

Prévention du Covid-19 hors vaccins

Pr Elisabeth Botelho-Nevers

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Inserm CIC 1408- Axe Vaccinologie, I-Reivac, Covireivac
Team GIMAP, CIRI, Inserm, U1111, CNRS, UMR530





Chaire Prévention, Vaccination, Contrôle de l'Infection PRESAGE

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

Intervenant : Nom/Prénom **Elisabeth BOTELHO-NEVERS**

Titre : Intitulé de l'intervention **PREVENTION du COVID-19 hors vaccins**

 L'orateur ne souhaite pas répondre

-  Consultant ou membre d'un conseil scientifique OUI NON
 -  Conférencier ou auteur/rédacteur rémunéré d'articles ou documents OUI NON
 -  Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations OUI NON
 -  Investigateur principal d'une recherche ou d'une étude clinique (CIC) OUI NON
- (AZ, Janssen)

PI de Covidaxis PHRC 2020,

Avec les vaccins, stratégie encore utile?

- **OUI!**
- **Non réponse/mauvaise réponse à la vaccination**
- **Disponibilité des vaccins**
- **Variants...**

COVID-19 prophylaxis: 27059 citations pubmed!

Jusqu'en Décembre 2020

Clinical Microbiology and Infection 27 (2021) 532–537

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

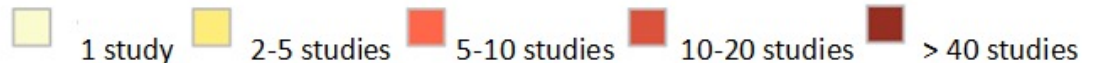
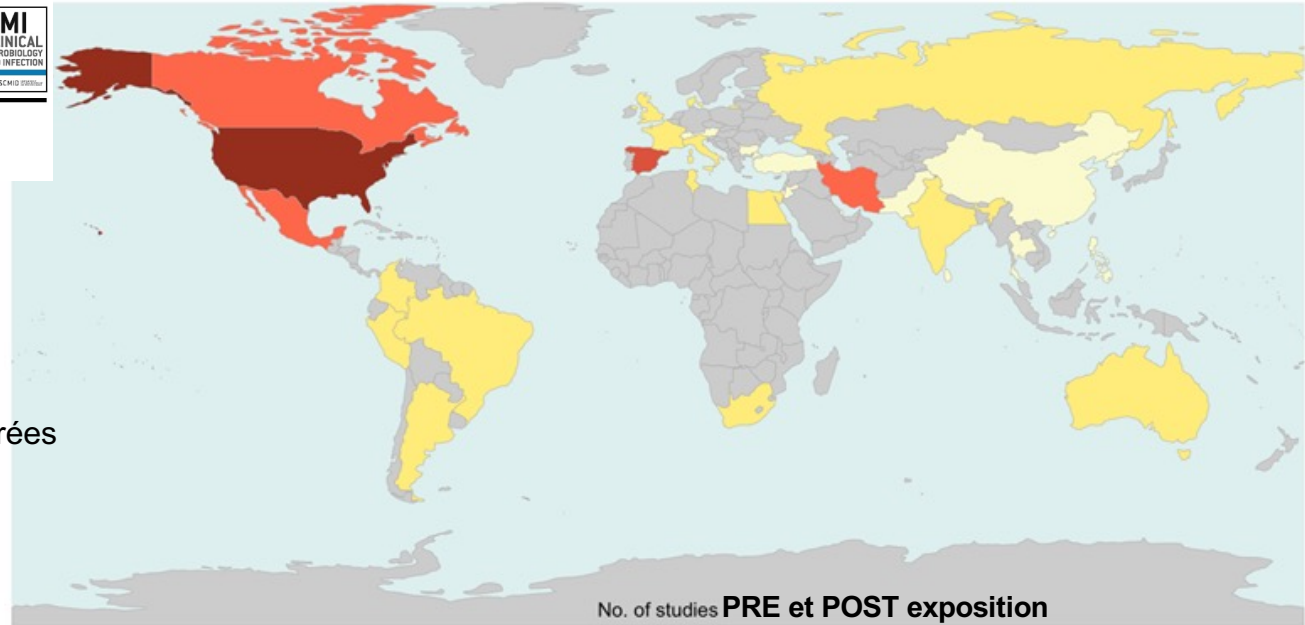


Systematic review

Prophylaxis for COVID-19: a systematic review

Mikaela Smit ^{1,3,*}, Annalisa Marinosci ^{1,1}, Thomas Agoritsas ^{2,3,4}, Alexandra Calmy ^{1,3}

COVID19 prophylaxis
Clinicaltrials.gov 1052 études enregistrées



La 1^{ère}: Hydroxychloroquine

Summary of RCT results of prophylactic candidates against COVID-19 and/or SARS-CoV-2

