SIG FARMACO

Grupo de Interesse Especial (SIG)

em Farmacologia e Terapêutica

RNP REDE NACIONAL DE ENSINO E PESQUISA

RUTE REDE UNIVERSITÁRIA DE TELEMEDICINA

Uma iniciativa para uso da estrutura de vídeo e web-conferências da Rede Universitária de Telemedicina (RUTE-MCT) ***para reduzir as distâncias geográficas e integrar ações em ensino e pesquisa em farmacologia e terapêutica no Brasil***

Apoio SBFTE

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www.sbfte.org.br/sigfarmaco

sigfarmaco@gmail.com

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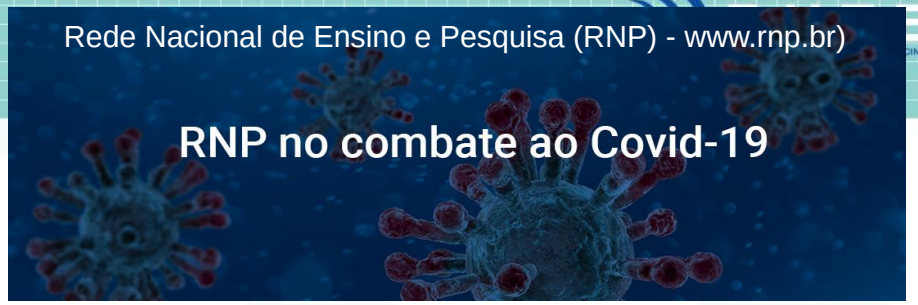

30 de março (2a f), 10:00 às 11:30 h

Farmacologia, Terapêutica Experimental e COVID-19

Local: Sala Virtual WebConf

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Durante a sessão: A todos os participantes:

Mantenham os **microfones da videoconferência no MUDO enquanto não estiverem falando**, medida que se faz necessária para evitar ruídos e perda de qualidade de áudio durante a conferência.

Perguntas, Comentários ***pelo Chat***

Inscrições para perguntas por audio ***pelo Chat*** (nome, instituição)

Estrutura da sessão

1. Apresentação do tema (Palestrantes): ~40 min

2. Debate do tema com participantes: ~30 min

3. Revisão Agenda SIG-Farmaco 2020: ~5 min

4. Encerramento e Registro Participação: ~5 min

Ambiente Restrito:
AS SESSÕES NESSE AMBIENTE SÃO GRAVADAS
Em conformidade a Lei dos Direitos Autorais 9.160

Registro de Presença nas Sessões RUTE

1) Do navegador do seu smartphone, tablet ou notebook, acesse:

www.rute.rnp.br/presenca

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2) Informe seu **CPF**, **E-mail** e clique em "**Registrar Presença**"

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3) Selecione o **SIG: Farmacologia e Terapêutica**

4) A **SENHA DA SESSÃO** do SIG é: **21254**

Informe a senha e clique em **"Registrar Presença – Etapa 2"**

Avalie a sessão após registrar sua presença

O registro deve ser feito **no mesmo dia (até 23h59)** da sessão

Em caso de dúvidas ou suporte, contate o e-mail: sig@rute.rnp.br

SIG FARMACO

Rede Nacional de Ensino e Pesquisa (RNP) - www.rnp.br)

RNP no combate ao Covid-19

Farmacologia, Terapêutica Experimental e COVID-19

Palestrantes:

Prof. Dr. François Noël (SIG-Farmaco, ICB/UFRJ)

Prof. Jaderson Lima (Aliança Pesquisa Clinica Brasil)

Coordenadores da Sessão:

Maria Christina W. Avellar (SIG-Farmaco, UNIFESP-EPM)

Emiliano Barreto (SIG-Farmaco, UFAL)

Paulo Ghedini (SIG-Farmaco, UFG)

Rosely O. Godinho (UNIFESP-EPM

SINOPSE

I. COVID-19 & HYDROXYCHLOROQUINE (HCQ):

HISTORICAL ASPECT – MECHANISM OF ACTION

II. DRUG ALTERNATIVES:

BRAZIL & ON-GOING INTERNATIONAL CLINICAL TRIALS

I. COVID-19 & HYDROCHLOROQUINE (HCQ): *HISTORICAL ASPECT*

1. 2007 Review: proposal of HCQ use for different intracellular bacteria & virus infections (*Raoult-France*)

2. *In vitro* data of HCQ effect on SARS-CoV-2 infected cells

3. Clinical experience of China (and South Korea) in COVID-19 treatment

4. First published open-label clinical trial data with HCQ in COVID-19 patients (*Raoult-France*)

5. Results of other clinical trials

International Journal of Antimicrobial Agents 30 (2007) 297–308

1

Review

Recycling of chloroquine and its hydroxyl analogue to face bacterial, fungal and viral infections in the 21st century

Jean-Marc Rolain *, Philippe Colson, Didier Raoult

H=166
>135.000
citações

Table 1
Bacteria, fungi and viruses inhibited by chloroquine and/or hydroxychloroquine (in vitro data)

Bacteria	Reference	Fungi	Reference	Virus	Reference
Coxiella burnetii	[5,13]	*Histoplasma capsulatum*	[24]	HIV	[2,29–32]
Tropheryma whipplei	[7,8]	*Cryptococcus neoformans*	[15,25]	SARS-CoV	[33,34]
Legionella pneumophila	[11]	*Paracoccidioides brasiliensis*	[26]	Influenza viruses	[35–38]
Francisella tularensis	[12]	*Penicillium marneffei*	[15,27]	Flavivirus, including yellow fever virus	[39]
Mycobacterium tuberculosis	[14]	*Aspergillus fumigatus*	[28]	Rubella virus	[40,41]
Mycobacterium avium	[15]			HAV	[42]
Salmonella Typhi	[16]			HBV	[43,44]
Escherichia coli	[17]			HCV	[45]
Bacillus anthracis	[18]			Arenavirus	[46]
Bacillus subtilis	[19]				
Borrelia burgdorferi	[20]			Lymphocytic choriomeningitis virus	[47]
Brucella abortus	[21]			Rabies virus	[48]
Staphylococcus aureus	[22]			Varicella–Zoster virus	[49]
Listeria monocytogenes	[23]			Respiratory syncytial virus	[50]
				Sindbis virus	[51]
				Herpes simplex viruses	[41,52,53]
				Epstein–Barr virus	[54]
				Polioviruses	[55–57]
				Newcastle disease virus	[58]
				Borna disease virus	[59]
				Vesicular stomatitis virus	[37,60–62]
				Vaccinia virus	[63]
				Murine RNA tumour virus	[64]
				FMDV	[65]
				Mayaro virus	[66]
				Feline calicivirus	[67]
				African swine fever virus	[68]
				Bovine leukaemia virus	[69]
				Canine parvovirus	[70]
				Minute Virus of Mice	[71]

HIV, human immunodeficiency virus; SARS-CoV, SARS coronavirus; HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; FMDV, foot and mouth disease virus.

