Collège National des Cardiologues des Hôpitaux

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WEBINAR « Partage d'expérience du Covid entre la France et le Québec et l'approche du déconfinement »

Mise à jour du traitement contre le coronavirus

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Chair Tele-cardiology Working Group isfteh.org

@alex_mischie

Les trois gros essais en cours pour le traitement de la pandémie COVID19

Essai SOLIDARITY (WHO)

- Soins classiques (bras de contrôle)
- Soins classiques + Remdesivir
- Soins classiques + Lopinavir + Ritonavir
- Soins classiques + Lopinavir + Ritonavir + IFN-β
- Soins classiques + Hydroxychloroquine

Essai DISCOVERY (Pays UE)

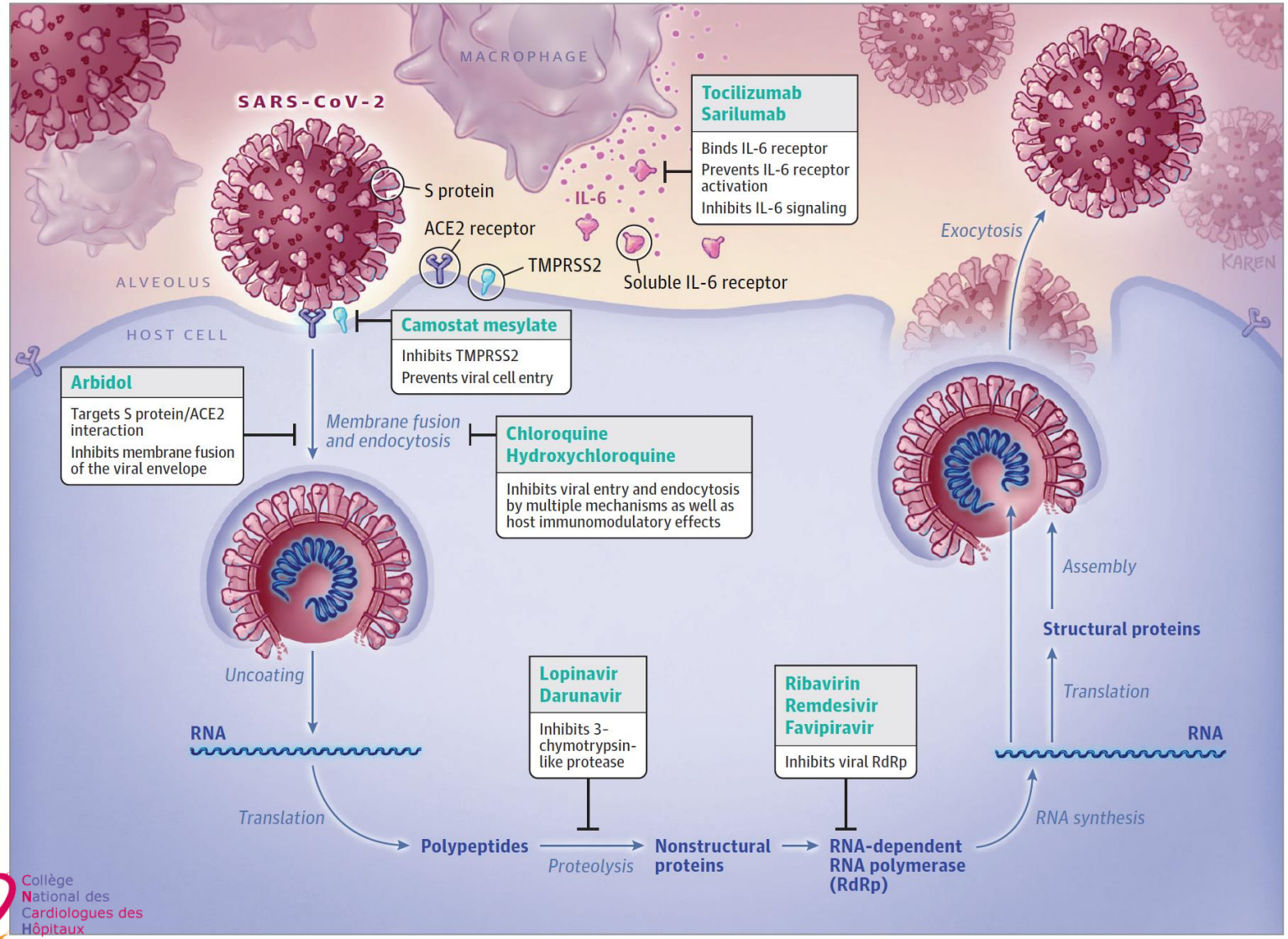
- Soins classiques (bras de contrôle)
- Soins classiques + Remdesivir (dose de charge intraveineuse de 200 mg le premier jour, suivie d'une dose d'entretien intraveineuse de 100 mg une fois par jour pendant la durée de l'hospitalisation jusqu'à une durée totale de 10 jours)
- Soins classiques + Lopinavir + Ritonavir (Lopinavir 400 mg / Ritonavir 100 mg sera administré toutes les 12 h pendant 14 jours sous forme orale ou sous forme de suspension de 5 ml toutes les 12 h pendant 14 jours via une sonde nasogastrique préexistante ou nouvellement placée)
- Soins classiques + Lopinavir + Ritonavir + IFN-β (Lopinavir / Ritonavir comme ci-dessus; L' IFN-β sera administré par voie sous-cutanée à la dose de 44 µg pour un total de 3 doses en 6 jours (jour 1, jour 3, jour 6))
- Soins classiques + Hydroxychloroquine (sera administrée par voie orale sous forme d'une dose de charge de 400 mg deux fois par jour pendant une journée, suivie de 400 mg une fois par jour pendant 9 jours ; la dose de charge d'Hydroxychloroquine à travers une sonde nasogastrique sera augmentée à 600 mg deux fois par jour pendant une journée, suivie d'une dose d'entretien de 400 mg une fois par jour pendant 9 jours)