Study	P(r)EP type	Intervention	Control	Target population	Intention to treat	Sample size	Study conclusions
Abella [27]	PrEP	HCQ (600 mg daily, 8 weeks)	Placebo	HCW	HCQ 4/64, 6.3% vs control 4/61, 6.6% (p > 0.99)	Total: 132 HCQ: 66 Control: 66	No observed effect
Barnabas [28]	PEP	HCQ (400 mg daily; 3 days and 200 mg daily; 11 days)	Ascorbic acid (500 mg daily; 250 mg daily)	Contacts	HR = 1.1 (95% CI 0.73–1.66, p > 0.20)	Total: 671 HCQ: 337 Control: 334	No observed effect
Boulware [29]	PEP	HCQ (800 mg once; 600 mg in 6–8 hours, 600 mg for 4 days)	Placebo	Household contacts; HCW	HCQ 49/414, 11.8% vs control 58/407, 14.3% (p 0.35)	Total: 821 HCQ: 414; Control: 407	No observed effect
Mitja [32] ^a	PEP	HCQ (800 mg once; 400 mg daily for 6 days)	No intervention	Contacts	Risk ratio = 0.89 (95% CI 0.54–1.46)	Total: 2314 HCQ: 1116 Control: 1198	No observed effect
Rajasingham [30]	PrEP	HCQ (400 mg twice in 6–8 hours; 400 mg once weekly for 12 weeks or 400 mg twice weekly for 12 weeks)	Placebo	HCW	Once weekly: HR = 0.72 (95% CI 0.44–1.16; p 0.18) Twice weekly: HR = 0.74 (95% CI 0.46–1.19; p 0.22)	Total: 1483 HCQ once weekly: 494 HCQ twice weekly: 495 Control: 494	No observed effect

Abbreviation: CI, confidence intervals; COVID-19, coronavirus disease 19; HCQ, hydroxychloroquine; HCW, healthcare workers; PEP, postexposure prophylaxis; PrEP, pre-exposure prophylaxis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VH-Fc, heavy variable domain fragment crystallization region.

** Studies identified post database search.

^a Studies identified through medRxiv.

Hydroxychloroquine en PRE exposition

Acceptability of a COVID-19 pre-exposure prophylaxis trial with hydroxychloroquine in French healthcare workers during the first wave of COVID-19 pandemic

Amandine Gagneux-Brunon^{1,2}, Clémentine Schilte³, Arnaud Garcin⁴, Nathalie Jolly³, Muriel Vray⁵, Laura Schaeffer⁵, Xavier Duval⁶, Bruno Hoen⁷ and Elisabeth Botelho-Nevers^{1,2*}

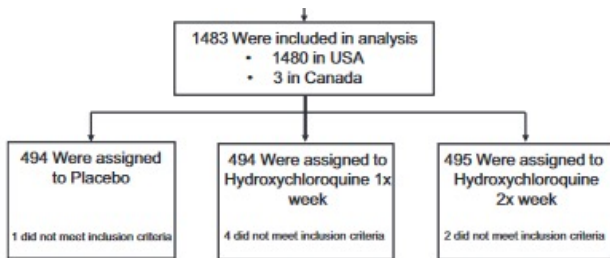


- 695 répondants, 79,8% déclaraient être prêts à participer à l'essai
- 342 répondants prêts à participer sur le CHU de Saint-Etienne, 91 (27%) effectivement inclus

Hydroxychloroquine as Pre-exposure Prophylaxis for Coronavirus Disease 2019 (COVID-19) in Healthcare Workers: A Randomized Trial

Radha Rajasingham,^{1,2} Ananta S. Bangdiwala,¹ Melanie R. Nicol,¹ Caleb P. Skipper,¹ Katelyn A. Pastick,^{1,2} Margaret L. Axelrod,² Matthew F. Pullen,¹ Alanna A. Nascene,¹ Darlisha A. Williams,¹ Nicole W. Engen,¹ Elizabeth C. Okafor,¹ Brian L. Rini,¹ Ingrid A. Mayer,² Emily G. McDonald,² Todd C. Lee,³ Peter Li,⁴ Lauren J. MacKenzie,⁵ Justin M. Balko,² Stephen J. Dunlop,^{1,6} Katherine H. Hullsiek,¹ David R. Boulware,^{1,2} and Sarah M. Lofgren^{1,4}; on behalf of the COVID PREP team

- Randomisation 2:2:1:1 .HCQ 800mg dose de charge puis 400 mg par semaine ou 400mg 2 fois par semaine et leur matching a placebo.



Outcome	Placebo		Hydroxychloroquine Once Weekly			Hydroxychloroquine Twice Weekly		
	No. of Infections (%)	Event Rate per Person-year (95% CI)	No. of Infections (%)	Event Rate per Person-year (95% CI)	Hazard Ratio (95% CI)	No. of Infections (%)	Event Rate per Person-year (95% CI)	Hazard Ratio (95% CI)
PCR positive or probable COVID-19	39 (7.9)	.38 (.26–.50)	29 (5.9)	.27 (.17–.37)	.72 (.44–1.16)	29 (5.9)	.28 (.18–.38)	.74 (.46–1.19)
PCR confirmed COVID-19	6 (1.2)	.06 (.01–.10)	4 (0.8)	.04 (.00–.07)	.65 (.18–2.32)	7 (1.4)	.07 (.02–.12)	1.18 (.40–3.51)
COVID-19 compatible with symptoms	38 (7.7)	.38 (.26–.49)	29 (5.9)	.28 (.18–.38)	.73 (.45–1.19)	28 (5.7)	.28 (.17–.38)	.74 (.45–1.20)

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction.