2 Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro

Wang et al. *Wuhan Institute of Virology, Chinese Academy of Sciences,*

Cell Research (2020) 30:269–271 Published online: 4 February 2020

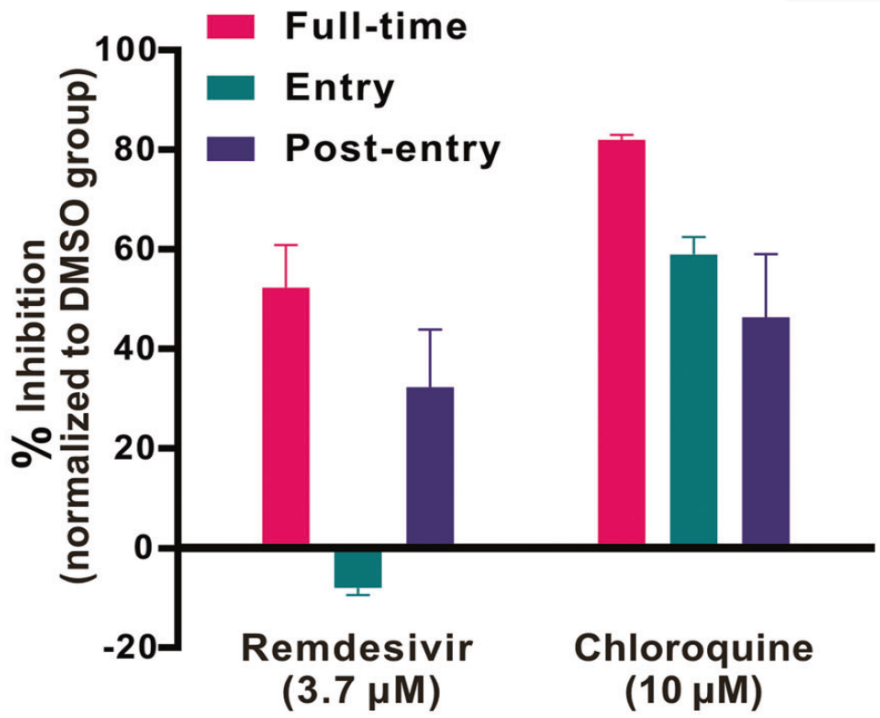


Fig. 1 The antiviral activities of the test drugs against 2019-nCoV in vitro.

100 μm. **c** and **d** Time-of-addition experiment of remdesivir and chloroquine. For "Full-time" treatment, Vero E6 cells were pre-treated with the drugs for 1 h, and virus was then added to allow attachment for 2 h. Afterwards, the virus–drug mixture was removed, and the cells were cultured with drug-containing medium until the end of the experiment. For "Entry" treatment, the drugs were added to the cells for 1 h before viral attachment, and at 2 h p.i., the virus–drug mixture was replaced with fresh culture medium and maintained till the end of the experiment. For "Post-entry" experiment, drugs were added at 2 h p.i., and maintained until the end of the experiment. For all the experimental groups, cells were infected with 2019-nCoV at an MOI of 0.05, and virus yield in the infected cell supernatants was quantified by qRT-PCR **c** and NP expression in infected cells was analyzed by Western blot **d** at 14 h p.i.

2 In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).

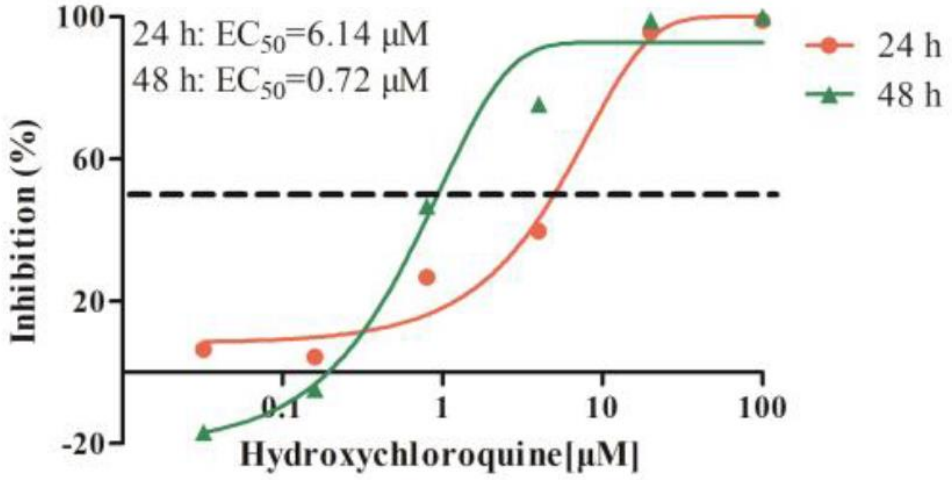
Yao X[1], Ye F[2], Zhang M[1], Cui C[1], Huang B[2], Niu P[2], Liu X[1], Zhao L[2], Dong E[3], Song C[4], Zhan S[5], Lu R[2], Li H[1,3], Tan W[2], Liu D[1].

Clin. Infect. Dis. 2020 Mar 9. pii: ciaa237

[1] Drug Clinical Trial Center, Peking University Third Hospital, Beijing, 100191, China.

Results. Hydroxychloroquine (EC_{50}=0.72 μM) was found to be more potent than chloroquine (EC_{50}=5.47 μM) *in vitro*. Based on PBPK models results, a loading dose of 400 mg twice daily of hydroxychloroquine sulfate given orally, followed by a maintenance dose of 200 mg given twice daily for 4 days is recommended for SARS-CoV-2 infection, as it reached three times the potency of chloroquine

Vero cells
Infection during 2 h
Washing
Treated for 24 and 48h
End-point: RT-PCR in supernatant



2 HC: *IN VITRO* EFFECTS ON SARS-CoV-2

Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro

On line: 18/03/2020

Cell Discovery (2020)6:16

Jia Liu[1], Ruiyuan Cao[2], Mingyue Xu[1,3], Xi Wang[1], Huanyu Zhang[1,3], Hengrui Hu[1,3], Yufeng Li[1,3], Zhihong Hu[1], Wu Zhong[2] and Manli Wang[1]

