IVERMECTIN

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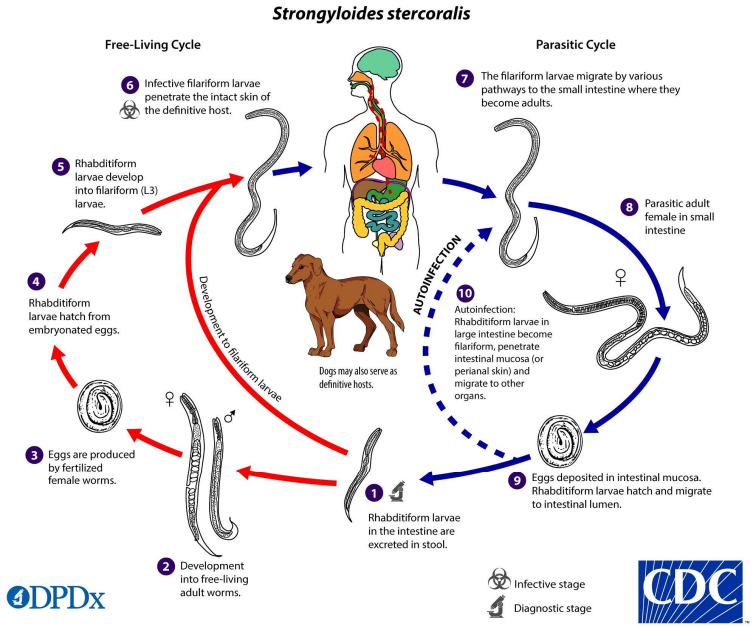
Ivermectin: Indication and Posology

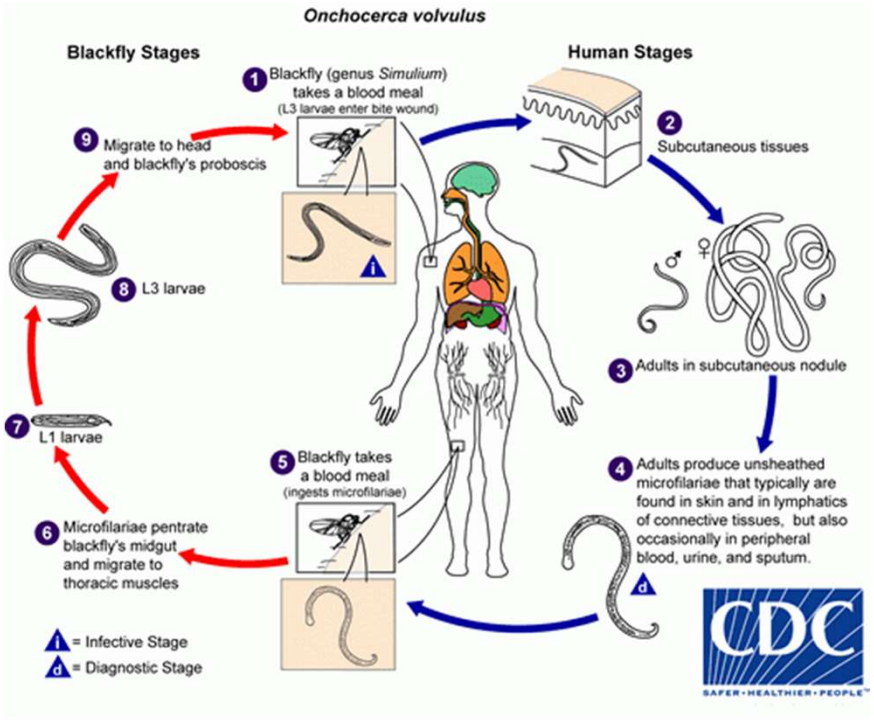
A semisynthetic, anthelmintic agent for oral administration.
Derived from the avermectins, a class of highly active broad-spectrum, anti-parasitic agents isolated from the fermentation products of *Streptomyces avermitilis*

Strongyloidiasis

- Nematode parasite *Strongyloides stercoralis*.
- RCT open-label designs, in which 64-100% of infected patients were cured following *a single 200-mcg/kg dose of ivermectin*
- 0.15 mg/kg orally once



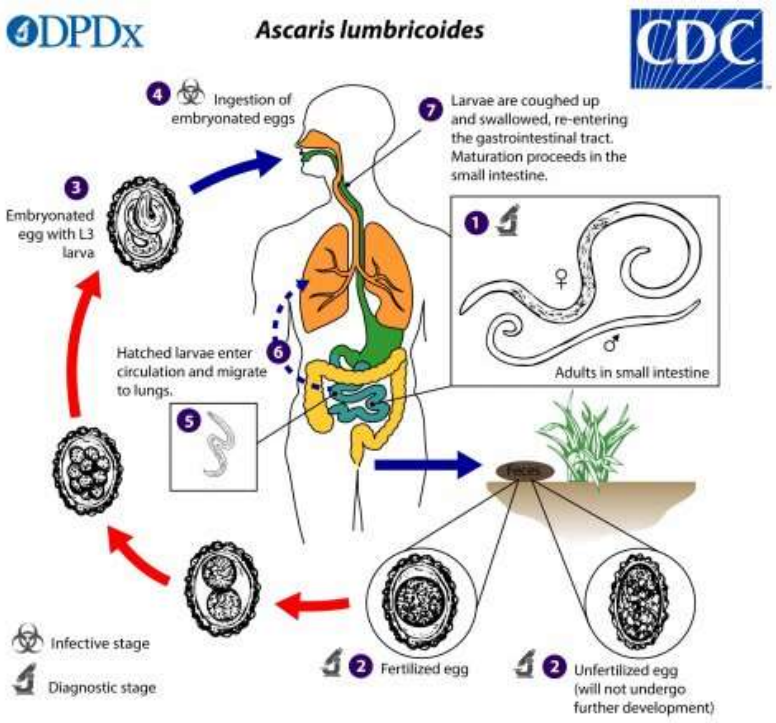
Ivermectin: Indication and Posology



Onchocerciasis

- Nematode parasite *Onchocerca volvulus*.
- RCT, double-blind, placebo-controlled in 1278 patients with moderate to severe onchocerciasis received *a single dose 150 mcg/kg ivermectin* experienced an 83.2% and 99.5% decrease in skin microfilariae count 3 days and 3 months after the dose, respectively.
- 0.15 mg/kg orally once every 12 months

Ivermectin: Indication and Posology



Others

- Ascariasis
- Filariasis: *Wuchereria bancrofti, Brugia malayi, Brugia timori*
- Cutaneous Larva Migrans
- Scabies

- 0.2 mg/kg orally once every 12 months

Pharmacokinetics of Ivermectin

Following oral administration of ivermectin, plasma concentrations are approximately proportional to the dose.