Hydroxychloroquine en PRE exposition

JAMA Internal Medicine | Original Investigation

Efficacy and Safety of Hydroxychloroquine vs Placebo for Pre-exposure SARS-CoV-2 Prophylaxis Among Health Care Workers: A Randomized Clinical Trial

Benjamin S. Abella, MD, MPH; Eliana L. Jolkovsky, BA; Barbara T. Biney, MPH; Julie E. Uspal, MD; Matthew C. Hyman, MD, PhD; Ian Frank, MD; Scott E. Hensley, PhD; Saar Gill, MD, PhD; Dan T. Vogl, MD, MSCE; Ivan Maillard, MD, PhD; Daria V. Babushok, MD; Alexander C. Huang, MD, PhD; Sunita D. Nasta, MD; Jennifer C. Walsh; E. Paul Wiletyo, PhD; Phyllis A. Gimotty, PhD; Michael C. Milone, MD, PhD; Ravi K. Amaravadi, MD; and the Prevention and Treatment of COVID-19 With Hydroxychloroquine (PATCH) Investigators

- 600mg HCQ/j vs matching placebo 8 semaines
- 132/200, 125 inclus dans l'analyse
- 4 of 64 [6.3%] vs 4 of 61 [6.6%]; $P > .99$.

Certains considèrent Utilité dans des pays avec moins de moyens (EPI...), taux d'incidence plus élevés....????
Souci: Inde l'a recommandé sans aucune preuve, donc pas de RCT

Juin 2021...

Hydroxychloroquine for SARS CoV2 Prophylaxis in Healthcare Workers – A Multicentric Cohort Study
Assessing Effectiveness and Safety

Badyal Dinesh¹, Chandu Sujith J², Chugh Preeta Kaur³, Faruqui Atiya⁴, Gupta YK⁵, Hazra Avijit⁶, Kamat Sandhya⁷, Kamboj VP⁵, Kaul Rajani⁸, Kshirsagar Nilima⁹, Maulik Subir¹⁰, Medhi Bikash¹¹, Menon Geetha¹², Ranjalkar Jaya², Rao Vishnu¹³, Shetty Yashashri⁷, Tripathi Raakhi⁷, Xavier Denis⁴

Journal of the association of the physicians of India (pas référencé Pubmed)



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

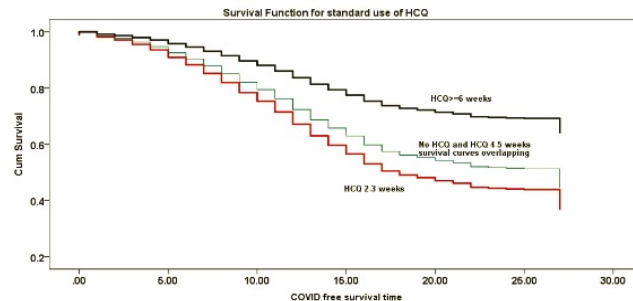


Fig. 1: Survival plots for COVID-positivity, stratified by pattern of HCQ use after adjustment for other covariates

12000 répondants
Questionnaire online!!!!
Analyse sur 2700 questionnaires??!

Hydroxychloroquine en PRE exposition

PAS d'efficacité démontrée

Beaucoup d'argent public, d'énergie et de temps perdu

Pas de collaboration nationale ou internationale

Des schémas trop hétérogènes

Des critères de jugement parfois trop « mous »

Des problèmes de méthodologies

Hydroxychloroquine en POST exposition

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 6, 2020

VOL. 383 NO. 6

A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19

D.R. Boulware, M.F. Pullen, A.S. Bangdiwala, K.A. Pastick, S.M. Lofgren, E.C. Okafor, C.P. Skipper, A.A. Nascene, M.R. Nicol, M. Abassi, N.W. Engen, M.P. Cheng, D. LaBar, S.A. Lothar, L.J. MacKenzie, G. Drobot, N. Marten, R. Zarychanski, L.E. Kelly, I.S. Schwartz, E.G. McDonald, R. Rajasingham, T.C. Lee, and K.H. Hullsiek

- Essai dématérialisé+++ : rend possible la faisabilité
- 4 jours post exposition d'un cas index confirmé
- 800 mg HCQ suivi 600 mg 6-8 h plus tard et 600 mg/j pendant 4j
- Endpoint COVID-19 confirmé ou des symptômes COVID à 14j

- 821 participants (414 HCQ vs 407 placebo)

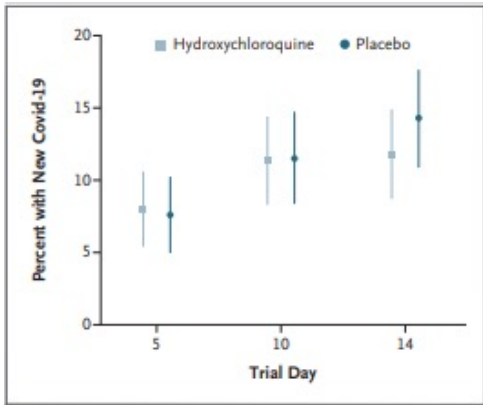


Table 2. Outcomes of Hydroxychloroquine Therapy for Postexposure Prophylaxis against Covid-19.*