2.1. Proof-of-Concept (efficacy *in vitro*)

Vero E6 cells: Pre-treatment for 1h

Infection with SARS-CoV-2

Viral RNA quantified by qPCR in supernatant 48h post-infection

HCQ: Potency: EC_{50}: 4.1 – 17.3 µM

Selectivity: SI (CC_{50}: / EC_{50}) = 14 - 61

2.2. Translationality ?

Serum level at safe dosage (400 mg HC sulfate / day) ≈ 1.4 µM

Large distribution to lungs (200 – 700 times > plasma)

3 CHINA: first published report of clinical trials

Letter

Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies

Gao et al. *BioScience Trends. 2020; 14(1):72-73.*

On line 19/02/2020

15 clinical trials... been quickly conducted in China to test the efficacy and safety of chloroquine or hydroxychloroquine in the treatment of COVID-19 associated pneumonia in more than 10 hospitals

results from more than 100 patients have demonstrated that chloroquine phosphate is superior to the control treatment in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course according to the news briefing. Severe adverse

3 CHINA: clinical experience & guidelines

Results of clinical trials registered with Chloroquine in China

19/02/2020: Guidelines for the Prevention, Diagnosis, and Treatment of Novel Coronavirus-induced Pneumonia issued by the National Health Commission (NHC) of the People's Republic of China for tentative treatment of COVID-19

Table 1. Antivirals included in the Guidelines (version 6) for treatment of COVID-19

Drug	Dosage	Method of administration	Duration of treatment
IFN-α	5 million U or equivalent dose each time, 2 times/day	Vapor inhalation	No more than 10 days
Lopinavir/ritonavir	200 mg/50 mg/capsule, 2 capsules each time, 2 times/day	Oral	No more than 10 days
Ribavirin	500 mg each time, 2 to 3 times/day in combination with IFN-α or lopinavir/ritonavir	Intravenous infusion	No more than 10 days
Chloroquine phosphate	500 mg (300 mg for chloroquine) each time, 2 times/day	Oral	No more than 10 days
Arbidol	200 mg each time, 3 times/day	Oral	No more than 10 days

Drug Discoveries & Therapeutics. 2020; 14(1):58-60.

"French" (*Prof. Raoult*) clinical trial

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial

Gautret et al. International Journal of Antimicrobial Agents
Available online 20 March 2020, 105949

LIMITATIONS - CRITICISMS

Open study, not randomized

Very small sample size, from different centers

Concerns about controls

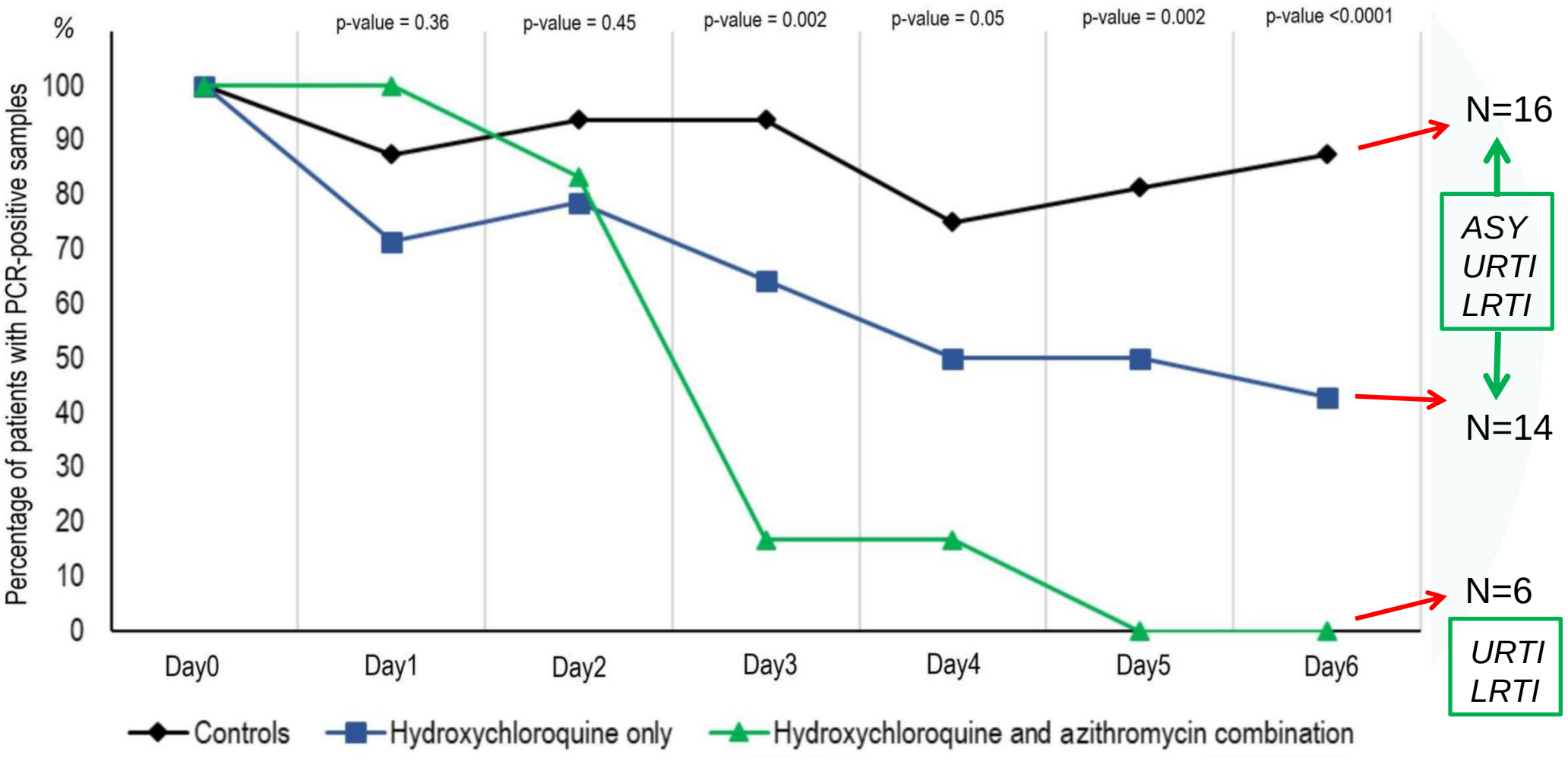
Drop-out of six HCQ treated patients without consideration of NNT

Absence of long-term outcome follow-up

End-point: nasopharyngeal swab – virus presence (qPCR)

BUT: *"However, in the current context, we believe that our resuts should be shared with the scientific community"*

Figure 2. Percentage of patients with PCR-positive nasopharyngeal samples from inclusion to day 6 post-inclusion in COVID-19 patients ….