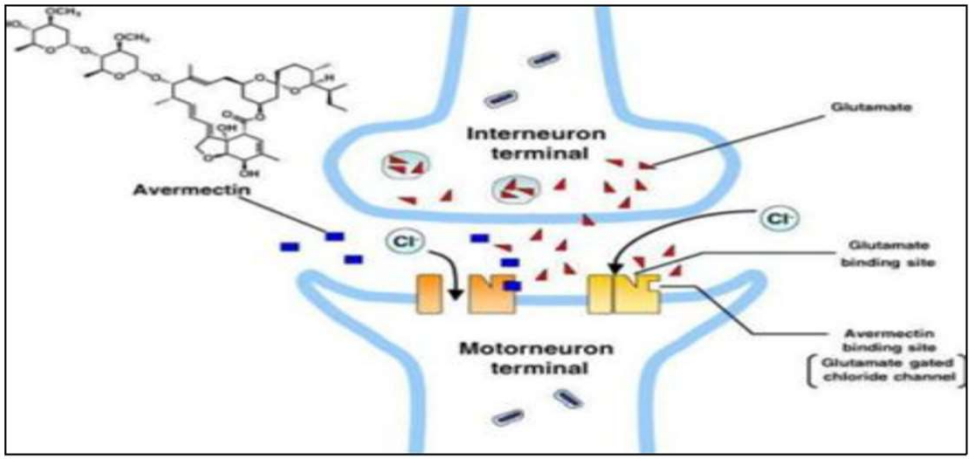
In two studies, after single 12-mg doses of ivermectin in fasting healthy volunteers (mean dose of 165 mcg/kg), 4 hours after dosing, the mean peak plasma concentrations were **46.6 (±21.9) (range: 16.4-101.1); and 30.6 (±15.6) (range: 13.9-68.4),** respectively.

Metabolized in the liver primarily by **CYP3A4**, excreted almost exclusively in the feces over an estimated 12 days, with less than 1% of the administered dose excreted in the urine.

The **plasma half-life of ivermectin is approximately 18 hours** following oral administration.

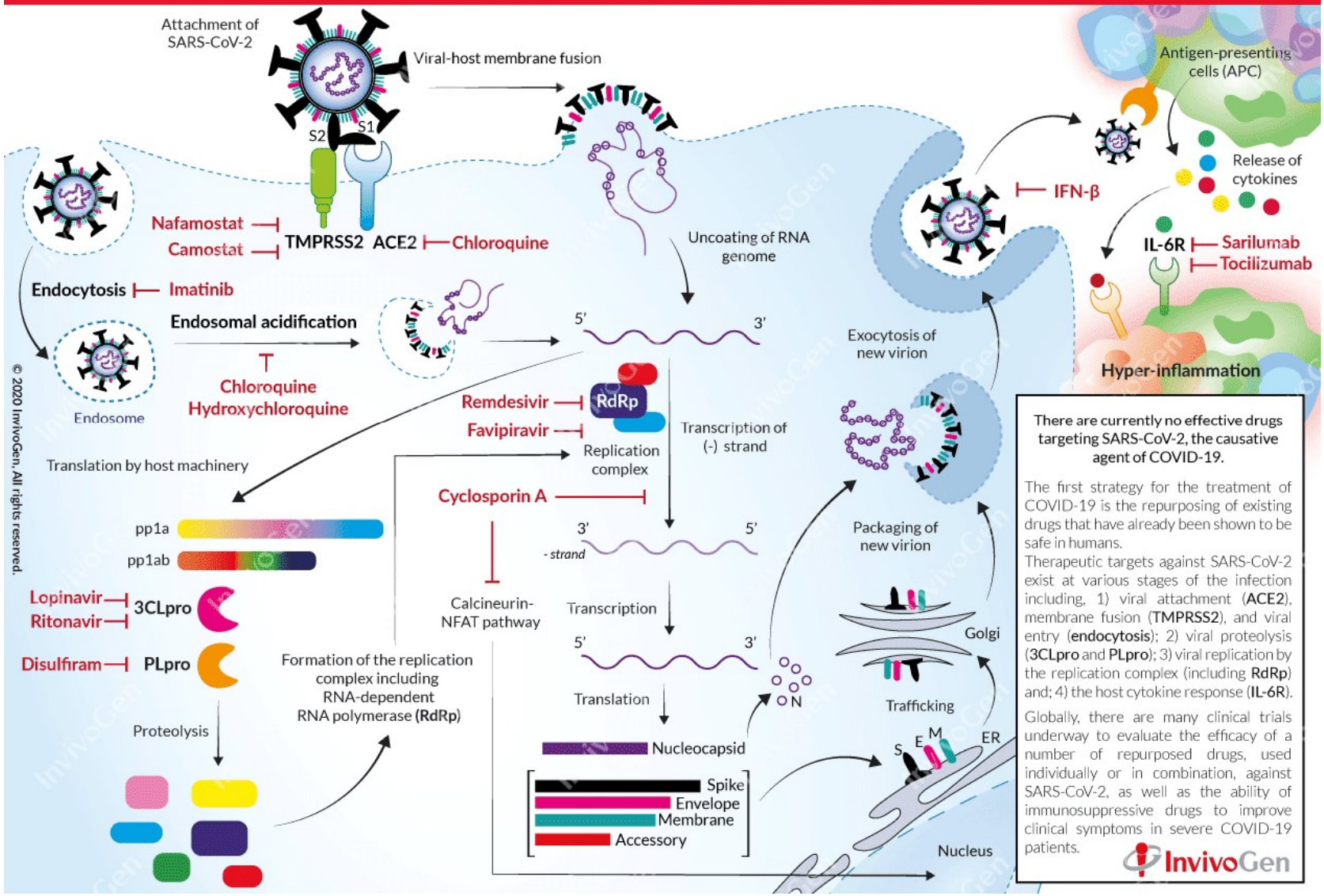
Pharmacodynamic

- It binds to **glutamate-gated chloride iron channels**, which are present in invertebrate nerve and muscle cells, and causes the **paralysis and death of the parasite**.