Outcome	Hydroxychloroquine (N=414)	Placebo (N=407)	P Value
	number (percent)		
Confirmed or probable Covid-19	49 (11.8)	58 (14.3)	0.35
Laboratory-confirmed diagnosis	11 (2.7)	9 (2.2)	0.82
Symptoms compatible with Covid-19	48 (11.6)	55 (13.5)	0.46
All new symptoms	57 (13.8)	59 (14.5)	0.84
Any hospitalization	1 (0.2)	1 (0.2)	0.99
Death	0	0	—

Hydroxychloroquine en POST exposition

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Cluster-Randomized Trial of Hydroxychloroquine for Prevention of Covid-19

O. Mitjà, M. Corbacho-Monné, M. Ubals, A. Alemany, C. Suñer, C. Tebé, A. Tobias, J. Peñafiel, E. Ballana, C.A. Pérez, P. Admella, N. Riera-Martí, P. Laporte, J. Mitjà, M. Clua, L. Bertran, M. Sarquella, S. Gavilán, J. Ara, J.M. Argimon, G. Cuatrecasas, P. Cañadas, A. Elizalde-Torrent, R. Fabregat, M. Farré, A. Forcada, G. Flores-Mateo, C. López, E. Muntada, N. Nadal, S. Narejos, A. Nieto, N. Prat, J. Puig, C. Quiñones, F. Ramírez-Viaplana, J. Reyes-Urueña, E. Riveira-Muñoz, L. Ruiz, S. Sanz, A. Sentís, A. Sierra, C. Velasco, R.M. Vivanco-Hidalgo, J. Zamora, J. Casabona, M. Vall-Mayans, C. González-Beiras, and B. Clotet, for the BCN-PEP-CoV2 Research Group*

- 1225 dans 338 clusters HCQ vs 1300 dans 334 pas d'intervention
- 1064 HCQ vs 1186 groupe controle

- Essai randomisé, en ouvert. Randomisation en cluster
- HCQ 800 mg puis 400 mg/j pdt 6 j
- Critère principal= cas symptomatiques confirmés J14

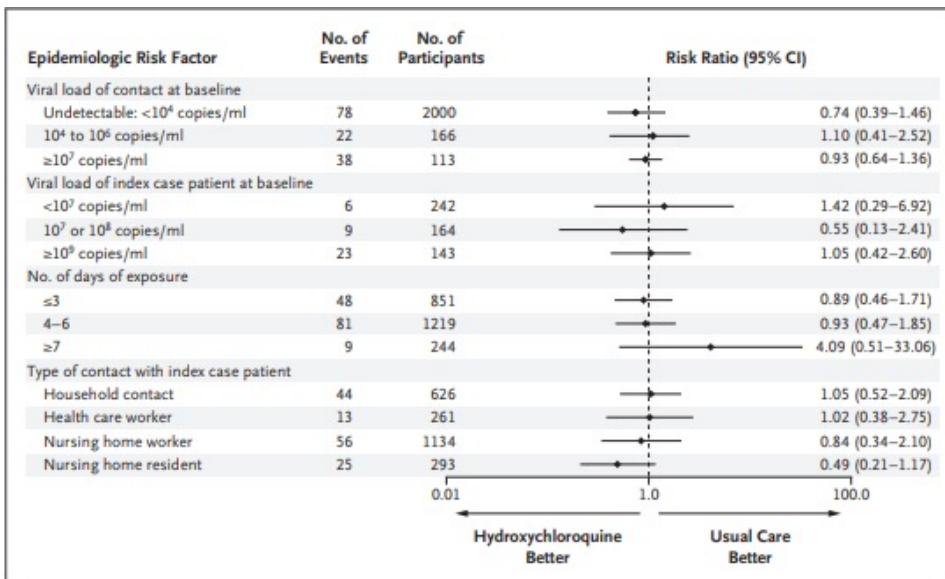


Figure 2. Subgroup Analyses of the Primary Outcome, According to Epidemiologic Risk Factors (Intention-to-Treat Population).

The primary outcome was PCR-confirmed, symptomatic coronavirus disease 2019 within 14 days.

