

Montpellier et la région Occitanie - Méditerranée

LE CORUM, Montpellier

du lundi 30 août 2021 au mercredi 1<sup>er</sup>septembre 2021



Dr Paul Loubet



22es JNI, Montpellier du 30/08 au 1er/09/2021





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L'orateur ne souhaite

pas répondre

Déclaration de liens d'intérêt avec les industries de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

Intervenant : Paul Loubet

**Titre :** Pneumonies à SARS-CoV-2 Actualités et perspectives thérapeutiques

Consultant ou membre d'un conseil scientifique : Astrazeneca, GSK, Pfizer



Conférencier ou auteur/rédacteur rémunéré d'articles ou documents



Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations Gilead, Pfizer



JNE

Investigateur principal d'une recherche ou d'une étude clinique





### Plan

- Thérapies antivirales
  - Remdesivir
  - Plasma convalescents
  - Ac Monoclonaux
- Thérapies Immunomodulatrices
  - Corticoïdes
  - Anti-IL6
  - Anti-IL1
  - Inhibiteur JAK





### Thérapies antivirales Remdesivir, Plasma de convalescents, mAbs



# Remdesivir (analogue nucleosidique)



Figure 3. Time to Recovery According to Subgroup.

### CJS: Mortalité Patient sous 02 HR 0.30 (0.14-0.64)

Heterogeneity:  $I^2 = 71\%$ 

	SULIDARITI NEJM 2021							
Subgroup	Remdesivir	Observed No. of I Control Remdes		-Expecte eaths in <i>i</i> ir Group	d Rate Ratio f (99% CI; 95% C	or Death CI for totals)		
			Value	Variance				
	no. of deaths reporte	d/no. of patients (%	%)					
Solidarity (stratified according to oxygen use and ventilation)								
No supplemental oxygen	11/661 (2.0)	13/664 (2.1)	-0.6	6.0		0.90 (0.31-2.58)		
Low-flow or high-flow oxygen	192/1828 (12.2)	219/1811 (13.8)	-16.9	101.8		0.85 (0.66-1.09)		
Ventilation	98/254 (43.0)	71/233 (37.8)	7.6	40.8	÷.	1.20 (0.80-1.80)		
Stratified total: Solidarity	301/2743 (12.5)	303/2708 (12.7)	-10.0	148.6	$\diamond$	0.94 (0.80-1.10)		

COLIDADITY

0.32 (0.15-0.66)

0.83 (0.34-2.04)

0.87 (0.72-1.04)

0.81 (0.68-0.96)

		Meta				
						Kaka Ann Inter Med 202
Supplemental oxygen and not ventilated	at baseline					
Beigel et al [ACTT-1], 2020 (5)	Placebo	9	232	25	203	
Wang et al, 2020 (13)	Placebo	11	129	7	68	+
Pan et al [Solidarity], 2020 (4)	Usual care	192	1828	219	1811	
Fixed-effects model		212	2189	251	2082	•

CJS: Evolution vers VM/ECMO

J	N	22")
		1710

HR 0.7 (0.6-0.9) 22es JNI, Montpellier du 30/08 au 1er/09/2021

### Plasma de convalescents

### • Meta-analyse, 10 RCTs, mortalité J15-30

A All-cause mortality

	Events, N	lo./total		Favors	Favors	
Trial	Plasma	Control	RR (95% CI)	plasma	control	Weight, %
Studies published in peer-review	ed journals			-		
PLACID <sup>17</sup>	34/235	31/229	1.07 (0.68-1.68)			3.7
PlasmAr <sup>18</sup>	25/228	12/105	0.96 (0.50-1.83)		1 1	1.8
ChiCTR2000029757 <sup>19</sup>	8/52	12/51	0.65 (0.29-1.47)	- 	1 1 1	1.2
NCT04479163 <sup>16</sup>	2/80	4/80	0.50 (0.09-2.65)		1 1 1	0.3
Summary for peer-reviewed st	udies		0.93 (0.63-1.38)	$\sim$		6.9
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ ,	P=.65				1 1 1	
Studies published as preprints						
ILBS-COVID-02 <sup>21</sup>	3/14	1/15	3.21 (0.38-27.40)	) — — — — — — — — — — — — — — — — — — —	<b>→</b>	0.2
PICP19 <sup>24</sup>	10/40	14/40	0.71 (0.36-1.41)	- 	1 3 3	1.6
ConCOVID <sup>22</sup>	6/43	11/43	0.55 (0.22-1.34)	- 	1 1 1	0.9
NCT04356534 <sup>20</sup>	1/20	2/20	0.50 (0.05-5.08)	- 	<b>→</b>	0.1
ConPlas-19 <sup>23</sup>	0/38	4/43	0.13 (0.01-2.26)	<b>~</b>	a <u>a</u> d	0.1
Study published as press release					3 3 3 1	
RECOVERY <sup>8</sup>	NA/NA	NA/NA	1.04 (0.95-1.14)	-		90.2
Summary for all studies			1.02 (0.92-1.12)	-	<b>&gt;</b>	100.0
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , P	=.48					
Test for overall effect: <i>P</i> = .68				01	1 5	
				DD (05%	د <u>،</u> ۲	
				RR (95%	CI)	