Essai RECOVERY (UK/NHS)

- Soins classiques (bras de contrôle)
- Soins classiques + Lopinavir + Ritonavir (Lopinavir 400 mg-Ritonavir 100 mg par voie orale (ou sonde nasogastrique) toutes les 12 heures pendant 10 jours ou jusqu'à la sortie)
- Soins classiques + IFN-β1a (solution nébulisée d'IFN-β1a 6MIU (0,5 ml d'une solution contenant 12MIU / ml) une fois par jour pendant 10 jours ou jusqu'à la sortie)
- Soins classiques + corticostéroïde (Dexaméthasone administrée par voie orale ou par voie intraveineuse 6 mg une fois par jour pendant 10 jours ou jusqu'à la sortie. il est permis de basculer entre les deux voies d'administration en fonction des circonstances cliniques)
- Soins classiques + Hydroxychloroquine (administration orale pendant 10 jours au total, comme suit : dose initiale 800 mg, 800 mg à + 6 heures, 400 mg à + 12 heures, 400 mg à + 24 heures, puis 400 mg toutes les 12 heures pendant 9 jours)

Quels médicaments pouvons-nous utiliser contre le COVID19?

Figure. Simplified Representation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Viral Lifecycle and Potential Drug Targets



https://jamanetwork.com/journals/jama/fullarticle/2764727?utm_source=twitter&utm_campaign=content-shareicons&utm_content=article_engagement&utm_medium=social&utm_term=041320&fbclid=IwAR3JvkNvlQ2CjoNmv2vkyyQy7Yf8Q3YY8c10dYJKZ1pbLm14lSK_2XWgIak#.XpTK4k3IJiw.twitter

- Repurposed Drugs (Médicaments réutilisés – indication tt autres maladis)
- Médicaments expérimentaux
- Thérapies Adjuvantes

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Repurposed Drugs (Médicaments réutilisés) : Hydroxychloroquine

Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19

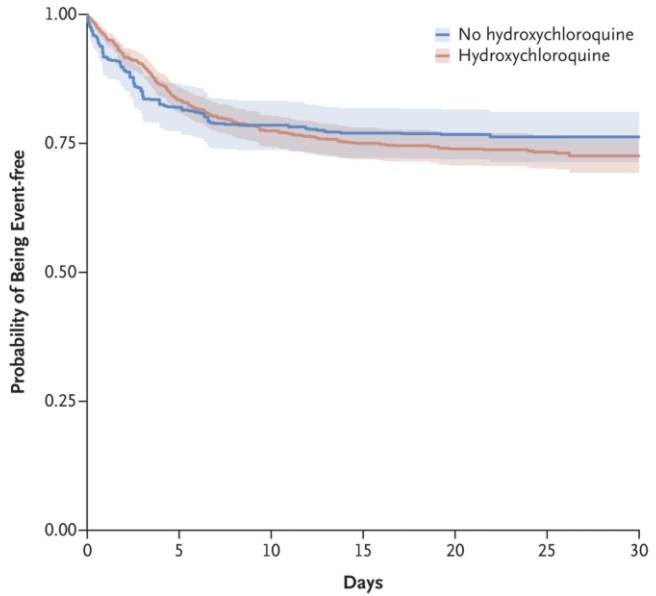
Joshua Geleris, M.D., Yifei Sun, Ph.D., Jonathan Platt, Ph.D., Jason Zucker, M.D., Matthew Baldwin, M.D., George Hripcsak, M.D., Angelena Labella, M.D., Daniel K. Manson, M.D., Christine Kubin, Pharm.D., R. Graham Barr, M.D., Dr.P.H., Magdalena E. Sobieszczyk, M.D., M.P.H., and Neil W. Schluger, M.D.

RESULTS

Of 1446 consecutive patients, 70 patients were intubated, died, or discharged within 24 hours after presentation and were excluded from the analysis. Of the remaining 1376 patients, during a median follow-up of 22.5 days, 811 (58.9%) received hydroxychloroquine (600 mg twice on day 1, then 400 mg daily for a median of 5 days); 45.8% of the patients were treated within 24 hours after presentation to the emergency department, and 85.9% within 48 hours. Hydroxychloroquine-treated patients were more severely ill at baseline than those who did not receive hydroxychloroquine (median ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen, 223 vs. 360). Overall, 346 patients (25.1%) had a primary end-point event (180 patients were intubated, of whom 66 subsequently died, and 166 died without intubation). In the main analysis, there was no significant association between hydroxychloroquine use and intubation or death (hazard ratio, 1.04, 95% confidence interval, 0.82 to 1.32). Results were similar in multiple sensitivity analyses.