Al-Fatlawi et al, QJVMS (2019) Vol. 18 No. (1)

Repurposing approved drugs for targeting SARS-CoV-2



There are currently no effective drugs targeting SARS-CoV-2, the causative agent of COVID-19.

The first strategy for the treatment of COVID-19 is the repurposing of existing drugs that have already been shown to be safe in humans.

Therapeutic targets against SARS-CoV-2 exist at various stages of the infection including, 1) viral attachment (**ACE2**), membrane fusion (**TMPRSS2**), and viral entry (**endocytosis**); 2) viral proteolysis (**3CLpro** and **PLpro**); 3) viral replication by the replication complex (including **RdRp**) and; 4) the host cytokine response (**IL-6R**).

Globally, there are many clinical trials underway to evaluate the efficacy of a number of repurposed drugs, used individually or in combination, against SARS-CoV-2, as well as the ability of immunosuppressive drugs to improve clinical symptoms in severe COVID-19 patients.

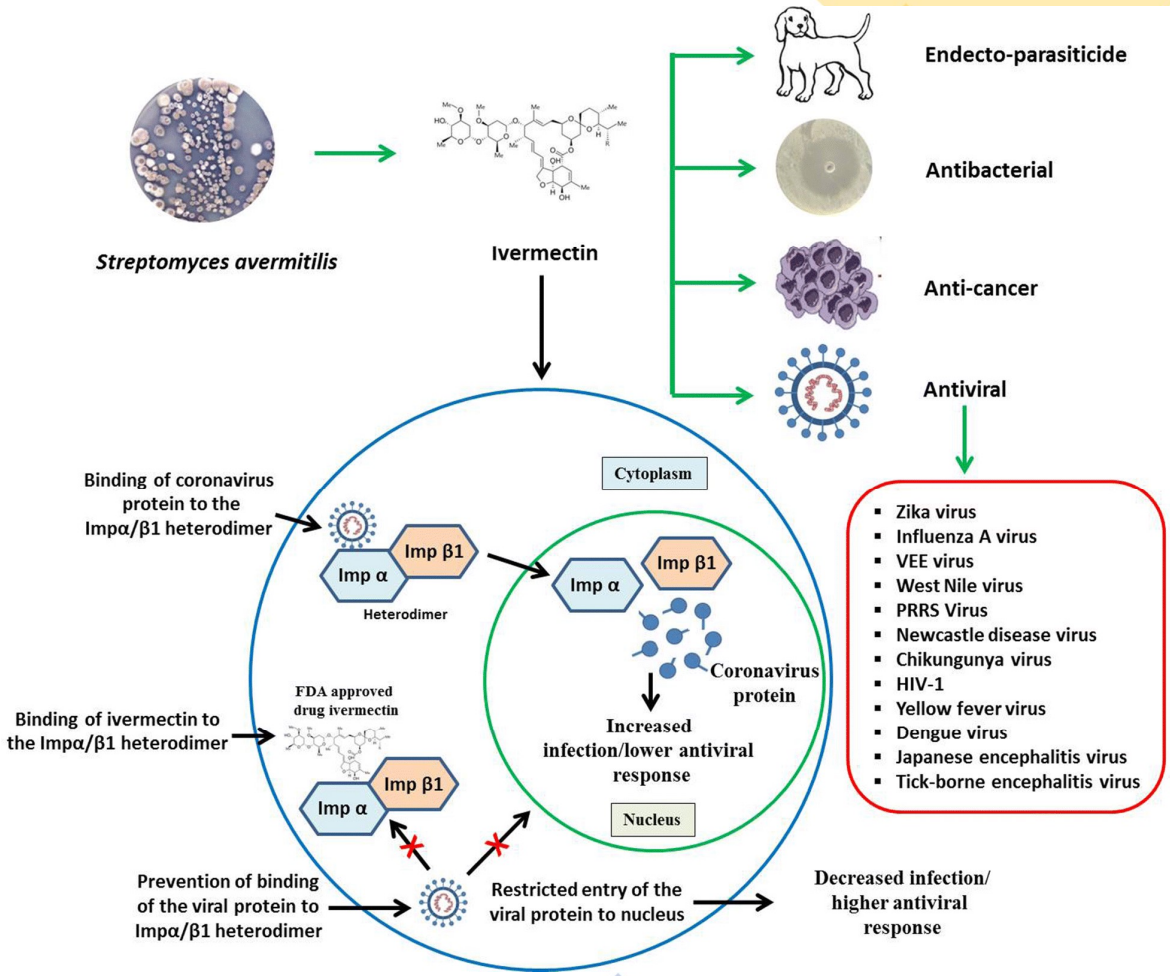
InvivoGen

IVM as Antiviral

Ivermectin against several RNA viruses is due to its ability to specifically inhibit importin α/β-mediated nuclear transport, which in turn blocks the nuclear trafficking of viral proteins.

Several RNA viruses depend on Impα/β1 during the process of infection.