ASY: asymtomatic
URTI: upper tract respiratory infection, LRTI: lower tract respiratory infection,

"French" (*Prof. Raoult*) clinical trial: 2nd paper

Submitted, 27 March 2020

Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: an observational study *Gautret et al.*

DESIGN:

80 hospitalized patients - median age: 52 years
- 57.5% ≥ one chronic condition
- 53.8% LDCT compatible with pneumonia

Hydroxychloroquine: 3x200 mg/day for 10 days
+ Azithromycin: 500 mg (D1) then 250 mg/day (4 days)

PRIMARY OUTCOMES:

Clinical outcome
Contagiousness (PCR & culture)
Long of stay in infectious disease unit

CLINICAL OUTCOME

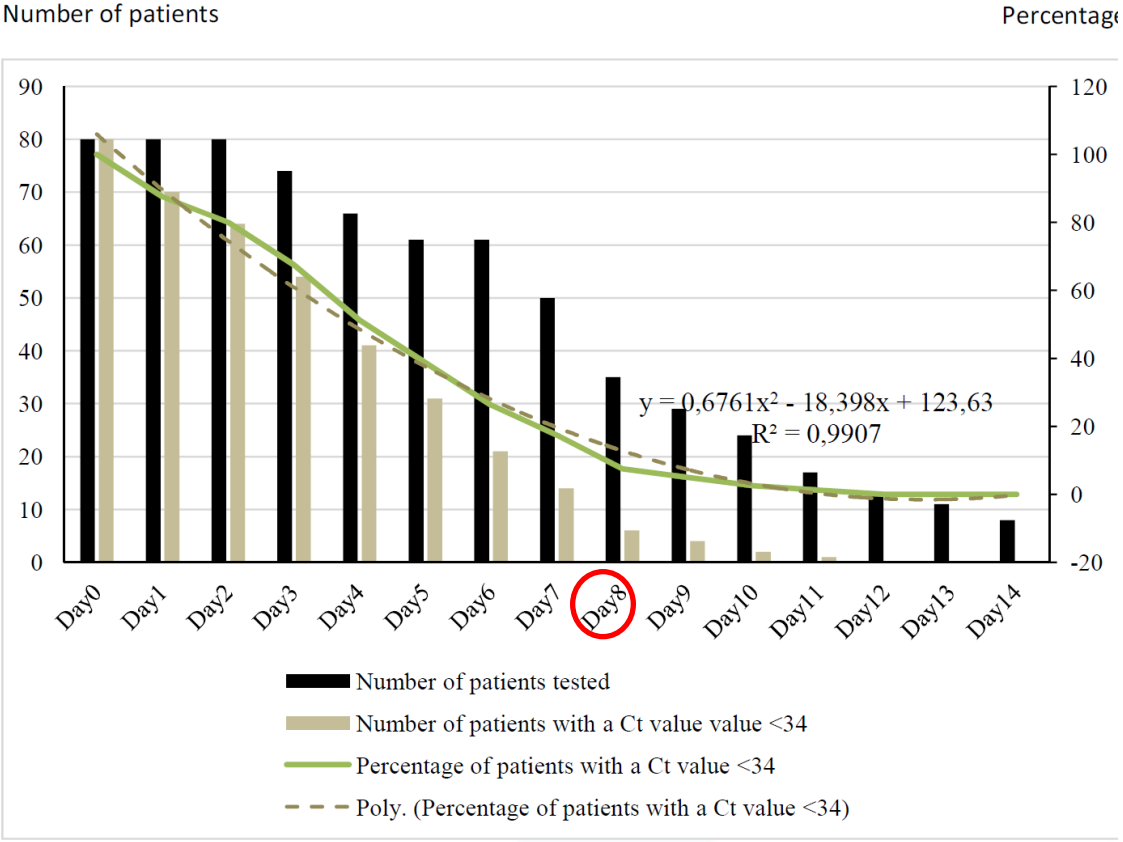
81.3% had favourable outcome and were discharged from Infectious Disease Unit
15% required oxygen therapy
3.8 % transfer to Intensive Care Unit
1.2 % death

CONTAGIOUSNESS (PCR)

↔ Literature:
high level for around 3 weeks

Length of stay in the IDU: 4.5 days

ADVERSE EVENTS: rare and minor



CHINA: Negative small clinical trial

A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19)

Chen et al. J. Zjeijang University. 2020 Apud Gautret et al., preprint march 27

"30 COVID-19 patients showed no significant differences between patients treated with 400 mg per day during five days (N=15) and controls (N=15) regarding pharyngeal carriage of viral RNA at day7.

However, patients received multiple additional treatments including antivirals"