CONCLUSIONS

In this observational study involving patients with Covid-19 who had been admitted to the hospital, hydroxychloroquine administration was not associated with either a greatly lowered or an increased risk of the composite end point of intubation or death. Randomized, controlled trials of hydroxychloroquine in patients with Covid-19 are needed. (Funded by the National Institutes of Health.)



The NEW ENGLAND JOURNAL of MEDICINE

Publié 7 Mai

Collège National des Cardiologues des Hôpitaux

Repurposed Drugs (Médicaments réutilisés): Lopinavir-Ritonavir vs. soins classiques (essai neutre)

RESULTS

A total of 199 patients with laboratory-confirmed SARS-CoV-2 infection underwent randomization; 99 were assigned to the lopinavir–ritonavir group, and 100 to the standard-care group. Treatment with lopinavir–ritonavir was not associated with a difference from standard care in the time to clinical improvement (hazard ratio for clinical improvement, 1.31; 95% confidence interval [CI], 0.95 to 1.80). Mortality at 28 days was similar in the lopinavir–ritonavir group and the standard-care group (19.2% vs. 25.0%; difference, –5.8 percentage points; 95% CI, –17.3 to 5.7). The percentages of patients with detectable viral RNA at various time points were similar. In a modified intention-to-treat analysis, lopinavir–ritonavir led to a median time to clinical improvement that was shorter by 1 day than that observed with standard care (hazard ratio, 1.39; 95% CI, 1.00 to 1.91). Gastrointestinal adverse events were more common in the lopinavir–ritonavir group, but serious adverse events were more common in the standard-care group. Lopinavir–ritonavir treatment was stopped early in 13 patients (13.8%) because of adverse events.

CONCLUSIONS

In hospitalized adult patients with severe Covid-19, no benefit was observed with lopinavir–ritonavir treatment beyond standard care. Future trials in patients with severe illness may help to confirm or exclude the possibility of a treatment benefit. (Funded by Major Projects of National Science and Technology on New Drug Creation and Development and others; Chinese Clinical Trial Register number, ChiCTR2000029308.)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

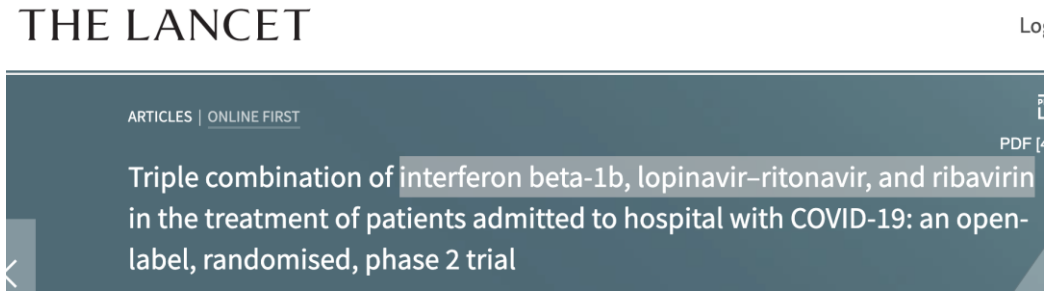
A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19

B. Cao, Y. Wang, D. Wen, W. Liu, Jingli Wang, G. Fan, L. Ruan, B. Song, Y. Cai, M. Wei, X. Li, J. Xia, N. Chen, J. Xiang, T. Yu, T. Bai, X. Xie, L. Zhang, C. Li, Y. Yuan, H. Chen, Huadong Li, H. Huang, S. Tu, F. Gong, Y. Liu, Y. Wei, C. Dong, F. Zhou, X. Gu, J. Xu, Z. Liu, Y. Zhang, Hui Li, L. Shang, K. Wang, K. Li, X. Zhou, X. Dong, Z. Qu, S. Lu, X. Hu, S. Ruan, S. Luo, J. Wu, L. Peng, F. Cheng, L. Pan, J. Zou, C. Jia, Juan Wang, X. Liu, S. Wang, X. Wu, Q. Ge, J. He, H. Zhan, F. Qiu, L. Guo, C. Huang, T. Jaki, F.G. Hayden, P.W. Horby, D. Zhang, and C. Wang