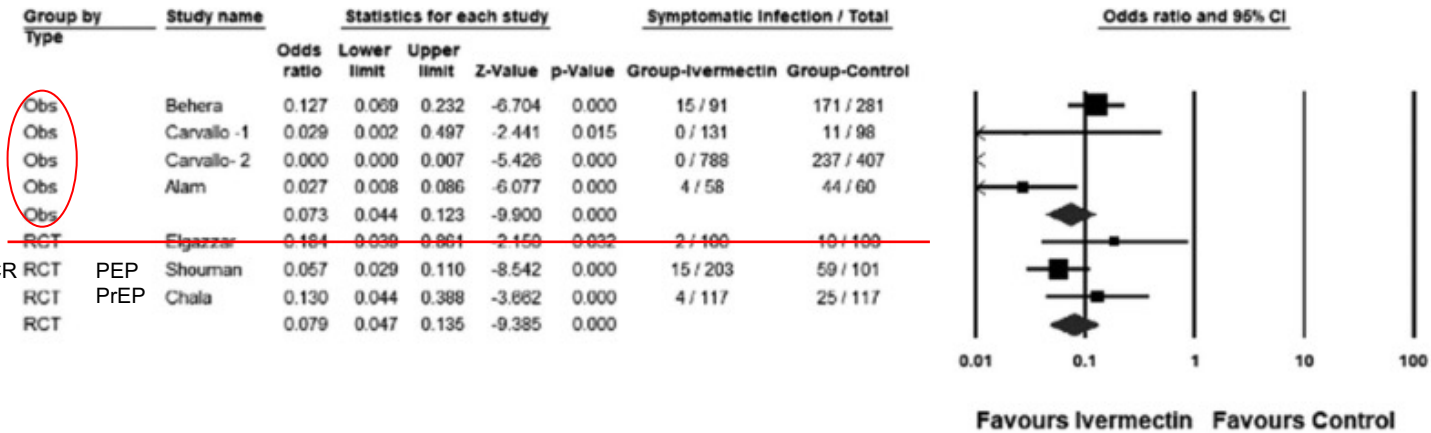
Ivermectine

American Journal of Therapeutics 28, e299–e318 (2021)

OPEN

Review of the Emerging Evidence Demonstrating the Efficacy of Ivermectin in the Prophylaxis and Treatment of COVID-19

Pierre Kory, MD,^{1*} Gianfranco Umberto Meduri, MD,² Joseph Varon, MD,³
Jose Iglesias, DO,⁴ and Paul E. Marik, MD⁵



Rétractée

Pas de placebo, pas de confirmation PCR

Pas de placebo, toujours pas publiée

FIGURE 1. Meta-analysis of ivermectin prophylaxis trials in COVID-19. OBS, observational study; RCT, randomized controlled trial. Symbols: Squares: Indicate treatment effect of an individual study. Large diamond: Reflect summary of study design immediately above. Size of each symbol correlates with the size of the confidence interval around the point estimate of treatment effect with larger sizes indicating a more precise confidence interval.

Findings 3. Ivermectin compared to no treatment for prevention of SARS-CoV-2 Infection

Ivermectin compared to no treatment for prevention of SARS-CoV-2 infection

Patient or population: people who were not infected with SARS-CoV-2, but were at high risk of developing the infection (e.g. after high-risk exposure)

Setting: inpatient or outpatients

Intervention: ivermectin

Comparison: no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N° of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no treatment	Risk with ivermectin				
SARS-CoV-2 infection (confirmed by RT-PCR or anti-gen testing) at 14 days	—	—	—	—	—	No study reported SARS-CoV-2 infection at 14 days.
Development of clinical COVID-19 symptoms up to 14 days	—	—	—	—	...a	No study with low risk or some concerns of bias reported development of clinical COVID-19 symptoms up to 14 days.
Adverse events (any grade) up to 14 days	—	—	—	—	...b	No study with low risk or some concerns of bias reported adverse events up to 14 days.
All-cause mortality up to 28 days	1 study assessed all-cause mortality during the study period, but 0 participants in either group died (Shoumann 2021).		Not estimable	304 (1 RCT)	⊕○○○ Very low ^c	We are uncertain whether ivermectin reduces or increases all-cause mortality up to 28 days.
Admission to hospital up to 14 days	—	—	—	—	—	No study reported admission to hospital up to 14 days.

Prophylaxis against covid-19: living systematic review and network meta-analysis

Jessica J Bartoszko,^{1,2} Reed A C Siemieniuk,¹ Elena Kum Long Ge,^{2,4} Mi Ah Han,¹ Behnam Sadeghirad,^{1,4} Arnab Derek K Chu,^{1,7} Rachel Couban,⁴ Andrea J Darzi,¹ Tahira Kimia Honarmand,⁸ Ariel Izcovich,⁹ Assem Khamis,¹⁰ Maura Marcucci,^{1,7} Shelley L McLeod,^{12,13} Sharhazad M Reem A Mustafa,¹⁵ John D Neary,⁷ Hector Pardo-Hernandez,¹⁶ Bram Rochweg,¹⁷ Charlotte Switzer,¹ Britta Tendal,²⁰ Robin W M Vernooij,^{22,23} Andrés Viteri-García,^{18,24} Yin Gordon H Guyatt,^{1,7} Romina Brignardello-Petersen¹