Hydroxychloroquine & COVID-19:
Putative Mechanisms of Action

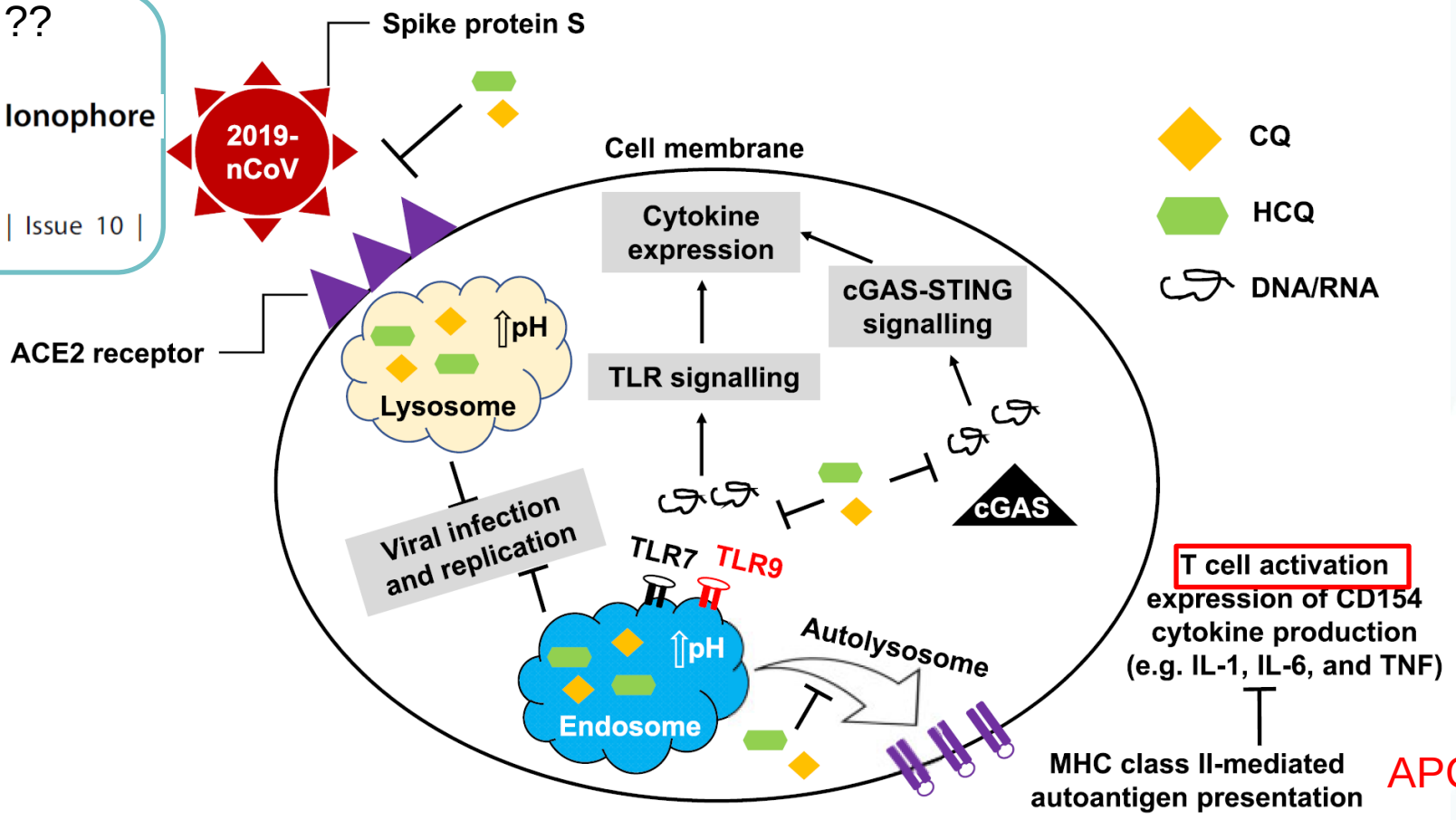
Zhou et al.
J. Antimicrob. Chemother. March 2020

1. Interference with glycosylation of ACE2 receptor (↓ infection)
2. ↑ pH of lysosomes (↓ infection) and endosomes (↓ replication)
3. Disruption of DNA/RNA interaction with TLRs and cGAS (↓ cytokine production)
4. Repression of T cell activation (↓ cytokine production) < effect on APCs

5. Zn ionophore ??

Chloroquine Is a Zinc Ionophore

PLOS ONE | October 2014 | Volume 9 | Issue 10 |



Hydroxychloroquine & COVID-19: Putative Mechanism of Action

SOMETHING ELSE?

Eva Schrezenmeier & Thomas Dörner
Nature Reviews Rheumatology **16**, p.155–166(2020)

"Although hydroxychloroquine is not an anticoagulant, this drug is widely believed to have vascular protective effects and prevent the development of thrombotic complications.

This protective effect seems to be most relevant for patients with a secondary coagulopathy owing to systemic inflammation[106] and in patients with primary APS"

ITALY: report that 50% of deaths are due to pulmonary embolism and not Hypoxia

II. DRUG ALTERNATIVES:
BRAZIL & INTERNATIONAL CLINICAL TRIALS

1. Drug alternatives in Brazil

2. On-going international clinical trials

II. DRUG ALTERNATIVES: *BRAZIL*

Fármacos com registro oficial

Fármaco	Mundo	Brasil
Sulfato de Hidroxicloroquina	SIM	SIM
Remdesivir *(Gilead Sciences)*	NÃO	NÃO
Lopinavir/Ritonavir	SIM	SIM
Favipiravir *(Toyama Chemical)*	Japão (2015) (Avigan®) – Influenza	NÃO

Journal Pre-proof

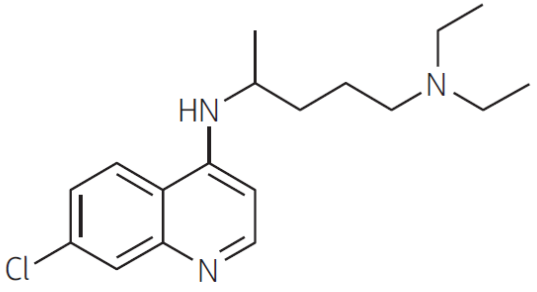
International Journal of Antimicrobial Agents (2020)

New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19?

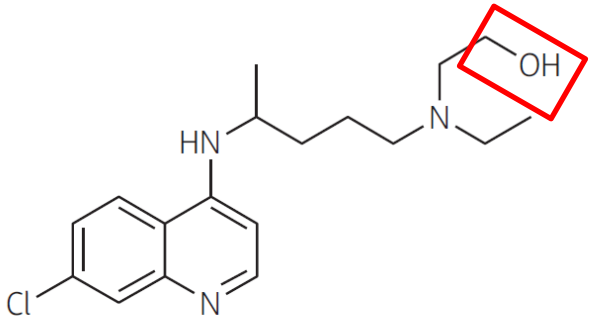
Christian A. Devaux [a,b,c,*], Jean-Marc Rolain [a,c], Philippe Colson [a,c], Didier Raoult [a,c]

[a] *Aix-Marseille Université, IRD, APHM, MEPHI, IHU–Méditerranée Infection, Marseille, France*

For decades, chloroquine was a front-line drug for the treatment and prophylaxis of malaria and is one of the most prescribed drugs worldwide hydroxychloroquine belong to the same molecular family (4-aminoquinoline) and is available for oral administration in the form of hydroxychloroquine sulfate.