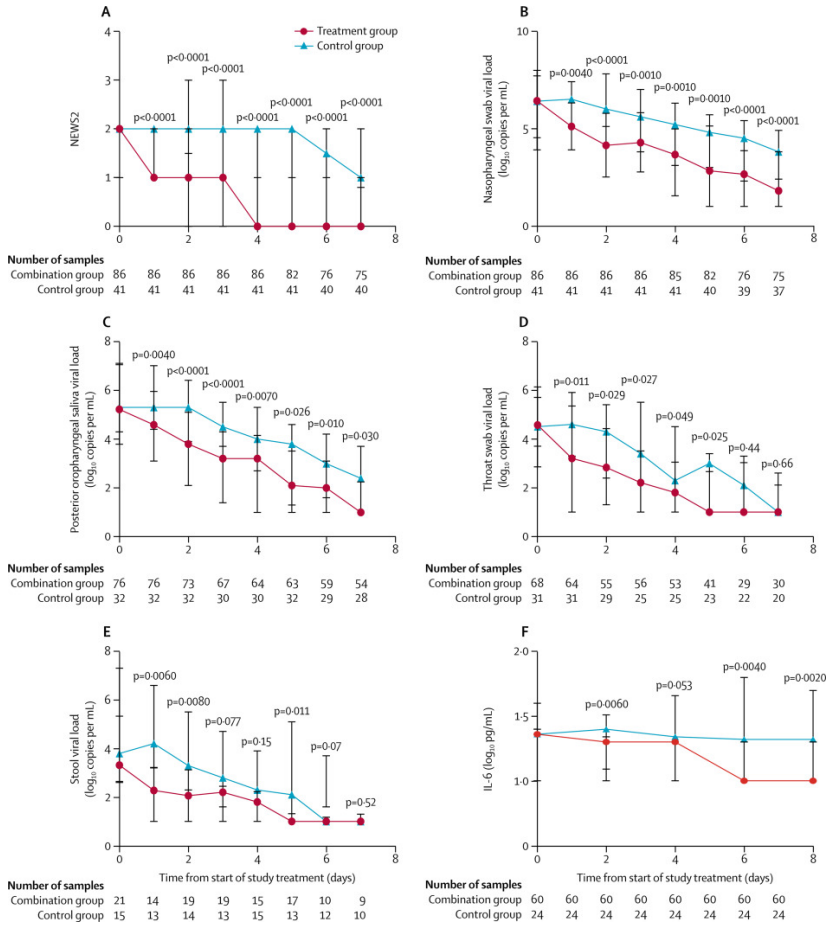
https://www.nejm.org/doi/pdf/10.1056/NEJMoa2001282?articleTools=true

Publié 18 Mars

Repurposed Drugs (Médicaments réutilisés): IFB1b+Lopinavir-Ritonavir+Ribavirin vs. Lopinavir-Ritonavir (essai positif)



La triple thérapie antivirale précoce était sûre et supérieure au lopinavir – ritonavir seul pour atténuer les symptômes et raccourcir la durée de l'excrétion virale et du séjour à l'hôpital chez les patients atteints de COVID-19 - maladie légère à modérée.



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https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31042-4/fulltext?fbclid=IwAR2QjTI_KZfy-uUowGily5klRkZImHWARRXCKDGLmHiRfpdzHF3n0gTzQBQ

Publié 8 Mai

Médicaments expérimentaux:
Redemsivir#1 vs. placebo (2 essais neutres)

THE LANCET

ARTICLES | ONLINE FIRST

Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial

Yeming Wang, MD † • Dingyu Zhang, MD † • Prof Guanhua Du, PhD † • Prof Ronghui Du, MD † • Prof Jianping Zhao, MD † • Prof Yang Jin, MD † • et al. Show all authors • Show footnotes

Published: April 29, 2020 • DOI: https://doi.org/10.1016/S0140-6736(20)31022-9 • Check for updates

Findings Between Feb 6, 2020, and March 12, 2020, 237 patients were enrolled and randomly assigned to a treatment group (158 to remdesivir and 79 to placebo); one patient in the placebo group who withdrew after randomisation was not included in the ITT population. Remdesivir use was not associated with a difference in time to clinical improvement (hazard ratio 1·23 [95% CI 0·87–1·75]). Although not statistically significant, patients receiving remdesivir had a numerically faster time to clinical improvement than those receiving placebo among patients with symptom duration of 10 days or less (hazard ratio 1·52 [0·95–2·43]). Adverse events were reported in 102 (66%) of 155 remdesivir recipients versus 50 (64%) of 78 placebo recipients. Remdesivir was stopped early because of adverse events in 18 (12%) patients versus four (5%) patients who stopped placebo early.

Interpretation In this study of adult patients admitted to hospital for severe COVID-19, remdesivir was not associated with statistically significant clinical benefits. However, the numerical reduction in time to clinical improvement in those treated earlier requires confirmation in larger studies.

Publié 29 Avril

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Compassionate Use of Remdesivir for Patients with Severe Covid-19

Patients were treated with compassionate-use remdesivir. Clinical improvement was observed in 36 of 53 patients (68%).

Data interpretation was very challenging because of the limitations of the study

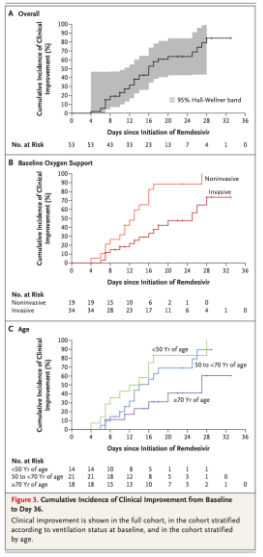

Figure 3. Cumulative Incidence of Clinical Improvement from Baseline to Day 36.
Clinical improvement is shown in the full cohort, in the cohort stratified according to ventilation status at baseline, and in the cohort stratified by age.