SARS-CoV-2, is an RNA virus, is expected to show a similar mechanism of action



Sharun et al. Ivermectin, a new candidate therapeutic against SARS-CoV-2/COVID-1. Ann Clin Microbiol Antimicrob (2020) 19:23

ja3

Unproven efficacy for dengue

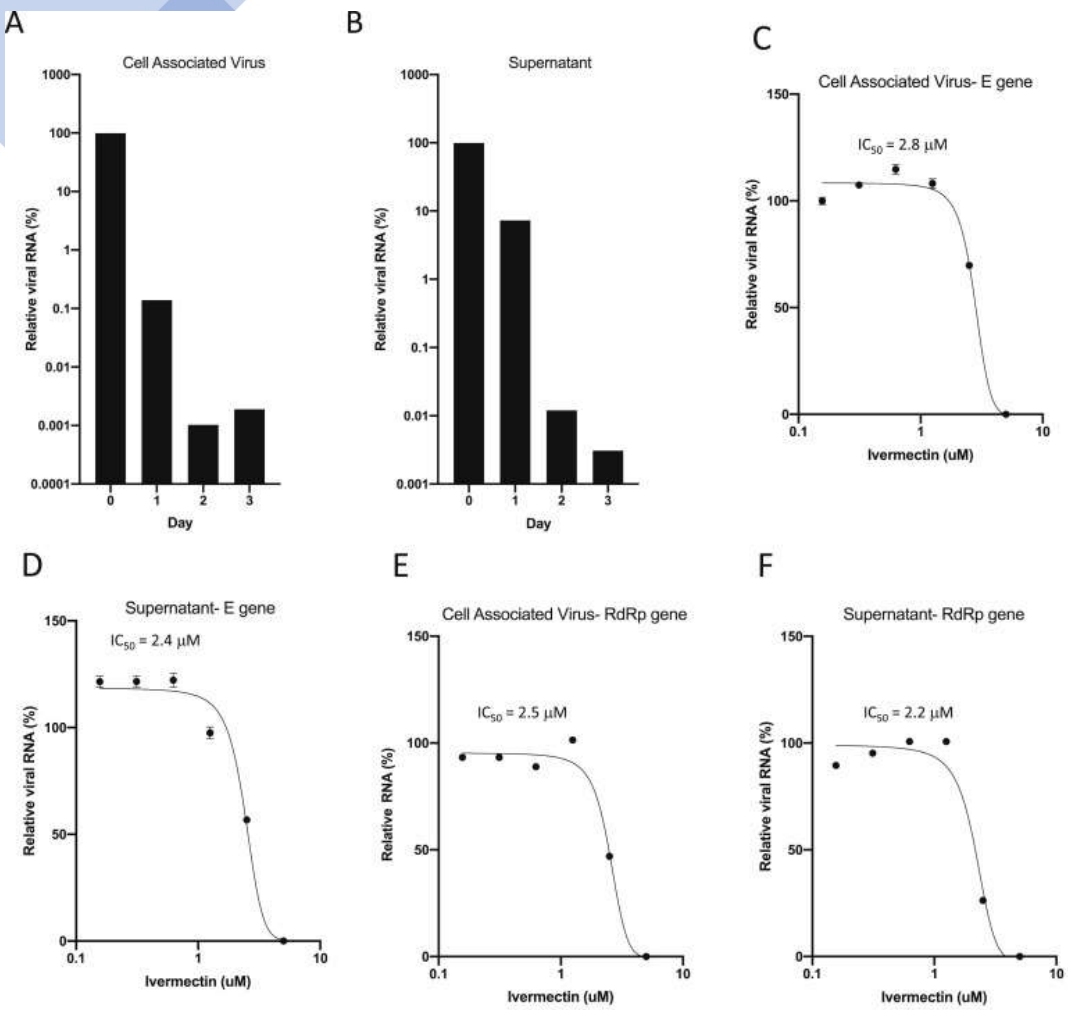
The 34th Annual Meeting The Royal College of Physicians of Thailand
'Internal Medicine and One Health'
26th - 28th April 2018, PEACH Royal Cliff Beach Resort, Pattaya, Chonburi, Thailand

Efficacy and Safety of Ivermectin against Dengue Infection: A Phase III, Randomized, Double-blind, Placebo-controlled Trial

Eakkawit Yamasmith[1]
Panisadee Avirutnan[2]
Dumrong Mairiang[2]
Sawalee Tanrumluk[1]
Yupin Suputtamongkol[1]
Fadhil A-hamad Saleh-arong[1]
Nasikarn Angkasekwinai[1]
Ekkarat Wongsawat[1]
Usanee Fongsri[1]

Slide 9

ja3 jarir atthobari, 7/21/2021



Antiviral Research 178 (2020) 104787

Contents lists available at ScienceDirect

Antiviral Research

journal homepage: www.elsevier.com/locate/antiviral

The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 *in vitro*

Leon Caly[a], Julian D. Druce[a], Mike G. Catton[a], David A. Jans[b], Kylie M. Wagstaff[b,*]