Chloroquine (CQ)



Hydroxychloroquine (HCQ)

- Hydroxychloroquine can be used in high doses for long periods with very good tolerance (but caution with QT prolongation).
- HCQ is 2-3 times less toxic than CQ, in animal studies (McChesney, 1983)

Preços no Brasil

Agência Nacional de Vigilância Sanitária
www.anvisa.gov.br

PREÇOS MÁXIMOS DE MEDICAMENTOS POR PRINCÍPIO ATIVO — **CMED**

PREÇO FÁBRICA - PF (PREÇO PARA LABORATÓRIOS E DISTRIBUIDORES)
PREÇO MÁXIMO AO CONSUMIDOR - PMC (PREÇO PARA FARMÁCIAS E DROGARIAS)

Publicada em 02/03/2020

GGREM	Medicamento (Laboratório)	Apresentação	ICMS 0%		ICMS 12%		ICMS 17%		ICMS 17,5%		ICMS 18%		ICMS 20%	
			PF	PMC	PF	PMC	PF	PMC	PF	PMC	PF	PMC	PF	PMC
PRINCÍPIO ATIVO: SULFATO DE HIDROXICLOROQUINA														
501602501113418	REUQUINOL (APSEN)	400 MG COM REV CT BL AL PLAS TRANS X 30	51,45		58,47	80,83	61,99	85,70	62,36	86,21	62,74	86,73	64,31	88,90
502819501113313	PLAQUINOL (SANOFI-AVENTIS)	400 MG COM REV CT BL AL PLAS INC X 30	67,35		76,53	105,80	81,14	112,17	81,64	112,86	82,13	113,54	84,19	116,39
541819010101806	SULFATO DE HIDROXICLOROQUINA (EMS)	400 MG COM REV CT BL AL PLAS PVC/PVDC OPC X 10	14,60		16,59	22,93	17,59	24,32	17,70	24,47	17,80	24,61	18,25	25,23
541819010101906	SULFATO DE HIDROXICLOROQUINA (EMS)	400 MG COM REV CT BL AL PLAS PVC/PVDC OPC X 20	29,18		33,16	45,84	35,16	48,61	35,37	48,90	35,59	49,20	36,48	50,43
541818100090106	SULFATO DE HIDROXICLOROQUINA (EMS)	400 MG COM REV CT BL AL PLAS PVC/PVDC OPC X 30	43,78		49,75	68,78	52,75	72,92	53,07	73,37	53,39	73,81	54,73	75,66
541819010102006	SULFATO DE HIDROXICLOROQUINA (EMS)	400 MG COM REV CT BL AL PLAS PVC/PVDC OPC X 60	87,55		99,49	137,54	105,48	145,82	106,12	146,70	106,77	147,60	109,44	151,29

10 comprimidos de 400 mg ≈ 1 tratamento ≈ R$ 14,60

Preço Fábrica

23 x

40 comprimidos = 1 tratamento ≈ R$ 340,00

GGREM	Medicamento (Laboratório)	Apresentação	ICMS 0%	
			PF	PMC
PRINCÍPIO ATIVO	LOPINAVIR;RITONAVIR			
506717070070706	LOPINAVIR + RITONAVIR (CRISTÁLIA QUÍMICO)	200 MG + 50 MG COM REV CT FR PLAS OPC X 120	1011,04	
543715110002117	KALETRA (ABBVIE .)	200 MG + 50 MG COM REV CT FR PLAS OPC X 120	1490,90	

Fontes de Hidroxicloroquina no Brasil

1. PRIVADO

   Aspen; Sanofi-Aventis; EMS

2. PÚBLICO

   Farmanguinhos – FIOCRUZ

   !! Somente difosfato de cloroquina

   Laboratório químico farmacêutico do Exército

   !! Somente (difosfato?) cloroquina

(Hidroxi)cloroquina: situação legal nos USA

Marketwatch Published: March 22, 2020 at 10:13 a.m. ETBy Jaimy Lee

March 19, President Donald Trump announced that the FDA had ***fast-tracked*** its approval for COVID-19.

The FDA denied that this was the case:

FDA commissioner Stephen Hahn said that while chloroquine would still need to go through clinical trials…….***an expanded use*** *approach to that could be done to actually see if that benefits patients*"

Expanded access (= USO COMPASSIVO):

Uso regulamentado pelo FDA para as pessoas usarem tratamentos em investigação se não houver outras opções aprovadas disponíveis em algumas circunstâncias com risco de vida.

II. DRUG ALTERNATIVES: *International Clinical Trials*

USA - ClinicalTrials.gov *(em 24/03/2020)*

128 ensaios clínicos,

vários envolvendo tratamento farmacológico:

Hidroxicloroquina:7
Cloroquina: 2
Remdesivir: 8
Lopinavir/Ritonavir: 10
Favipiravir: 2
Outros: 44

OMS - *International Clinical Trials Registry Platform*

382 ensaios clínicos (23/01/2020 – 08/03/2020)

108 com tratamento farmacológico

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

Cao et al. *N. Engl. J. Med. 2020 Mar 18*.

Controlled, randomized, open-label trial - 199 hospitalized patients
2 arms: Standard care +/- lopinavir-ritonavir (400-100 mg) / BID 14 days
End-point: time to clinical improvement

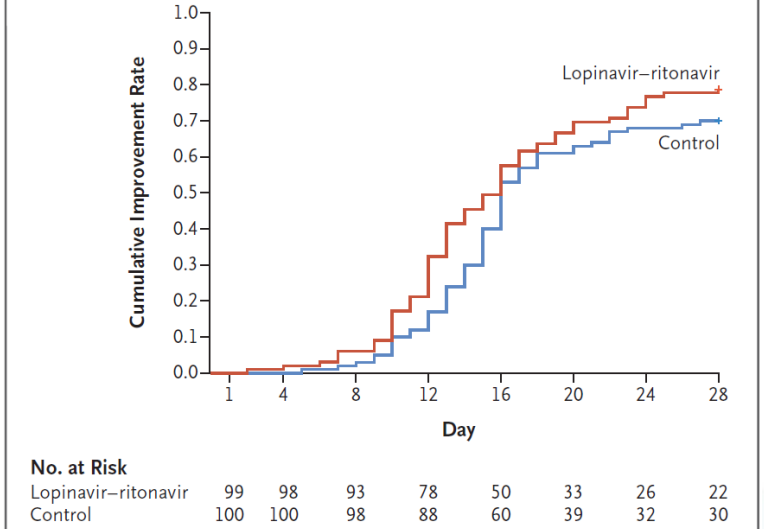


Figure 2. Time to Clinical Improvement in the Intention-to-Treat Population.

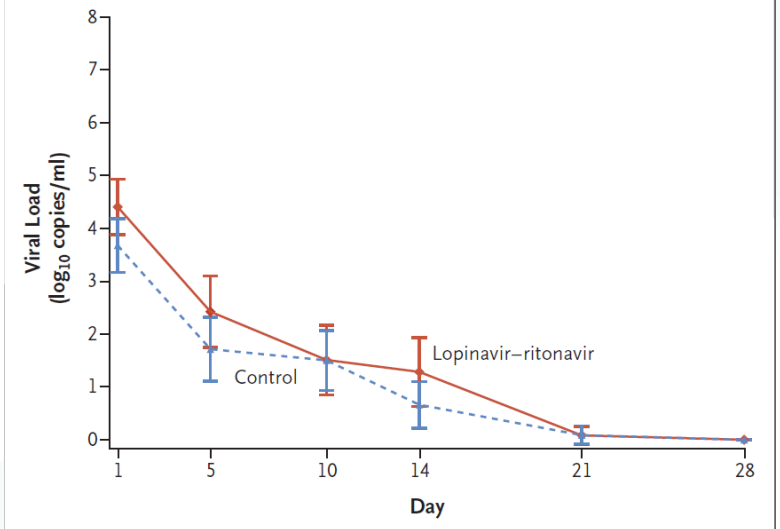


Figure 3. Mean Change from Baseline in SARS-CoV-2 Viral RNA Load by qPCR on Throat Swabs.