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Médicaments expérimentaux: Redemsivir#2 vs placebo (essai positif)

Adaptive COVID-19 Treatment Trial (ACTT)

adaptive, randomized, double-blind, placebo-controlled trial conducted in up to approximately 100 sites globally

Le critère d'analyse principal est le temps récupération au 29éme jour. Un critère de jugement secondaire clé évalue les améliorations liées au traitement sur une échelle de 8 points au 15éme jour.

Une analyse intermédiaire a montré que le remdesivir était meilleur que le placebo pour le critère d'évaluation principal qui était le temps de récupération.

Les patients qui ont reçu du remdesivir ont eu un temps de récupération 31% plus rapide que ceux qui ont reçu un placebo (p <0,001) (11 jours contre 15).

Il y a aussi un bénéfice de survie, avec un taux de mortalité de 8,0% pour le groupe recevant du remdesivir contre 11,6% pour le groupe placebo (p = 0,059).

Dose: 200 mg of Remdesivir administered intravenously on Day 1, followed by a 100 mg once-daily maintenance dose of Remdesivir while hospitalized for up to a 10 days total course.

Study Design

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	800 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Double (Participant, Investigator)
Primary Purpose:	Treatment
Official Title:	A Multicenter, Adaptive, Randomized Hospitalized Adults
Actual Study Start Date :	February 21, 2020
Estimated Primary Completion Date :	April 1, 2023
Estimated Study Completion Date :	April 1, 2023

https://clinicaltrials.gov/ct2/show/NCT04280705

https://www.niaid.nih.gov/news-events/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19

FDA / 1er Mai, 2020

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Thérapies Adjuvantes:
Tocilizumab vs. soins classiques (essai positif)

anticorps monoclonal bloquant le récepteur de la cytokine interleukine-6, utilisé cliniquement notamment dans le traitement de la polyarthrite rhumatoïde

Dose: Tocilizumab 8mg/kg D1 and if no response (no decrease of oxygen requirement) a second injection at D3.

Essai CORIMUNO-TOCI (France)

multicenter open-label randomized controlled trial

Inclue les patients hospitalisés pour une pneumonie modérée ou sévère COVID-19 ne nécessitant pas de soins intensifs à l'admission.

Au total, 129 patients ont été randomisés: 65 selon soins classiques + tocilizumab et 64 selon soins classiques seuls.

Une analyse intermédiaire a montré qu'une proportion significative de patients avaient atteint le résultat principal dans le bras tocilizumab (besoin de ventilation ou décès au jour 14).

Study Design

Study Type :	Interventional (Clinical Trial)
Actual Enrollment :	228 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Cohort Multiple Randomized Controlled Trials CORIMUNO-19 - TOCI (CORIMUNO-TOCI)
Actual Study Start Date :	March 30, 2020
Estimated Primary Completion Date :	March 31, 2021
Estimated Study Completion Date :	December 31, 2021

https://clinicaltrials.gov/ct2/show/NCT04331808

https://www.aphp.fr/contenu/tocilizumab-improves-significantly-clinical-outcomes-patients-moderate-or-severe-covid-19

Publié 27 Avril

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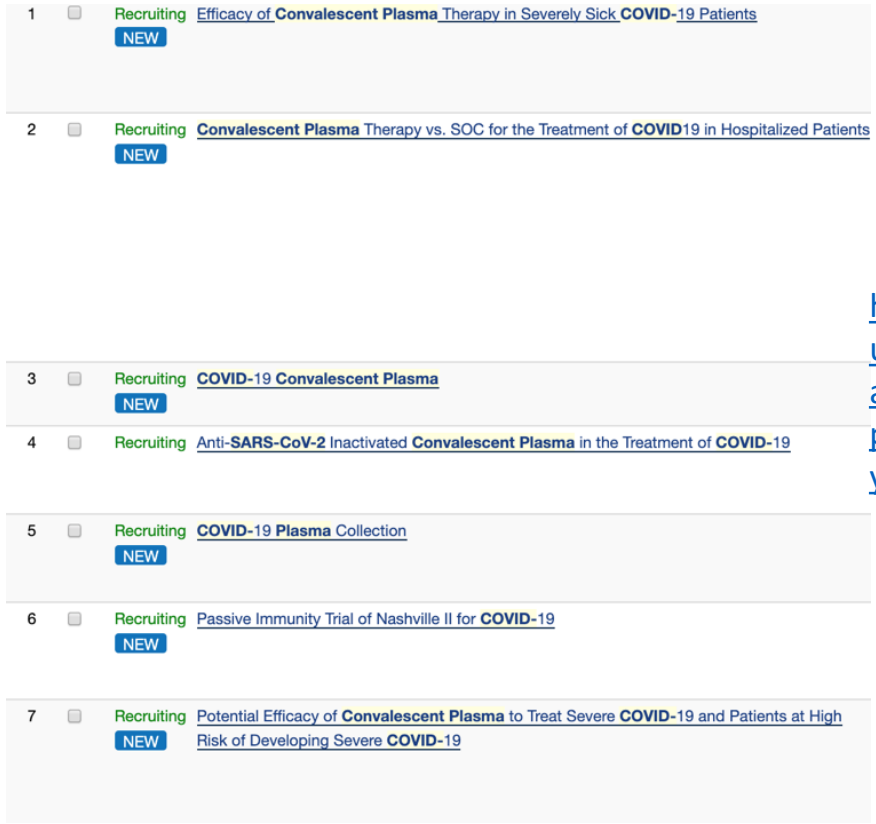
Thérapies Adjuvantes:
Les Immunoglobulines (essais en cours)