[a] Victorian Infectious Diseases Reference Laboratory, Royal Melbourne Hospital, At the Peter Doherty Institute for Infection and Immunity, Victoria, 3000, Australia
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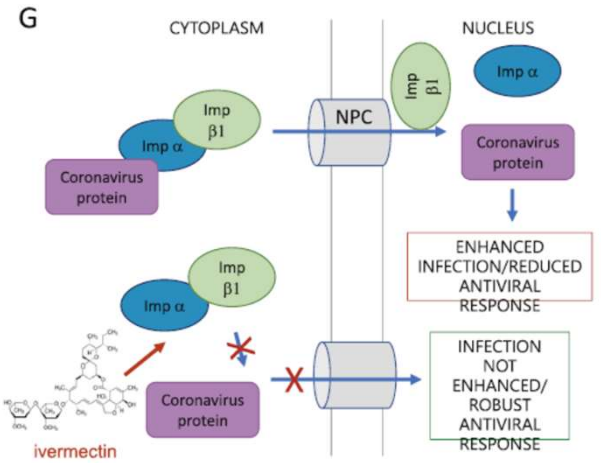
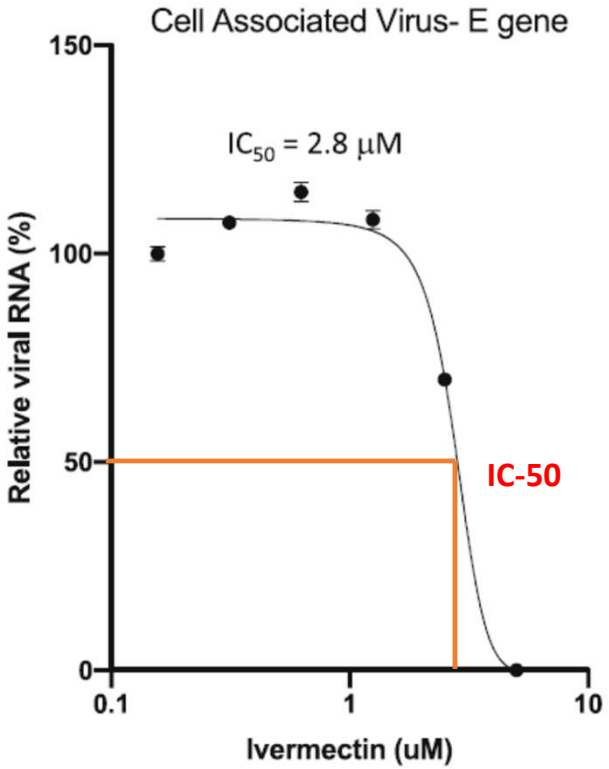
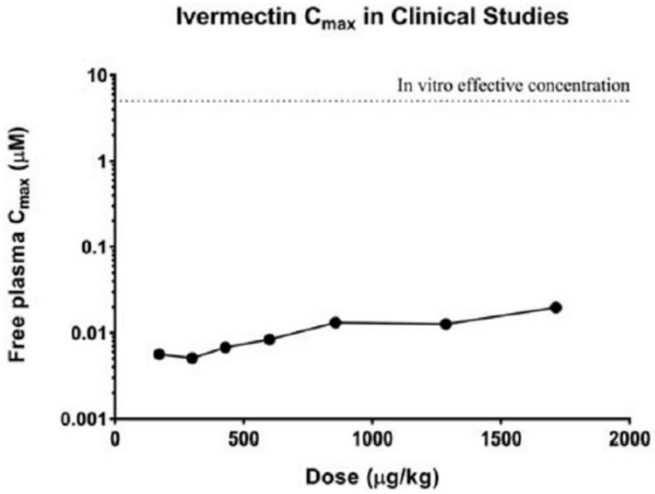
ABSTRACT

Although several clinical trials are now underway to test possible therapies, the worldwide response to the COVID-19 outbreak has been largely limited to monitoring/containment. We report here that Ivermectin, an FDA-approved anti-parasitic previously shown to have broad-spectrum anti-viral activity *in vitro*, is an inhibitor of the causative virus (SARS-CoV-2), with a single addition to Vero-hSLAM cells 2 h post infection with SARS-CoV-2 able to effect ~5000-fold reduction in viral RNA at 48 h. Ivermectin therefore warrants further investigation for possible benefits in humans.



Standard human dose vs. In-vitro dose





In the standard dose ivermectin (0.15 mg/kg= 150 µg/kg) , in Pharmacokinetic study, maximum plasma concentration was only ~ 0.025µM

The inhibitory concentration of the drug, ~5.0 µM (~200-fold more standard dosing)

Lung concentrations are a bit lower than blood concentrations but still ~100-fold more than what is needed to inhibit the virus in cells in culture.

R Peña-Silva et al., Pharmacokinetic considerations on the repurposing of ivermectin for treatment of COVID-19. Br J Clin Pharmacol. 2021 Mar;87(3):1589-1590

Published online:
06 July 202

ACCEPTED MANUSCRIPT

Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection

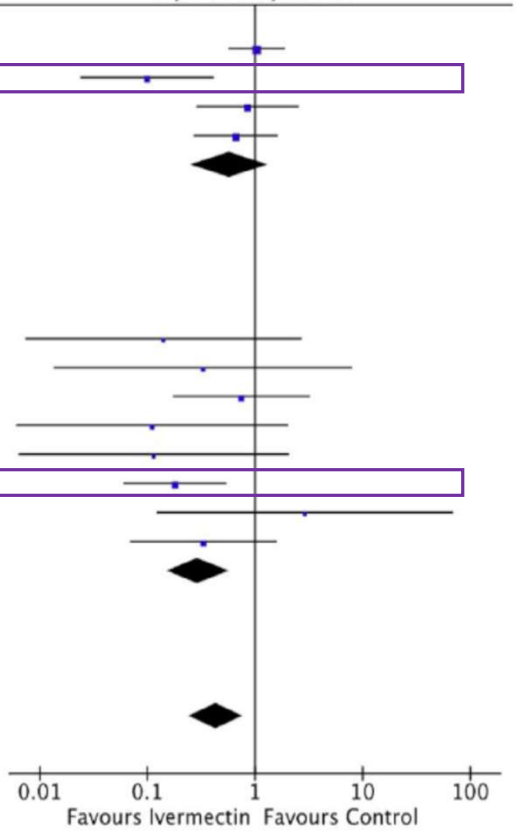
Andrew Hill ✉, Anna Garratt, Jacob Levi, Jonathan Falconer, Leah Ellis, Kaitlyn McCann, Victoria Pilkington, Ambar Qavi, Junzheng Wang, Hannah Wentzel

Open Forum Infectious Diseases, ofab358, https://doi.org/10.1093/ofid/ofab358

Peer reviewed	14 mg 3 days	Brazil Fonseca et al
Pre-print	0.4 mg/kg 5 days	Egypt Elgazzar Severe
Pre-print	0.2 mg/kg 1 days	Mexico Gonzalez et al
Peer reviewed	0.2 mg/kg 5 days	Turkey Okumus et al
Unpublished	0.2 mg/kg 1 days	Bangladesh Mahmud et al
Peer reviewed	0.3 mg/kg 5 days	Colombia Lopez-Medina et al
Unpublished	0.2 mg/kg 3 days	Egypt Abd-Elsalam et al
Pre-print	0.4 mg/kg 5 days	Egypt Elgazzar Moderate
Pre-print	12 mg 5 days	India Kirti et al
Pre-print	0.2 mg/kg 1-3 days	Iran Niaee et al
Unpublished	0.2 mg/kg 1 days	Iran Rezai et al
Pre-print	0.2-0.4 mg/kg 2-3 days	Iraq Hashim et al