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

HCQ: UNIVERSITY OF MINNESOTA - USA

(launched on 17/03/2020)

Post-exposure Prophylaxis and Preemptive Therapy for SARS-Coronavirus-2: A Pragmatic Randomized Clinical Trial

DESIGN:

3000 patients / Blind & Randomized interventional study

2 arms: Hydroxychloroquine: 800 mg + 600 mg (8h) + 600 mg / day for 4 days

Placebo

PRIMARY OUTCOMES:

- Prophylaxis: Incidence of COVID19 Disease (day 14) among those who are asymptomatic at trial entry
- Therapy: Ordinal Scale of COVID19 Disease Severity at 14 days among those who are symptomatic at trial entry

SECONDARY OUTCOMES:

- Incidence of hospitalization & death, severity of symptoms.....

HCQ: WHO-sponsored SOLIDARITY trial

(launched on 20/03/2020)

DESIGN: very simple (WHO says it had to balance scientific rigor against speed).

Not double-bind; design elaborated in 2 weeks

"ADAPTIVE DESIGN" with 4 arms, that can be added or eliminated any time.

Chloroquine *or* Hydroxychloroquine / Remdesivir / Lopinavir-Ritonavir / Lopinavir-Ritonavir+Interferon-beta

END-POINTS

- The day the patient left the hospital or died
- Duration of the hospital stay
- Whether the patient required oxygen or ventilation

PARTICIPANTS-10 COUNTRIES: Argentina, Bahrain, Canada, France, Iran, Norway, South Africa, Spain, Switzerland,Thailand (Brazil)

HCQ: INSERM-France: DISCOVERY trial

(launched on 22/03/2020)

DESIGN: similar to WHO trial (*Adaptive and open*) but randomized for treatment

INCLUSION CRITERIA: Severe forms of COVID-19

DRUGS: same as SOLIDARITY (but NOT chloroquine)

END-POINTS

- Efficacy and safety will be evaluated 15 days after inclusion of each patient

PARTICIPANTS - 8 COUNTRIES:

Belgium, France, Germany Luxembourg, the Netherlands, Spain, Sweden, UK

3200 patients (target)

BRASIL:
REGISTRO BRASILEIRO DE ENSAIOS CLÍNICOS - MS

http://ensaiosclinicos.gov.br/

The Brazilian Registry of Clinical Trials (ReBEC) launches the virtual service process in extended hours and the fast track for clinical research on COVID-19.

No clinical trial has been found with the term: COVID-19

Consultado em 26/03/2020 (14:00h)

HCQ

ALBERT EINSTEIN
SOCIEDADE BENEFICENTE ISRAELITA BRASILEIRA

HCor
Associação Beneficente Síria

SÍRIO-LIBANÊS

BRICNet
Brazilian Research in Intensive Care Network

RUTE
REDE UNIVERSITÁRIA DE TELEMEDICINA

COALIZÃO COVID-19 BRASIL I, II e III

(Launched on 25/03/2020)

Estudo nacional, multicêntrico, randomizado, controlado, aberto (30 centros)

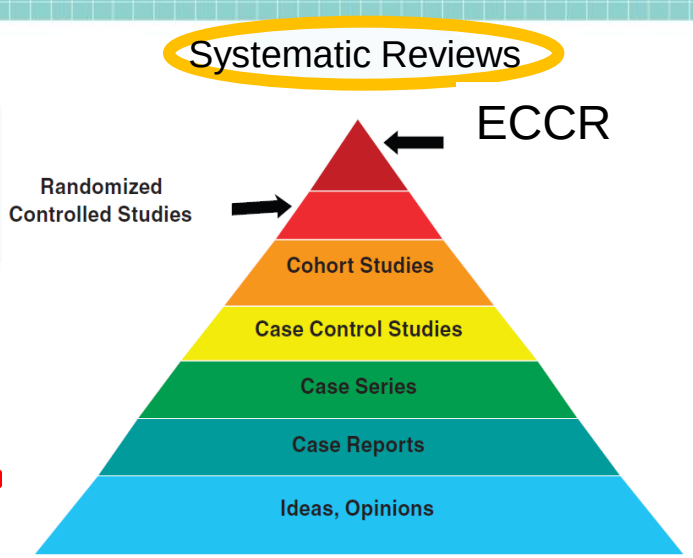
First Received	NCT ID	Brief Title	Sponsors	Phase	Commercial Product Info (Pharma)	Enrollment	Overall Status	Primary Completion Date	Intervention Type	Intervention Name
25/03/2020	NCT04321278	Safety and Efficacy of Hydroxychloroquine Associated With Azithromycin in SARS-CoV2 Virus (Alliance Covid-19 Brasil II)	Hospital Israelita Albert Einstein EMS Hospital do Coracao Hospital Sirio-Libanes Brazilian Research In Intensive Care Network	Phase 3		440	Not yet recruiting	30/08/2020	Drug	Hydroxychloroquine + azithromycin

Top

(sulfato de) Hidroxicloroquina funciona ???

- Esperamos que sim, mas

- Não "sabemos" pois não temos evidências clínicas seguras (ie. ECCR: Estudos Clínicos Controlados Randomizados com N elevado)



- Qual esquema posológico? Dose de ataque?
- Quando tratar ????

Dose de ATAQUE	MANUTENÇÃO	LOCAL
-	3X200 mg / dia (10 dias) + AZI	Raoult - Marseille
2 x 400 mg (2 dias)	400 mg / dia (3 dias)	MGH - Massachusetts
800 mg + 600 mg (8h)	600 mg / dia (4 dias)	Minnesota University
-	2x400 mg / dia (7 dias) + AZI	COVID-19 Brasil
3 x 400 mg (1 dia)	3x200 mg / dia (9 dias)	SANOFI-França

Lúpus ou artrite: ≈ 400 mg / dia (meses)
Câncer: até 1200 mg/dia

NOTA INFORMATIVA Nº 5/2020-DAF/SCTIE/MS

Brasília, 27 de março de 2020.