Lab confirmed covid-19

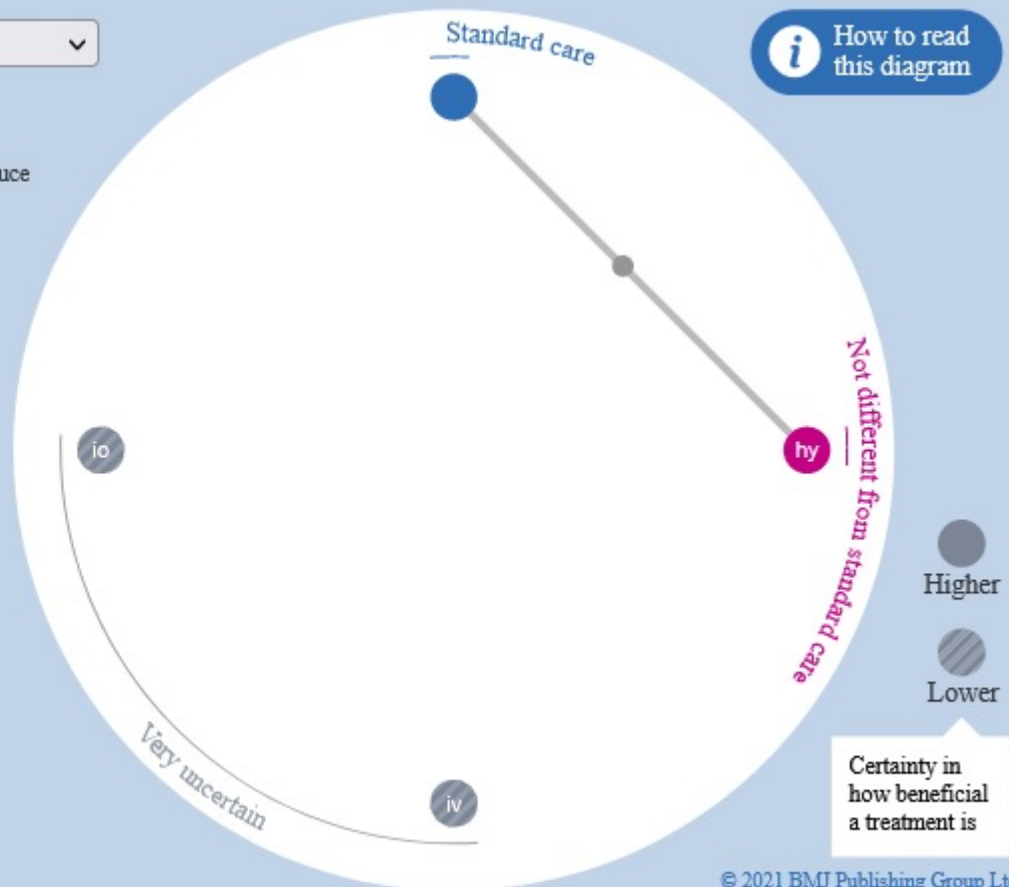
8 trials

5728 participants

Hydroxychloroquine probably does not reduce the risk of laboratory confirmed infection compared with standard care or placebo. Evidence for the effects of ivermectin, with or without iota-carrageenan, on laboratory confirmed infection is of very low certainty. The main limitations of the evidence are risk of bias and imprecision.

Evidence quality displayed:

- High
- Moderate
- Low
- Very low 



Ivermectine

- L'Inde recommande l'ivermectine pour ses soignants en pré-exposition....Les américains consomment des formulations pour animaux.....Besoin d'études de qualité+++

- PAS de RCT versus placebo publié à ce jour pour la prophylaxie

- Clinicaltrials.gov:

- Prophylaxis for COVID-19: Ivermectin in Close Contacts of COVID-19 Cases (IVERNEX-TUC) (IVERNEX-TUC): RCT 2:1 ivermectine (0,6mg/kg J1,J7) vs placebo, 750 personnes. Endpoint diagnostic de certitude. Argentine
- Effectiveness and Safety of Ivermectin for the Prevention of Covid-19 Infection in Colombian Health Personnel (IveprofCovid19): 200 mcg/kg par semaine 7 semaines vs placebo. 550 soignants; Endpoint clinique (pas de PCR). Colombie



Les anticorps monoclonaux: c'est pas du vaccin!

The NEW ENGLAND JOURNAL of MEDICINE

PEP

ORIGINAL ARTICLE

Subcutaneous REGEN-COV Antibody Combination to Prevent Covid-19

M.P. O'Brien, E. Forleo-Neto, B.J. Musser, F. Isa, K.-C. Chan, N. Sarkar, K.J. Bar, R.V. Barnabas, D.H. Barouch, M.S. Cohen, C.B. Hurt, D.R. Burwen, M.A. Marovich, P. Hou, I. Heirman, J.D. Davis, K.C. Turner, D. Ramesh, A. Mahmood, A.T. Hooper, J.D. Hamilton, Y. Kim, L.A. Purcell, A. Baum, C.A. Kyratsous, J. Krainson, R. Perez-Perez, R. Mohseni, B. Kowal, A.T. DiCiccio, N. Stahl, L. Lipsich, N. Braunstein, G. Herman, G.D. Yancopoulos, and D.M. Weinreich, for the Covid-19 Phase 3 Prevention Trial Team*

Table 3. Adverse Events.*

Event	REGEN-COV (N=1311)	Placebo (N=1306)
	<i>number of participants (percent)</i>	
Symptomatic Covid-19	15 (1.1)	112 (8.6)
Asymptomatic Covid-19	54 (4.1)	108 (8.3)
Headache	24 (1.8)	46 (3.5)
Injection-site reaction	55 (4.2)	19 (1.5)

- Casirivimab et imdevimab, actifs sur les variants B.1.1.7 (alpha), B.1.351 (beta), B.1.617.2 (delta), B.1.429 (epsilon), and P.1 (gamma)
- Efficacité sur COVID-19 en administration précoce, patients ambulatoires (<7j de symptômes)
- Inclusion si "household" cas index, dans les 72h, > 12 ans, PCR neg, sérologie neg, asymptomatiques
- 1200mg SC 1 injection

End Point	REGEN-COV (N=753)	Placebo (N=752)
Primary end point: symptomatic RT-qPCR-confirmed SARS-CoV-2 infection, broad-term definition†		
No. of participants (%)	11 (1.5)	59 (7.8)
Relative risk reduction — %	81.4	—
Odds ratio (95% CI)	0.17 (0.09–0.33)	—
P value‡	<0.001	—
Viral load >10 ⁴ copies/ml§		
No. of participants/total no. (%)	12/745 (1.6)	85/749 (11.3)
Relative risk reduction — %	85.8	—
Odds ratio (95% CI)	0.13 (0.07–0.24)	—
P value‡	<0.001	—

Les anticorps monoclonaux: c'est pas du vaccin!