1G)

Study or Subgroup	Ivermectin Events	Total	Control Events	Total	Weight	Risk Ratio IV, Random, 95% CI
4.3.1 Severe						
Brazil Fonseca et al	12	53	25	115	18.4%	1.04 [0.57, 1.91]
Egypt Elgazzar Severe	2	100	20	100	9.4%	0.10 [0.02, 0.42]
Mexico Gonzalez et al	5	36	6	37	12.5%	0.86 [0.29, 2.56]
Turkey Okumus et al	6	30	9	30	14.7%	0.67 [0.27, 1.64]
Subtotal (95% CI)		**219**		**282**	**55.0%**	**0.58 [0.25, 1.32]**
Total events	25		60			
Heterogeneity: $Tau^2 = 0.45$; $Chi^2 = 8.90$, df = 3 (P = 0.03); $I^2 = 66\%$						
Test for overall effect: Z = 1.30 (P = 0.19)						
4.3.2 Mild/moderate						
Bangladesh Mahmud et al	0	183	3	180	3.2%	0.14 [0.01, 2.70]
Colombia Lopez-Medina et al	0	200	1	198	2.8%	0.33 [0.01, 8.05]
Egypt Abd-Elsalam et al	3	82	4	82	9.1%	0.75 [0.17, 3.25]
Egypt Elgazzar Moderate	0	100	4	100	3.2%	0.11 [0.01, 2.04]
India Kirti et al	0	55	4	57	3.3%	0.12 [0.01, 2.09]
Iran Niaee et al	4	120	11	60	12.4%	0.18 [0.06, 0.55]
Iran Rezai et al	1	35	0	34	2.8%	2.92 [0.12, 69.20]
Iraq Hashim et al	2	70	6	70	8.4%	0.33 [0.07, 1.60]
Subtotal (95% CI)		**845**		**781**	**45.0%**	**0.30 [0.15, 0.58]**
Total events	10		33			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.42$, df = 7 (P = 0.61); $I^2 = 0\%$						
Test for overall effect: Z = 3.57 (P = 0.0004)						
Total (95% CI)		**1064**		**1063**	**100.0%**	**0.44 [0.25, 0.77]**
Total events	35		93			
Heterogeneity: $Tau^2 = 0.35$; $Chi^2 = 19.24$, df = 11 (P = 0.06); $I^2 = 43\%$						
Test for overall effect: Z = 2.85 (P = 0.004)						
Test for subgroup differences: $Chi^2 = 1.54$, df = 1 (P = 0.21), $I^2 = 35.1\%$						



RESEARCH ARTICLE

Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: A randomized multi-center clinical trial

Morteza Shakhsi Niaee, Nematollah Gheibi, Peyman Namdar, Abbas Allami, Leila Zolghadr, Amir Javadi, Amin Karampour, Mehran Varnaseri, Behzad Bizhani, Fatemeh Cheraghi, Yazdan Naderi, Fatemeh Amini, Masoumeh Karamyan, Mohammad Jafar Yadyad, Ramin Jamshidian

Point Estimates		Confidence Limits
Type	Value	Lower, Upper
Risk in Ivermectin groups	3.3%	1.0, 8.5
Risk in Control groups	18.3%	10.4, 30.1
Overall Risk	8.3%	5.0, 13.4
Risk Ratio	0.18	0.06, 0.55
Risk Difference	-15%	-25.3, -4.7°
Prevented fraction in Control groups	54.6%	23, 50
Prevented fraction in Ivermectin groups	81.8%	45.3, 94.0

		Group						
		Control groups (S +P)		Ivermectin Groups				
		S	P	Arm1	Arm2	Arm3	Arm4	Total
Sex	male	16 (53.3)	14 (46.7)	12 (40.0)	19 (63.3)	16 (53.3)	13 (43.3)	90 (50.0)
	female	14 (46.7)	16 (53.3)	18 (60.0)	11 (36.7)	14 (46.7)	17 (56.7)	90 (50.0)
Age (year)		55 [45 - 70]	58 [45 - 68]	61 [42 - 68]	53 [42 - 65]	54 [47 - 60]	54 [46 - 65]	56 [45 - 67]
BMI (Kg/m2)		26.0 [24.1 -27.6]	25 .6 [23.9 -26.9]	26.1 [24.8 - 28.0]	26.4 [25.5 -27.2]	27.7 [25.7 -32.6]	25.1 [23.9 -26.2]	26.0 [24.7 -27.4]
Severity on CT	negative	0 (0)	0 (0)	0 (0)	2 (6.7)	0 (0)	0 (0)	2 (1.1)
	mild	4 (13.3)	5 (16.7)	8 (26.7)	2 (6.7)	4 (13.3)	2 (6.7)	25 (13.9)
	mode	23 (76.7)	23 (76.7)	21 (70.0)	20 (66.7)	21 (70.0)	23 (76.7)	131 (72.8)
	sever	3 (10.0)	2 (6.7)	1 (3.3)	6 (20.0)	5 (16.7)	5 (16.7)	22 (12.2)
PCR	positive	18 (60.0)	14 (46.7)	23 (76.7)	23 (76.7)	29 (96.7)	21 (70.0)	128 (71.1)
	negative	12 (40.0)	16 (53.3)	7 (23.3)	7 (23.3)	1 (3.3)	9 (30.0)	52 (28.9)

Almost 30% subject is not COVID-19

ARTICLE

Efficacy and Safety of Ivermectin for Treatment and prophylaxis of COVID-19 Pandemic

Ahmed Elgazzar, Abdelaziz Eltaweel, Shaimaa Abo Youssef, Basma Hany, Mohy Hafez, Hany Moussa

Group I: 100 patients Mild/Moderate COVID-19 Ivermectin 0.4mg/kg
Group II: 100 patients Mild/Moderate COVID-19 hydroxychloroquine
Group III: 100 patients Severe COVID-19 Ivermectin 0.4mg/kg
Group IV: 100 patients Severe COVID-19 hydroxychloroquine
Group V: 100 health care (pre-exposure) ivermectin 0.4mg/kg
Group VI: 100 health care (pre-exposure) protective measures only

