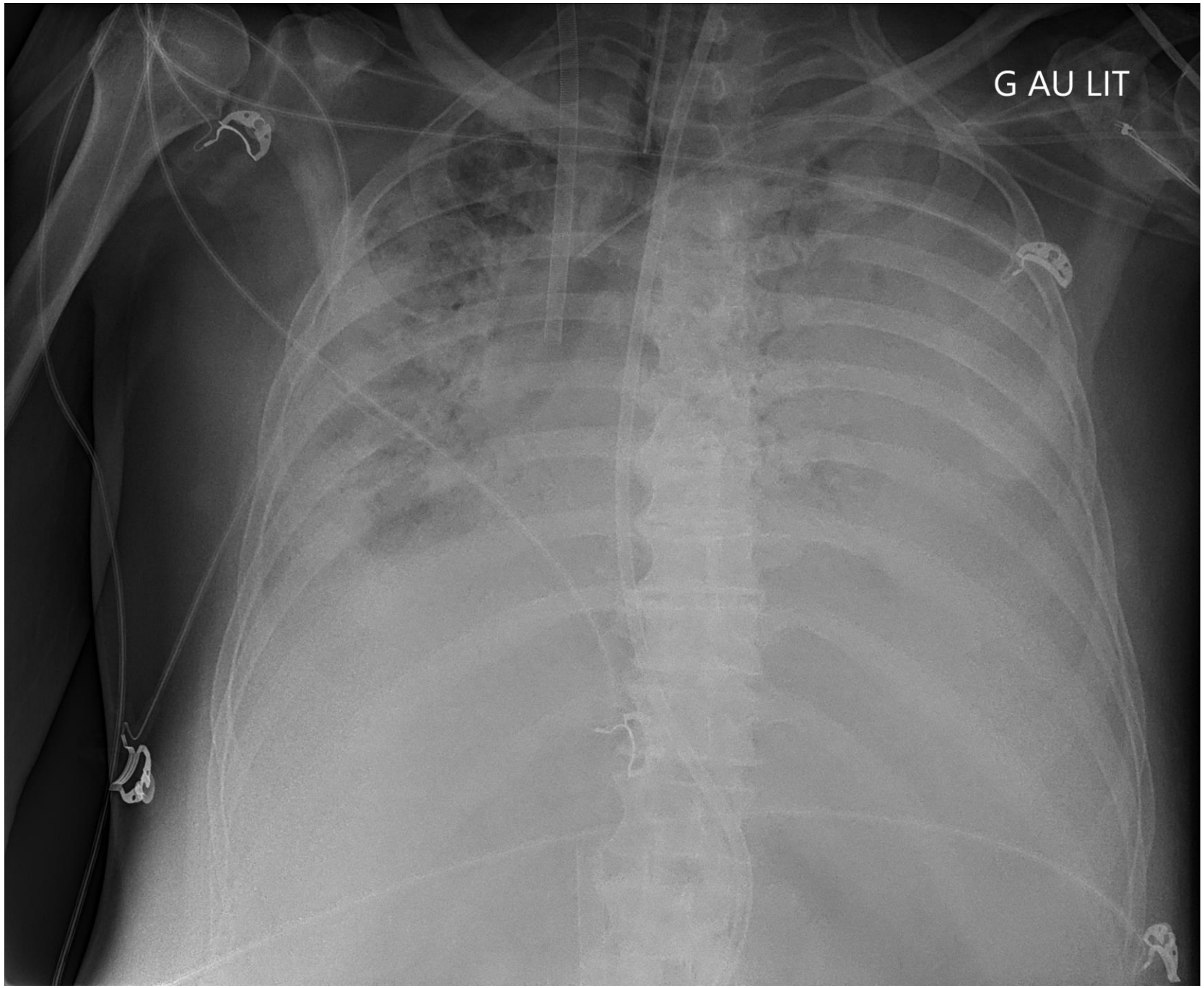
G AU LIT

COVID-19 et soins intensifs

- Antiviraux :
  - Bof
  - Sauf Ac monoclonaux en association chez les immunodéprimés PCR+ séronégatifs

- Immunomodulation
  - Corticoïdes
  - Quid d'une intensification : anti IL1 ? Anti IL6 ? Anti JAK ? Personnalisation ?

- Ventilation
  - Stratégies non invasives possibles
  - Y compris « frugales » si ressources limitées
  - Mais ne pas rater le timing de l'intubation
  - Et la place de l'ECMO

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EDITORIAL

Do not just sit there, do something … but do no harm: the worrying aspects of COVID-19 experimental interventions

Mervyn Singer[1*] and Andre Kalil[2]