utilisation de plasma convalescent ou d'immunoglobulines hyperimmunes contenant des anticorps anti-virus COVID19

En théorie, cette thérapie est tés efficace dans les 7 à 10 premiers jours de l'infection, lorsque la virémie est à son apogée et que la réponse immunitaire primaire ne s'est pas encore produite.

La FDA a émis des recommandations aux fournisseurs de soins de santé sur l'administration et l'étude du plasma de convalescence prélevé sur des individus qui se sont gueris de COVID-19.

https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma



7 essais qui recrutent des patients sur clinicaltrials.org

https://clinicaltrials.gov/ct2/results?term=Convalescent+Plasma+Transfusion+covid&Search=Apply&recrs=a&age_v=&gndr=&type=&rslt=

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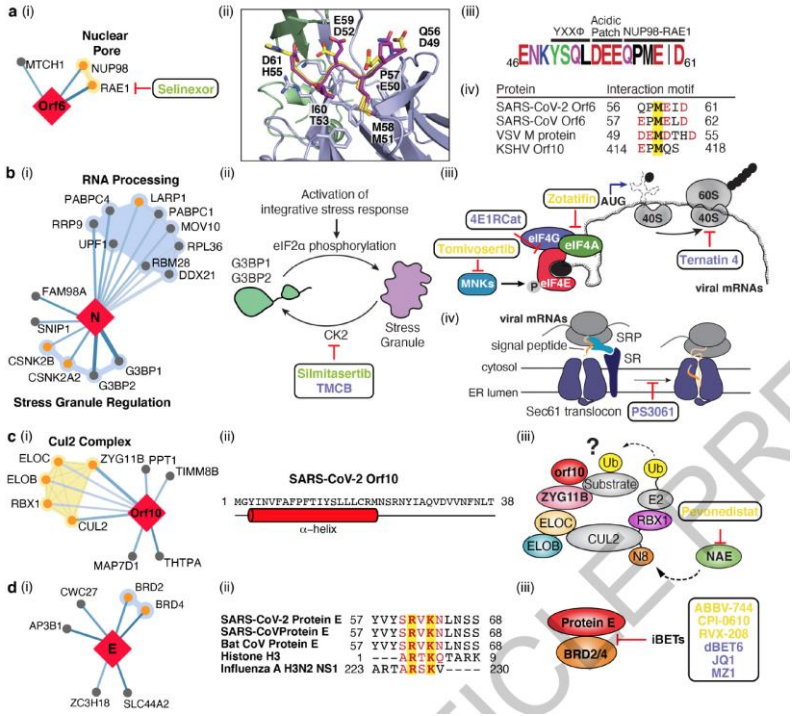
Publié 24 Mars

Une nouvelle carte d'interaction des protéines humains-protéines COVID19 révélant des cibles pour la réutilisation de médicaments

Dans cet étude, les chercheurs américains et français ont identifié 66 protéines humaines ciblées par 69 médicaments (médicaments existants approuvés par la FDA, médicaments en essais cliniques et / ou des médicaments expérimentaux).

nature

Article | Published: 30 April 2020



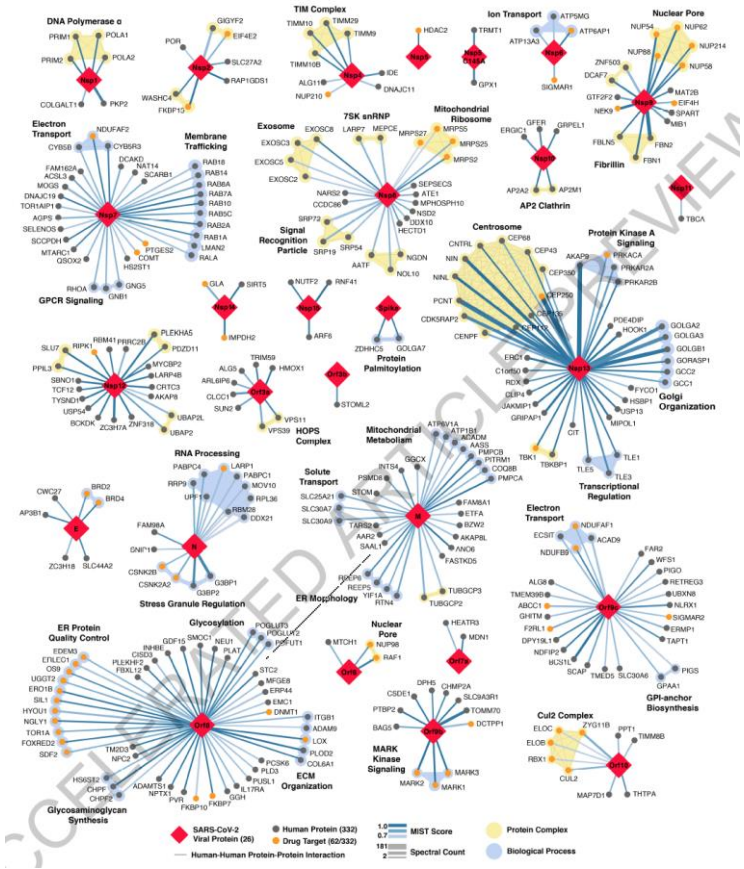
SARS-CoV-2 interactome reveals novel aspects of SARS-CoV-2 biology and pharmacological targets