Janiaud, JAMA 2021

### Plasma de convalescents

- RECOVERY Trial (UK)
  - 11 558 patients, Plasma + SOC vs SOC (1:1), mortalité à J28
    - 5% VM, 87% O<sub>2</sub>, 8% pas O<sub>2</sub>
    - Médiane début symptômes 9j (6-12)



Figure 3: Effect of allocation to convalescent plasma on 28-day mortality by prespecified characteristics at randomisation

Cor	nvalescent plasma	Usual care		RR (95% CI)
Age, years (χ <sub>1</sub> <sup>2</sup> =0.3; p=0.57	7)			
<70	533/3705 (14%)	545/3748 (15%)	_ <b>_</b>	1.00 (0.88-1.12)
70 to 79	495/1310 (38%)	494/1280 (39%)		0.99 (0.87-1.13)
≥80	370/780 (47%)	369/735 (50%)		0.94 (0.81–1.09)
Sex ( $\chi_1^2$ =1.3; p=0.25)				
Men	952/3643 (26%)	972/3787 (26%)		1.03 (0.94-1.13)
Women	446/2152 (21%)	436/1976 (22%)		0.94 (0.82–1.07)
Ethnicity (x <sup>2</sup> =0.2; p=0.62)				
White	1089/4362 (25%)	1096/4293 (26%)		0.98 (0.90-1.07)
Black, Asian or minority eth	nic 200/853 (23%)	203/889 (23%)	<b>-</b>	1.04 (0.85–1.26)
Days since symptom ons	et (χ <sub>1</sub> <sup>2</sup> =3.2; p=0.07)			
≤7	606/2226 (27%)	659/2240 (29%)		0.92 (0.83-1.03)
>7	789/3564 (22%)	749/3522 (21%)	+=-	1.06 (0.96–1.17)
Respiratory support recei	ived (χ <sub>1</sub> <sup>2</sup> =3.5; p=0.06)			
No oxygen received	56/442 (13%)	69/455 (15%)	<	0.83 (0.58-1.18)
Oxygen only	1184/5051 (23%)	1194/4993 (24%)		0.99 (0.91-1.07)
Invasive mechanical ventila	tion 158/302 (52%)	145/315 (46%)	+	1.19 (0.95–1.50)
Use of corticosteroids (x <sub>1</sub> <sup>2</sup>	=2.7; p=0.10)			
Yes	1313/5370 (24%)	1299/5311 (24%)	-#-	1.01 (0.93-1.09)
No	74/391 (19%)	100/413 (24%)	<+	0.78 (0.58–1.05)
Patient SARS-CoV-2 anti	ibody test result ( $\chi_1^2$ =1	.6; p=0.21)		
Positive	566/3022 (19%)	495/2752 (18%)		1.05 (0.93-1.19)
Negative	626/1982 (32%)	549/1629 (34%)		0.94 (0.84-1.06)
Not done	206/791 (26%)	364/1382 (26%)		1.01 (0.85–1.19)
All participants	1398/5795 (24%)	1408/5763 (24%)	\$	1.00 (0.93–1.07) p=0.93



Figure 2: Effect of allocation to convalescent plasma on 28-day mortality

Recovery Collaborative Group, Lancet 2021

Convalescent plasma Usual care better better

1.2 1.4 1.6

### <u>iasina ar convarsechis</u>

### Convalescent plasma therapy for B-cell-depleted patients with protracted COVID-19

Hueso, Blood 2020

Potential benefit of convalescent plasma transfusions in immunocompromised patients with COVID-19