Ministério da Saúde

Uso da Cloroquina como terapia adjuvante no tratamento de formas graves do COVID-19.

Ministério da Saúde do Brasil disponibilizará para uso, a critério médico, o medicamento **cloroquina como terapia adjuvante no tratamento de formas graves, em pacientes hospitalizados, sem que outras medidas de suporte sejam preteridas em seu favor.** A presente medida considera que não existe outro tratamento específico eficaz

*Dispneia, frequência respiratória ≥ 30/min, $SpO_2 \leq 93\%$, $PaO_2/FiO_2 < 300$ e/ou infiltração pulmonar > 50% dentro das 24 a 48 horas

**Falência respiratória, choque séptico e/ou disfunção de múltiplos órgãos

Situação clínica	Recomendação	Considerações
Pacientes hospitalizados com formas graves da COVID-19* Casos críticos da COVID-19**	Difosfato de Cloroquina: 3 comp. de 150mg 2x/dia no 1º dia (900mg de dose de ataque) seguido de 3 comp. 150 mg 1x/dia no 2º, 3º, 4º e 5º dias (450mg/dia) OU Hidroxicloroquina: 1 comp. 400mg 2x/dia no 1º dia (800mg dose de ataque), seguido de 1 comp. 400 mg 1x/dia no 2º, 3º, 4º e 5º dias (400mg/dia)	Verifique o eletrocardiograma (ECG) antes do início, risco de prolongamento do intervalo QT. O risco é maior em pacientes em uso de outros agentes prolongadores do intervalo QT. Manter monitoramento do ECG nos dias subsequentes Na presença de insuficiência renal ou insuficiência hepática graves, reduzir a dose de cloroquina para 50%.

LINKS DE INTERESSE

1. IUPHAR: https://www.guidetopharmacology.org/coronavirus.jsp

2. Centre for Evidence-Based Medicine (Oxford)
   https://www.cebm.net/covid-19/registered-trials-and-analysis/

SIG FARMACO

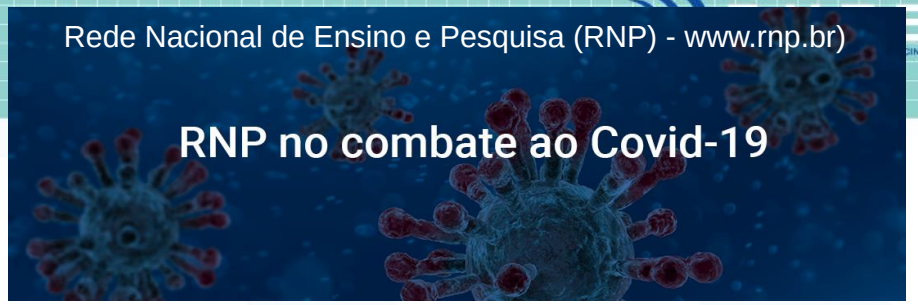
Horário das Reuniões: 9:00 as 10:30 h, terceira 4ª f de cada mês.

www.sbfte.org.br/sigfarmaco

sigfarmaco@gmail.com

2020	TEMA	COORDENADOR LOCAL/ APRESENTADOR
15/04	Metodologias ativas e o ensino de farmacologia, como inovar? (educação)	**Coordenador Local – UFAM** José Wilson N. Correa **Palestrante** - Aurea Elisabeth Linder – UFSC
20/05	Impacto da desnutrição na microbiota intestinal: importância de pre e probióticos (pesquisa)	**Coordenador Local – UFC -** Flávia Santos **Palestrante -** Aldo Ângelo Moreira Lima – UFC
17/06	Efeito do Canabidiol nas psicopatologias associadas ao Diabetes (pesquisa)	**Coordenador Local – UFPR -** Alexandra Acco **Palestrante -** Janaina Menezes Zanoveli - UFPR
15/07	Conceitos em Farmacologia: "Sinalização intra- e extracelular do cAMP: papeis complementares ou diferenciais? (pesquisa)	**Coordenador Local – UNIFESP -** Maria Christina W. Avellar **Palestrante -** Rosely Godinho/UNIFESP-EPM
19/08	Ligas acadêmicas de Farmacologia: como podem ser aliados na formação acadêmica de fato? (ensino)	**Coordenador Local – UFAM -** José Wilson N. Correa **Palestrante -** Cinthya Iamile – UFAM
16/09	Influência do Oua-Na,K-ATPase na sinalização inflamatória (pesquisa)	**Coordenador Local – UFG -** Paulo César Ghedini **Palestrante -** Jacqueline Alves Leite-UFG
21/10	Metabolômica e/ou proteômica aplicada a descoberta de fármacos (pesquisa)	**Coordenador Local – UFRJ -** Francois Noel **Palestrante -** CCS-UFRJ
18/11	Influência dos hormônios sexuais femininos no processo inflamatório e estudo das alterações e dos métodos de preservação dos enxertos empregados nos transplantes cardiotorácicos (pesquisa)	**Coordenador Local – USP -** Wothan Tavares de Lima **Palestrante** - Ana Cristina Breithaupt-Faloppa INCOR/USP
16/12	Avaliação e Agenda 2021	**Palestrantes -** Emiliano Barreto (UFAL) Maria Christina W. Avellar (UNIFESP-EPM)

SIG FARMACO



Local: Sala Virtual WebConf

http://conferenciaweb.rnp.br/webconf/rutesigfarmacologiaeterapeutica

(até a normallização do acesso em nossas instituições das salas de Telemedicina)

https://rute.rnp.br/sigs

www.sbfte.org.br/sigfarmaco

sigfarmaco@gmail.com

RNP REDE NACIONAL DE ENSINO E PESQUISA

RUTE REDE UNIVERSITÁRIA DE TELEMEDICINA

Registro de Presença nas Sessões RUTE

1) Do navegador do seu smartphone, tablet ou notebook, acesse:

www.rute.rnp.br/presenca

(ou solicite um computador disponível ao técnico de videoconferência local)

2) Informe seu **CPF**, **E-mail** e clique em "**Registrar Presença**"

(no 1º acesso, preencha **nome completo, data de nascimento, perfil, área** e **instituição**)

3) Selecione o **SIG: Farmacologia e Terapêutica**

4) A **SENHA DA SESSÃO** do SIG é: **21254**

Informe a senha e clique em **"Registrar Presença – Etapa 2"**

Avalie a sessão após registrar sua presença

O registro deve ser feito **no mesmo dia (até 23h59)** da sessão

Em caso de dúvidas ou suporte, contate o e-mail: sig@rute.rnp.br