Collège National des Cardiologues des Hôpitaux

https://www.nature.com/articles/s41586-020-2286-9

Publié 30 Avril

Une nouvelle carte d'interaction des protéines humains-protéines COVID19 révélant des cibles pour la réutilisation de médicaments



Les classes de molécules suivantes ont été efficaces pour réduire l'infectiosité virale:

Protein biogenesis inhibitors:

- Totatifin (elongation factor-4A (eIF4A) inhibitor), is currently in a phase I clinical trial for cancer therapy
- Ternatin-4 (eEF1A inhibitor).
- Plitidepsin (eEF1A inhibitor) is used clinically in multiple myeloma patients and is currently under consideration by the Spanish Medicines Agency for a Phase II trial in hospitalized COVID-19 patients.
- PS3061

Ligands of the Sigma1 and Sigma2 receptors (perturb the virus through different mechanisms than the translation inhibitors, potentially including cell stress response):

- Haloperidol inhibits the dopamine D2 and histamine H1 receptors
- PD-144418
- Hydroxychloroquine
- PB28 (~20 times more potent than hydroxychloroquine)

Sigma R1/ R2 active drugs:

- Clemastine and Cloperastine (antihistamines)
- Progesterone (this could explain why men appear to be more susceptible to COVID-19 and more often suffer severe complications)
- Siramesine

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https://www.nature.com/articles/s41586-020-2286-9

Vaccins - essais en cours

Astra Zeneca - ChAdOx1 nCoV-19

https://clinicaltrials.gov/ct2/show/NCT04324606?term=ChAdOx1+nCoV-19&draw=2&rank=1

Study Design

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	1112 participants
Allocation:	Randomized
Intervention Model:	Sequential Assignment
Masking:	Single (Participant)
Primary Purpose:	Treatment
Official Title:	A Phase I/II Study to Determine Efficacy, Healthy Adult Volunteers
Estimated Study Start Date :	April 2020
Estimated Primary Completion Date :	May 2021
Estimated Study Completion Date :	May 2021

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Vaccins - essais en cours

Astra Zeneca - ChAdOx1 nCoV-19

https://clinicaltrials.gov/ct2/show/NCT04324606?term=ChAdOx1+nCoV-19&draw=2&rank=1

Moderna Inc - mRNA-1273

https://clinicaltrials.gov/ct2/show/NCT04283461?term=mrna&cond=Coronavirus&draw=2&rank=1

Study Design

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	105 participants
Allocation:	Non-Randomized
Intervention Model:	Sequential Assignment
Masking:	None (Open Label)
Primary Purpose:	Prevention
Official Title:	Phase I, Open-Label, Dose-Ranging
Actual Study Start Date :	March 16, 2020
Estimated Primary Completion Date :	September 20, 2021
Estimated Study Completion Date :	September 20, 2021

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Vaccins - essais en cours

Astra Zeneca - ChAdOx1 nCoV-19

https://clinicaltrials.gov/ct2/show/NCT04324606?term=ChAdOx1+nCoV-19&draw=2&rank=1

Moderna Inc - mRNA-1273

https://clinicaltrials.gov/ct2/show/NCT04283461?term=mrna&cond=Coronavirus&draw=2&rank=1

Biontech SE & Pfizer - BNT162abc

https://clinicaltrials.gov/ct2/show/NCT04368728?term=vaccine+covid&recrs=a&draw=2&rank=9

Study Design

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	7600 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Triple (Participant, Care Provider, Investigator)
Primary Purpose:	Prevention
Official Title:	A PHASE 1/2, PLACEBO-CONTROLLED, RANDOMIZED, IMMUNOGENICITY, AND POTENTIAL EFFICACY OF **SAR**
Actual Study Start Date :	April 29, 2020
Estimated Primary Completion Date :	January 27, 2023
Estimated Study Completion Date :	January 27, 2023

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Vaccins - essais en cours

Astra Zeneca - ChAdOx1 nCoV-19

https://clinicaltrials.gov/ct2/show/NCT04324606?term=ChAdOx1+nCoV-19&draw=2&rank=1