Rodionov, Lancet 2021

JAMA Oncology | Original Investigation

### Association of Convalescent Plasma Therapy With Survival in Patients With Hematologic Cancers and COVID-19

Thompson, JAMA Oncol 2021

- 966 patients, 70 centres ۲
- 143 PC vs 843 contrôles •
- 1/3 sous VM
- **Score Propension**
- HR 0.52 (IC95% 0.29-0.92)



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# Anticorps monoclonaux





### Anticorps monoclonaux : Casirivimab + Indevimab

### • RECOVERY Trial (UK)

- 9 785 patients, RONAPREVE (8g) + SOC vs SOC (1:1), mortalité à J28 chez les séro puis globale
  Outcome, subgroup
  REGEN-COV
  Usual care
  RR (95% Cl)
  - 54% Séro +, 32% séro -, 14% inconnu
  - 6% VM, 24% VNI, 62% O<sub>2</sub>, 8% pas O<sub>2</sub>
  - Médiane début symptômes 9j (6-12)



Outcome, subgroup	REGEN-COV	Usual care		RR (95% CI)
Death within 28 days (χ	<sup>2</sup> <sub>1</sub> = 10.1; p=0.001)			
Seronegative	396/1633 (24%)	451/1520 (30%)	_ <b>_</b>	0.80 (0.70-0.91)
Seropositive	411/2636 (16%)	383/2636 (15%)		- 1.09 (0.95-1.26)
Unknown	137/570 (24%)	192/790 (24%)		- 0.98 (0.78-1.22)
All participants	944/4839 (20%)	1026/4946 (21%)	$\diamond$	0.94 (0.86–1.03)
Discharge alive from ho	ospital (χ²=16.6; p<0	0.001)		
Seronegative	1046/1633 (64%)	878/1520 (58%)	- <b> </b>	- 1.19 (1.08-1.30)
Seropositive	1970/2636 (75%)	2031/2636 (77%)	-	0.94 (0.88-1.00)
Unknown	359/570 (63%)	504/790 (64%)		0.96 (0.83-1.10)
All participants	3375/4839 (70%)	3413/4946 (69%)	<	1.01 (0.97–1.07)
Invasive mechanical ve	ntilation or death (χ	<sup>2</sup> =12.0; p<0.001)		
Seronegative	487/1599 (30%)	542/1484 (37%)		0.83 (0.75-0.92)
Seropositive	456/2449 (19%)	415/2450 (17%)	- <b>-</b> -	- 1.10 (0.97-1.24)
Unknown	146/508 (29%)	194/708 (27%)		- 1.05 (0.87-1.26)
All not on invasive mechanical ventilation at randomisation	1089/4556 (24%)	1151/4642 (25%)	<	0.96 (0.90–1.04)
			0.6 0.8 1 1	.2 1.4 1.6
			Outcome	Outcome
			less likely with mo	ore likely with
			REGEN-COV RE	EGEN-COV

# Synthèse

- Remdesivir
  - Si 0<sub>2</sub>
- Plasma convalescent
  - Pas effet
  - Déficit Immunité B
- mABs
  - Uniquement chez les séro nég
  - Attente plus de données



### Perspectives

- Autres Ac monoclonaux
  - AZD 7442 (Discovery 2.0, EU Response, ACTIV3, NIH)
- Anticorps polyclonaux (XAV-19, Résultats phase 2 POLYCOR) (Gaborit, Trials 2021)
- Antiviraux direct
  - Molnupiravir (MK 4482, analogue nucléotidique)
    - résultats phase 2a, patients ambulatoires clairance virale plus rapide, négativation PCR tous les patients traités à J5 (Fischer, MedRxiv 2021).
    - Essai phase 2/3 à venir patients hospitalisés avec O2 simple, USA (NCT04575584)
  - AT-527/RO7496998 (analogue nucléotidique). Phase 2 : Réduction charge virale patients hospitalisés
  - Inhibiteurs protéases (PF 07304814 et PF 07321332)