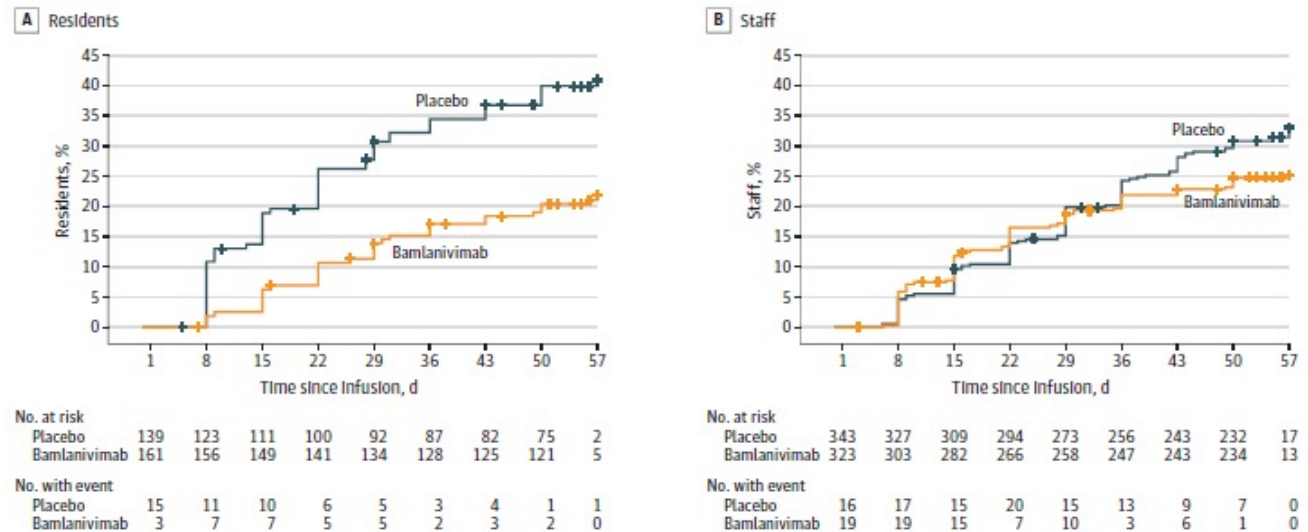
JAMA | Original Investigation

Effect of Bamlanivimab vs Placebo on Incidence of COVID-19 Among Residents and Staff of Skilled Nursing and Assisted Living Facilities A Randomized Clinical Trial PrEP/ PEP

Myron S. Cohen, MD; Ajay Nirula, MD, PhD; Mark J. Mulligan, MD; Richard M. Novak, MD; Mary Marovich, MD; Catherine Yen, MD; Alexander Stermer, MD; Stockton M. Mayer, DO; David Wohl, MD; Blair Brengle, MD; Brian T. Montague, DO; Ian Frank, MD; Russell J. McCulloch, MD; Carl J. Fichtenbaum, MD; Brad Lipson, DO; Nashwa Gabra, MD; Julio A. Ramirez, MD; Christine Thai, MD; Wairimu Chege, MD, MPH; Margarita M. Gomez Lorenzo, MD; Nirupama Sista, PhD; Jennifer Farnior, MS; Meredith E. Clement, MD; Elizabeth R. Brown, ScD; Kenneth L. Custer, PhD; Jacob Van Naarden, BS; Andrew C. Adams, PhD; Andrew E. Schade, MD, PhD; Matan C. Dabora, MD; Jack Knorr, PhD; Karen L. Price, PhD; Jay L. Tuttle, PhD; Paul Klekotka, MD, PhD; Lei Shen, PhD; Daniel M. Skovronsky, MD, PhD; for the BLAZE-2 Investigators

- 1 cas dans l'établissement
- 4200mg IV, PCR négative, sérologie négative

Figure 3. Time From Infusion to Detection of SARS-CoV-2 by RT-PCR With Bamlanivimab vs Placebo and Viral Load in Participants Who Tested Positive for SARS-CoV-2 During the Study



Les anticorps monoclonaux : c'est pas des vaccins



Bamlanivimab et Bamlanivimab+ Etesevimab
pas efficaces contre les variants avec les mutations E484 and K417
mutations (comme B.1.351, B.1.1.28, B.1.617.1 et B.1.526)

Chen RE, et al., Nature. 2021 Aug;596(7870):103-108.