Moderna Inc - mRNA-1273

https://clinicaltrials.gov/ct2/show/NCT04283461?term=mrna&cond=Coronavirus&draw=2&rank=1

Biontech SE & Pfizer - BNT162abc

https://clinicaltrials.gov/ct2/show/NCT04368728?term=vaccine+covid&recrs=a&draw=2&rank=9

Sinovac Biotech Co

https://clinicaltrials.gov/ct2/show/NCT04352608?term=vaccine+covid&recrs=a&draw=2&rank=7

Study Design

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	744 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Quadruple (Participant, Care Provider, Investigator, Ou
Primary Purpose:	Prevention
Official Title:	A Randomized, Double-Blinded, Placebo-Controlled, I
	Vaccine in Healthy Adults Aged 18~59 Years
Actual Study Start Date :	April 16, 2020
Estimated Primary Completion Date :	August 13, 2020
Estimated Study Completion Date :	December 13, 2020

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Vaccines – résultats dans 3-6 mois/1 an

Astra Zeneca - ChAdOx1 nCoV-19

https://clinicaltrials.gov/ct2/show/NCT04324606?term=ChAdOx1+nCoV-19&draw=2&rank=1

Moderna Inc - mRNA-1273

https://clinicaltrials.gov/ct2/show/NCT04283461?term=mrna&cond=Coronavirus&draw=2&rank=1

Biontech SE & Pfizer - BNT162abc

https://clinicaltrials.gov/ct2/show/NCT04368728?term=vaccine+covid&recrs=a&draw=2&rank=9

Sinovac Biotech Co

https://clinicaltrials.gov/ct2/show/NCT04352608?term=vaccine+covid&recrs=a&draw=2&rank=7

Shenzhen Medical Institute - LV-SMENP-DC

https://clinicaltrials.gov/ct2/show/NCT04276896?term=vaccine+covid&recrs=a&draw=2&rank=3

Shenzhen Medical Institute - LV-SMENP-DC

https://clinicaltrials.gov/ct2/show/NCT04299724?term=vaccine+covid&recrs=a&draw=2&rank=1

Study Design

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	100 participants
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Phase I/II Multicenter Trial of Lentiviral
Estimated Study Start Date :	March 24, 2020
Estimated Primary Completion Date :	July 31, 2023
Estimated Study Completion Date :	December 31, 2024

Study Design

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	100 participants
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Safety and Immunity Evaluation
Actual Study Start Date :	February 15, 2020
Estimated Primary Completion Date :	July 31, 2023
Estimated Study Completion Date :	December 31, 2024

Vaccines BCG – plusieurs essais en cours

THE LANCET

Considering BCG vaccination to reduce the impact of COVID-19

« Des essais contrôlés randomisés sont en cours aux Pays-Bas et en Australie pour évaluer si le BCG-danois réduit l'incidence et la gravité du COVID-19 chez les travailleurs de la santé »

NIH U.S. National Library of Medicine
ClinicalTrials.gov

		recruiting NEW	Limitation, and Immunoglobulin Enhancement	• Therapeutic **Vaccine** • **BCG** • (and 2 more...)	• Biological: Placebo	Campinas, SP, Brazil
4	☐	Not yet recruiting NEW	Performance Evaluation of **BCG Vaccination** in Healthcare Personnel to Reduce the Severity of **SARS-COV-2** Infection	• **COVID**-19	• Biological: **vaccine BCG** • Other: Placebo	• Program for Research and Control in Tropical Diseases - PECET Medellín, Antioquia, Colombia
5	☐	Recruiting	Reducing Health Care Workers Absenteeism in **Covid**-19 Pandemic Through **BCG Vaccine**	• **COVID**-19	• Drug: **BCG Vaccine** • Drug: Placebo	• Jeroen Bosch ziekenhuis Den Bosch, Brabant, Netherlands • Canisius Wilhelmina Ziekenhuis Nijmegen, Gelderland, Netherlands • Radboud UMC Nijmegen, Gelderland, Netherlands • (and 6 more...)
6	☐	Recruiting NEW	**BCG Vaccine** for Health Care Workers as Defense Against **COVID** 19	• Coronavirus • Coronavirus Infection • Coronavirus as the Cause of Diseases Classified Elsewhere	• Biological: **BCG Vaccine** • Biological: Placebo **Vaccine**	• Cedars-Sinai Medical Center Los Angeles, California, United States • Harvard T.H. Chan School of Public Health Boston, Massachusetts, United States • Texas A&M Family Care Clinic Bryan, Texas, United States • (and 4 more...)
7	☐	Not yet recruiting NEW	Using **BCG Vaccine** to Protect Health Care Workers in the **COVID**-19 Pandemic	• **COVID**-19 • Non-specific Effects of **Vaccines** • Morbidity • (and 2 more...)	• Biological: **BCG**-Denmark • Biological: Saline	
8	☐	Recruiting NEW	Outcome of **COVID**-19 Cases Based on Tuberculin Test: Can Previous **BCG** Alter the Prognosis?	• **COVID**-19 • **BCG Vaccination**	• Diagnostic Test: Tuberculin test	• AssiutU Assiut, Egypt

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