### Immunomodulateurs Corticoides, Anti-IL1, Anti-IL6, Inhib JAK



22es JNI, Montpellier du 30/08 au 1er/09/2021

## Corticoïdes systémiques



### Mortality (%) Mortality (%) 60. 40 40 Usual care Devamethasone 20 Dexamethasone Usual care 21 14 28 14 21 28 Days since Randomization Days since Randomization No. at Risk No. at Risk Usual care 2604 2195 2018 1950 1916 1034 98 928 897 889 Usual care Dexamethasone 1279 1036 1006 981 Dexamethasone 501 477 440 420 411





**Recovery Collaborative Group, NEJM 2021** 

### Meta-Analyse •

### 7 essais, 1700 patients, CTC vs Placebo, mortalité à J28

Figure 2. Association Between Corticosteroids and 28-Day All-Cause Mortality in Each Trial, Overall, and According to Corticosteroid Drug

Drug and trial	ClinicalTrials.gov identifier	Initial dose and administration	No. of de No. of pa	aths/total tients	Odds ratio	Favors	Favors no steroids		Weight, %
Dexamethasone	lucititiei		Steroids	No steroids		steroids	Steroids		70
DEXA-COVID 19	NCT04325061	High: 20 mg/d intravenously	2/7	2/12	2.00 (0.21-18.69) —			<b>→</b>	0.92
CoDEX	NCT04327401	High: 20 mg/d intravenously	69/128	76/128	0.80 (0.49-1.31)		<u> </u>		18.69
RECOVERY	NCT04381936	Low: 6 mg/d orally or intravenously	95/324	283/683	0.59 (0.44-0.78)	-			57.00
Subgroup fixed e	ffect		166/459	361/823	0.64 (0.50-0.82)				76.60
Hydrocortisone									
CAPE COVID	NCT02517489	Low: 200 mg/d intravenously	11/75	20/73	0.46 (0.20-1.04)		÷		6.80
COVID STEROID	NCT04348305	Low: 200 mg/d intravenously	6/15	2/14	4.00 (0.65-24.66)			<b>—</b>	1.39
REMAP-CAP	NCT02735707	Low: 50 mg every 6 h intravenously	26/105	29/92	0.71 (0.38-1.33)				11.75
Subgroup fixed e	ffect		43/195	51/179	0.69 (0.43-1.12)		λ		19.94
Methylprednisolon	e								
Steroids-SARI	NCT04244591	High: 40 mg every 12 h intravenously	13/24	13/23	0.91 (0.29-2.87)				3.46
Overall (fixed effec	:t)		222/678	425/1025	0.66 (0.53-0.82)	$\diamond$			100.0
P = .31 for heteroge	eneity;								
Overall (random ef	fects <sup>a</sup> )		222/678	425/1025	0.70 (0.48-1.01)	$\sim$			
WHO		king Group JAMA 2020			0.2	1		14	

Odds ratio (95% CI)

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WHO REACT Working Group, JAMA 2020

# Corticoïdes systémiques

- RCT, double aveugle, Europe/Inde, 982 patients
- 10 I/min ou VM
- 10j DXM 6mg vs 12 mg
- Survie sans support à J28