Les anticorps monoclonaux : c'est pas des vaccins

ÉVALUER LES TECHNOLOGIES DE SANTÉ

AVIS SUR LE
MÉDICAMENTS REUTERS®

World Business Legal Markets Breakingviews Technology Inven

August 20, 2021
7:11 PM CEST
Last Updated 9 days ago

Healthcare & Pharmaceuticals

AstraZeneca's antibody therapy prevents COVID-19, study shows

AZD7442: AZD8895 and AZD1061

Effet long terme

- Astra in frame to launch new prevention tool on top of vaccines
- Antibody combo 77% effective in preventing COVID-19
- New hope for immunocompromised with low vaccine protection
- AstraZeneca pursuing initial approval well before year-end

vaccination et qui présentent une immunodépression sévère et qui sont à haut risque de forme sévère de COVID-19.

Les anticorps monoclonaux : c'est pas des vaccins

AstraZeneca

AstraZeneca Websites Global site

What science can do R&D Our therapy areas Our company Careers Investors Media Sustainability Partnering

Update on AZD7442 STORM CHASER trial in post-exposure prevention of symptomatic COVID-19

15 June 2021 07:00 BST

AstraZeneca today announced results from the STORM CHASER trial assessing the safety and efficacy of AZD7442, a long-acting antibody (LAAB) combination, for the prevention of symptomatic COVID-19 in participants recently exposed to the SARS-CoV-2 virus. **The trial did not meet the primary endpoint of post-exposure prevention of symptomatic COVID-19** with AZD7442 compared to placebo.



Trial participants were unvaccinated adults 18 years and over with confirmed exposure to a person with a case of the SARS-CoV-2 virus within the past eight days. In the overall trial population, AZD7442 reduced the risk of developing symptomatic COVID-19 by 33% (95% confidence interval (CI): -26, 65) compared to placebo, which was not statistically significant (Table 1).

Tout le reste.....

Lopinavir/ritonavir

- Pas d'efficacité

BMJ Open Efficacy of pragmatic same-day ring prophylaxis for adult individuals exposed to SARS-CoV-2 in Switzerland (COPEP): protocol of an open-label cluster randomised trial

Mikaela Smit ,^{1,2} Annalisa Marinosci,¹ Giovanni Jacopo Nicoletti,³ Thomas Perneger ,^{2,4} Silvio Ragozzino,⁵ Diego O Andrey,^{1,2,6} Marcel Stoeckle,⁵ Frederique Jacqueroiz ,⁷ Dan Lebowitz,^{8,9} Thomas Agoritsas,^{2,10,11} Benjamin Meyer,¹² Herve Spechbach,⁷ Julien Salamun,⁷ Moritz Back,¹³ Carla Schaubhut,¹³ Simon Fuchs,¹³ Laurent Decosterd,¹⁴ Manuel Battegay,⁵ Idris Guessous,⁷ François Chappuis,⁷ Laurent Kaiser,^{15,16} Niklaus D Labhardt,^{3,5} Alexandra Calmy^{1,2}

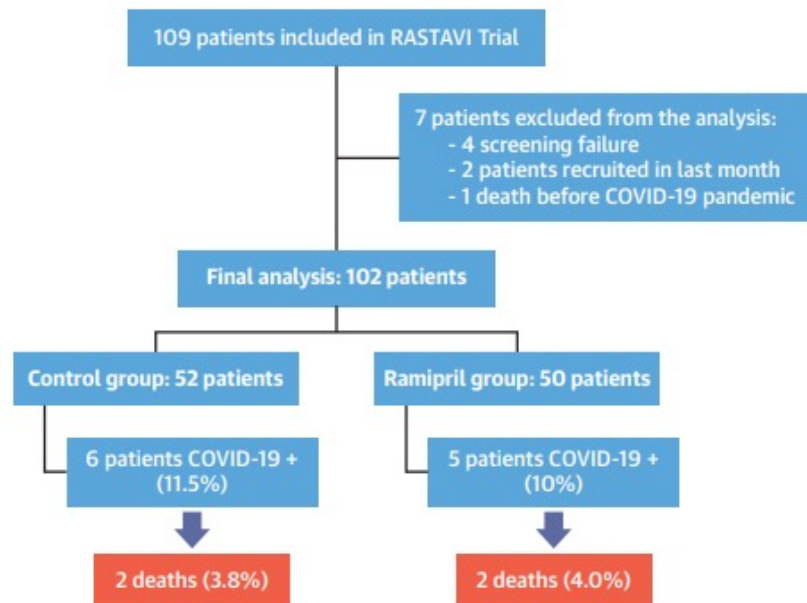
Ramipril: recyclage

Ramipril in High-Risk Patients With COVID-19



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FIGURE 1 Patient Flowchart



Clinical trials

- COVID-19 Prophylaxis; RCT, placebo; Active/completed, hors vaccin
 - Melatonin 2mg PREP
 - Nitazoxanide PEP
 - Niclosamide PREP
 - Nicotine patch PREP
 - Iota-Carrageenan PREP
 - Autres AC monoclonaux
 - Molnupiravir PEP
 - Amantadine
 - Ivermectine
 - Emtricitabine/tenofovir disoproxil
 - Divers composés: GLS-1200, PUL-042 en pulvérisation PREP
 - RTB101 PEP
 - Divers compléments nutritionnels
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Merci pour votre attention