Subgroup (no. of patients)	Dexamethasone 12 mg	Dexamethasone 6 mg	Adjusted mean	difference (95%Cl)	P value for heterogeneity
Geographical region Me	edian days alive wit	hout life support (IQR)			0.57
Europe (298 vs. 315)	22.0 (7.0-28.0)	20.0 (4.0-28.0)	-	1.8 (0.2 to 3.	4)
India (187 vs. 182)	28.0 (4.8-28.0)	25.0 (5.0-28.0)		0.5 (-1.7 to 2	.6)
Age					0.83
≥70 yr (167 vs. 167)	12.0 (3.0-28.0)	8.0 (3.0-28.0)	<b>-</b>	1.6 (-0.7 to 4	.0)
< 70 yr (318 vs. 330)	26.0 (9.0-28.0)	25.0 (5.0-28.0)	<b>.</b>	1.2 (-0.4 to 2	.8)
Chronic use of steroids					0.53
Yes (16 vs. 13)	22.0 (6.0-28.0)	5.0 (0.8-8.0)		8.4 (-5.9 to 2	2.7)
No (469 vs. 484)	22.0 (6.0-28.0)	21.5 (4.0-28.0)	-	1.0 (-0.3 to 2	2.3)
Limitations of care					0.11
Yes (25 vs. 30)	9.0 (3.3-28.0)	6.0 (3.0-28.0)		6.6 (0.1 to 13	3.1)
No (460 vs. 467)	22.0 (7.0-28.0)	22.0 (5.0-28.0)	-	1.2 (-0.1 to 2	.5)
Invasive mechanical ventila	tion				0.44
Yes (99 vs. 107)	9.0 (0.0-21.0)	2.5 (0.0-15.0)	<b>-</b>	2.4 (-0.2 to 5	.0)
No (386 vs. 390)	28.0 (9.0-28.0)	28.0 (6.0-28.0)	<b>.</b>	1.1 (-0.5 to 2	.6)
Interleukin-6 inhibitors		, ,			0.59
Yes (47 vs. 52)	27.0 (9.5-28.0)	28.0 (24.0-28.0)	<b>_</b>	-1.4 (-5.3 to 2	2.4)
No (438 vs. 445)	22.0 (5.0-28.0)	18.0 (4.0-28.0)	-	1.7 (0.3 to 3.	1)
Corticosteroid use before ra	andomization				0.64
0-2 days (355 vs. 384	) 22.0 (4.5-28.0)	23.0 (5.0-28.0)	-	1.6 (0.1 to 3.	1)
3-4 days (130 vs. 113	) 22.0 (6.8-28.0)	19.0 (4.0-28.0)	_ <b>-</b> _	-0.4 (-3.4 to	2 7)
All patients (491 vs. 480)	22.0 (6.0-28.0)	20.5 (4.0-28.0)	-	1.3 (0.0 to 2.	6)
	11.0 (0.0 10.0)	-10	0 10	20	-,





### Anti-IL6

- Meta-Analyse •
  - 27 essais, 10 930 patients (4299 Tocilizumab, 2073 Sarilumab vs placebo ou SOC), mortalité à J28

Mortalité J28 23%

Anti-IL6 OR 0.86 (IC95% 0.79-0.95) Tocilizumab OR 0.83 (IC95% 0.74-0.92) Sarilumab OR 1.08 (IC 95% 0.86-1.36)

	All anti-IL-6 agents							
	No. of events/	total patients	_					
Subgroup	Anti-IL-6	Anti-IL-6 Control		OR (95% CI)				
28-d mortality	28-d mortality							
Respiratory support at randomization								
Oxygen flow rate ≤15 L/min	277/2246	283/1708	0	0.81 (0.67-0.98)				
Noninvasive ventilation	588/2209	544/1655	8	0.83 (0.72-0.96)				
IMV or ECMO	496/1289	305/728	0	0.95 (0.78-1.16)				



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WHO REACT Working Grout

## Anti-IL1

- Anakinra : Pas de nouveauté
- Meta-Analyses

The CORIMUNO-19 Collaborative group\*†

Lancet Respir Med 2021

Effect of anakinra versus usual care in adults in hospital with  $\Re$ 

- 1 185 patients, 9 études
- (8 études observationnelles, 1 essai), mortalité

	Anakinra		Control Weig		Weight		Odds ratio (95% CI)	
	Events	Total	Events	Total				
Balkhair et al (2021) <sup>30</sup>	13	45	11	24	8.0%		0.48 (0.17–1.34)	
Bozzi et al (2021) <sup>25</sup>	9	65	19	55	13.9%	<u> </u>	0.30 (0.12-0.75)	
Cauchois et al (2020) <sup>22</sup>	0	12	1	10	0.9%	• • • • • • • • • • • • • • • • • • •	• 0·07 (0·00-46·88)	
Cavalli et al (2021) <sup>26</sup>	3	62	62	275	17.0%		0.17 (0.05-0.58)	
Huet et al (2020) <sup>23</sup>	7	52	19	44	13.9%	— <u> </u>	0.20 (0.08-0.55)	
Kooistra et al (2020) <sup>28</sup>	4	21	7	39	3.1%	<b>a</b>	1.08 (0.28-4.20)	
Kyriazopoulou et al (2021) <sup>29</sup>	15	130	29	130	20.1%	-0-1	0.45 (0.23-0.90)	
The CORIMUNO-19 Collaborative group (2021) <sup>24</sup>	13	59	13	55	8.2%		0.91 (0.38-2.19)	
Pontali et al (2021) <sup>27</sup>	9	63	19	44	15.0%		0.22 (0.09-0.55)	
Total (95% CI)		509		676	100.0%	$\diamond$	0-37 (0-27-0-51)	
Heterogeneity: $\tau^2$ = 0-2966; $\chi^2$ =11-52, df=8 (p=0-17)	); l²=31%						1 20	





Kyriazopoulou, Lancet Rheum 2021

### En attente de plus de données

COVID-19 and mild-to-moderate pneumonia (CORIMUNO-ANA-1): a randomised controlled trial

## Anti-IL1

- Canakimumab
- RCT, double aveugle, Canada, 454 patients
- Canakimumab dose unique IV + SOC vs SOC + Placebo
- 70% O<sub>2</sub> simple
- Survie sans VM à J29

89% Canakimumab 86% Placebo OR 1.4 (0.8-2.5) A Use of IMV or death





### Inhibiteurs de JAK

- Baricitinib (JAK 1&2)
- COV-BARRIER, RCT, double aveugle, 1 525 patients (1:1)



Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19

• Baricitinib 4mg/j + SOC vs SOC + Placebo, 14j, Aggravation à J28





Kalil, NEJM 2021

## Inhibiteurs de JAK

- Tofacitinib (JAK 1&3)
  - RCT double aveugle (Brésil, 15 sites), 289 patients (1:1)
  - Tofacitinib (10mgx2/j) + SOC vs SOC + Placebo, 14 j, <u>Décès ou défaillance respiratoire à J28</u>
    - 25% pas  $0_2$ , 63%  $O_2$  simple, 13% OHD



Subgroup	No. of Patients	Risk Ratio (95% CI	)
Overall	289	F-	0.63 (0.41-0.97)
Sex			
Male	188	⊢ <b></b>	0.66 (0.34-1.30)
Female	101	⊢ <b></b> (	0.36 (0.13-0.96)
Age			
<u>≤60 yr</u>	171		0.81 (0.37-1.78)
>60 yr	118	F	0.41 (0.18-0.93)
Antiviral therapy		1	
No	251	F₩1	0.46 (0.25-0.85)
Yes	38	⊢►	1.08 (0.28-4.13)
Glucocorticoids			
No	62	►	0.71 (0.20-2.55)
Yes	227	<b>⊢</b>	0.50 (0.27-0.93)
Days since symptom onset			
<8	81		0.55 (0.21-1.44)
8 to 11	100	⊨I	0.86 (0.35-2.07)
>11	106	<b>←</b>	0.27 (0.08-0.92)
0 to 10	183		0.67 (0.35-1.27)
>10	104	<b>←</b>	0.28 (0.08-0.96)
		0.13 0.25 0.50 1.0 2.00 4.00	



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Guimaraes NEJM 2021

Tofacitinib Better Placebo Better

ORIGINAL ARTICLE

Tofacitinib in Patients Hospitalized

with Covid-19 Pneumonia

# Synthèse

- Corticoïdes
  - SOC
  - Posologie, durée, molécules
- Anti-IL6, Anti-JAK
  - En association aux CTC
- Anti-IL1
  - Manque données de qualité



### Perspectives

- Cadre utilisation Anti-IL6, JAK. Comparaison IL-6 vs JAK (+ CTC)
- Molécules inhalées
  - INF-β1-a,
    - Essai petite taille 48 patients vs 50 placebo, 2/3 sous 0<sub>2</sub>, 14j, Amélioration clinique + fréquente (Monk, Lancet Resp Med 2020)
    - Phase 3
- Autres immunomodulateurs
  - Anti GM-CSF (Mavrilimumab) (De Luca, Lancet Rheumatol 2020 ; Cremer Lancet Rheumatol 2021)
  - Inhibiteur du complément
    - Anti-C5a (Vilobelimab) (Vlaar, Lancet Rheumatol 2021)
    - Anti-C5aR1 (Avdoralimab) : résultats négatifs phase 2, Essai Force (Communiqué Presse, Juillet 2021)
  - Antagoniste récepteur bradykinine 2 (van de Veerdonk, JAMA Open Net 2021)

## Conclusions

Attente d'autres molécules antivirales
Utilisation mAbs chez les séronégatifs?

 A associer au traitement immunomodulateur actuel (SOC) qui risque évoluer

### CTC $\rightarrow$ CTC + Anti-IL6/Inhib JAK



Notions de timing administration et sous groupe patients essentielles

### Merci de votre attention



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