Table (1): Initial Laboratory data of the studied patients before starting treatment:

Variable		Group I (n =100)	Group II (n =100)	Group III (n = 100)	Group IV (n =100)	Test
Hgb (gm/dl)	Mean ±SD	12.6 ± 1.8	12.9 ± 2.1	11.2 ± 1.9	10.9 ± 1.2	ANOVA-test F = 69.1 P <0.001
	Range	10 -14	9 – 15	9 -12	10 -13	
TLC (X 103/ mL)	Mean ±SD	5.8± 1.2	6.2± 1.8	7.3± 1.4	6.9± 2.1	ANOVA-test F=11.71 P <0.001
	Range	4-9	4.3-10.2	4.8-11.2	5.1-13.7	
Lymphocyte (%)	Mean ±SD	18 ± 2.3	17 ± 3.1	16 ± 2.8	17 ± 1.9	ANOVA-test F=430 P<0.001
	Range	14 – 20	15 – 18	13 - 19	9 – 18	
CRP (mg/l)	Mean ±SD	48.4 ± 14.6	50.6 ± 18.3	64.8 ± 16.4	68.2 ± 18.5	ANOVA-test F=280 P <0.001
	Range	10 – 69	12 – 89	18 - 64	24 – 82	
Serum ferritin (ng/ml)	Mean ±SD	168.4±12.6	172±18.6	420±72.8	334±108.6	ANOVA-test F=523 P <0.001
	Range	154-186	158-194	188-472	192-630	
D dimer (mg/l)	Mean ±SD	4.8±1.8	5.4±2.1	9.6±1.2	10.2±2.8	ANOVA-test F=478 P <0.001
	Range	4.3-5.6	3.2-6.2	8.2-10.4	8.6-11.2	

STUDY WAS WITHDRAWN

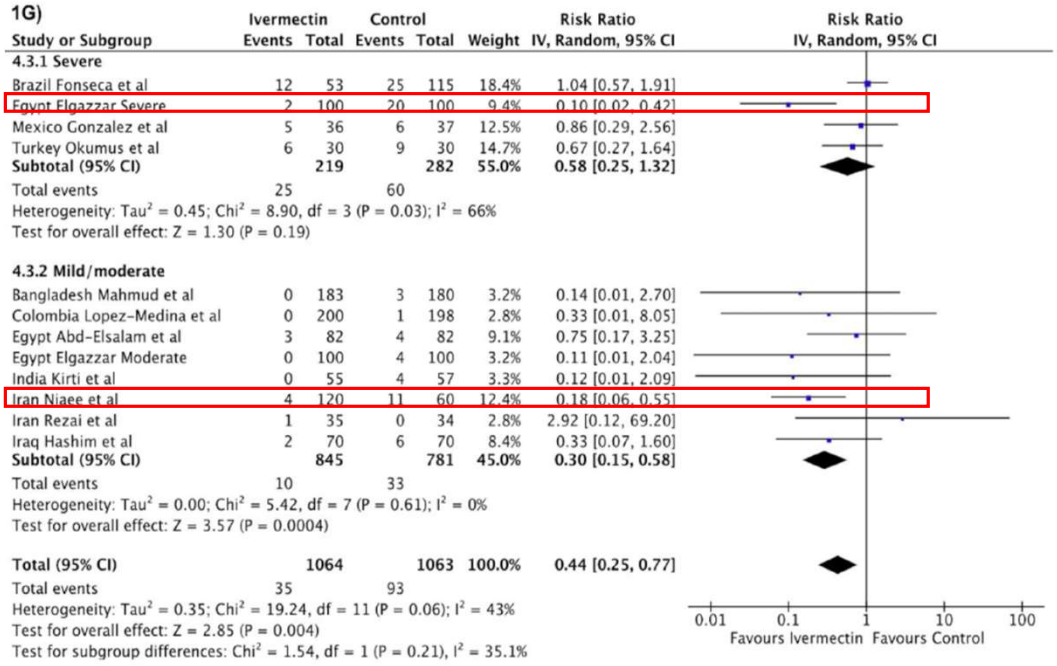
ACCEPTED MANUSCRIPT

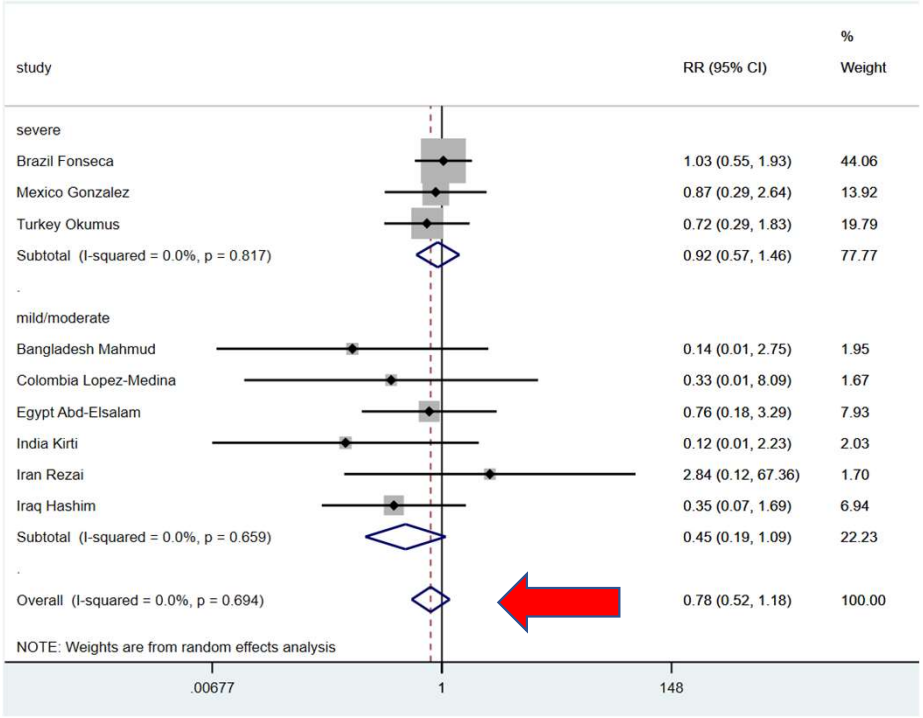
Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection

Andrew Hill ✉, Anna Garratt, Jacob Levi, Jonathan Falconer, Leah Ellis, Kaitlyn McCann, Victoria Pilkington, Ambar Qavi, Junzheng Wang, Hannah Wentzel

Open Forum Infectious Diseases, ofab358, https://doi.org/10.1093/ofid/ofab358

Excluded 2 studies with high RoB





American Journal of Therapeutics 28, e434–e460 (2021)

OPEN

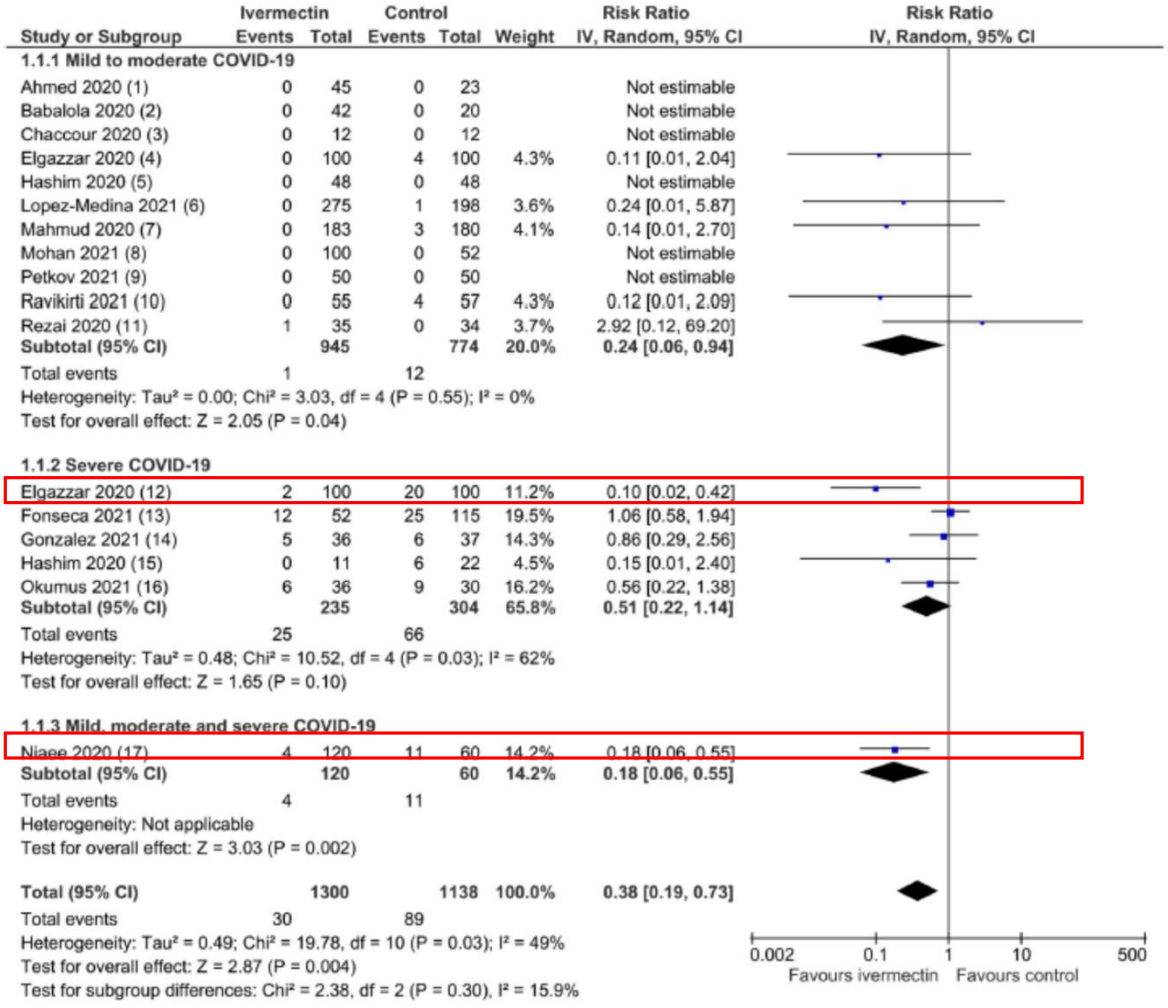
Published online 2021 Jun 21

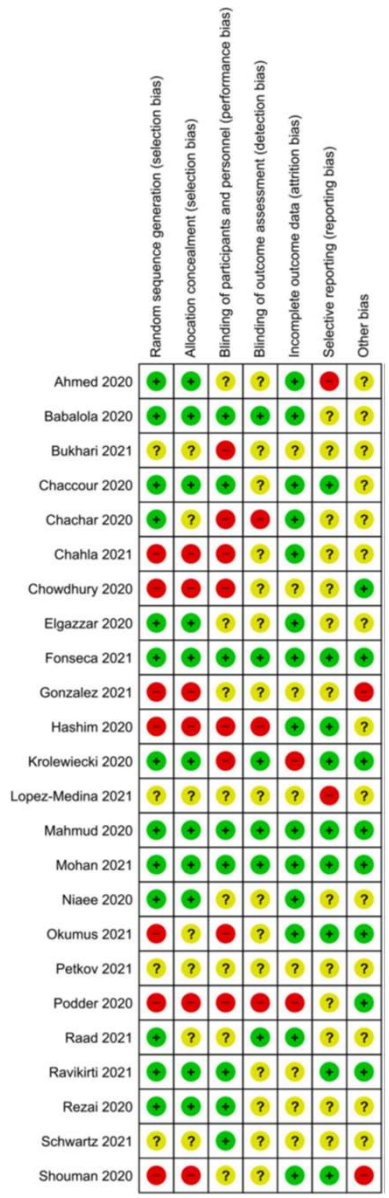
Ivermectin for Prevention and Treatment of COVID-19 Infection: A Systematic Review, Meta-analysis, and Trial Sequential Analysis to Inform Clinical Guidelines

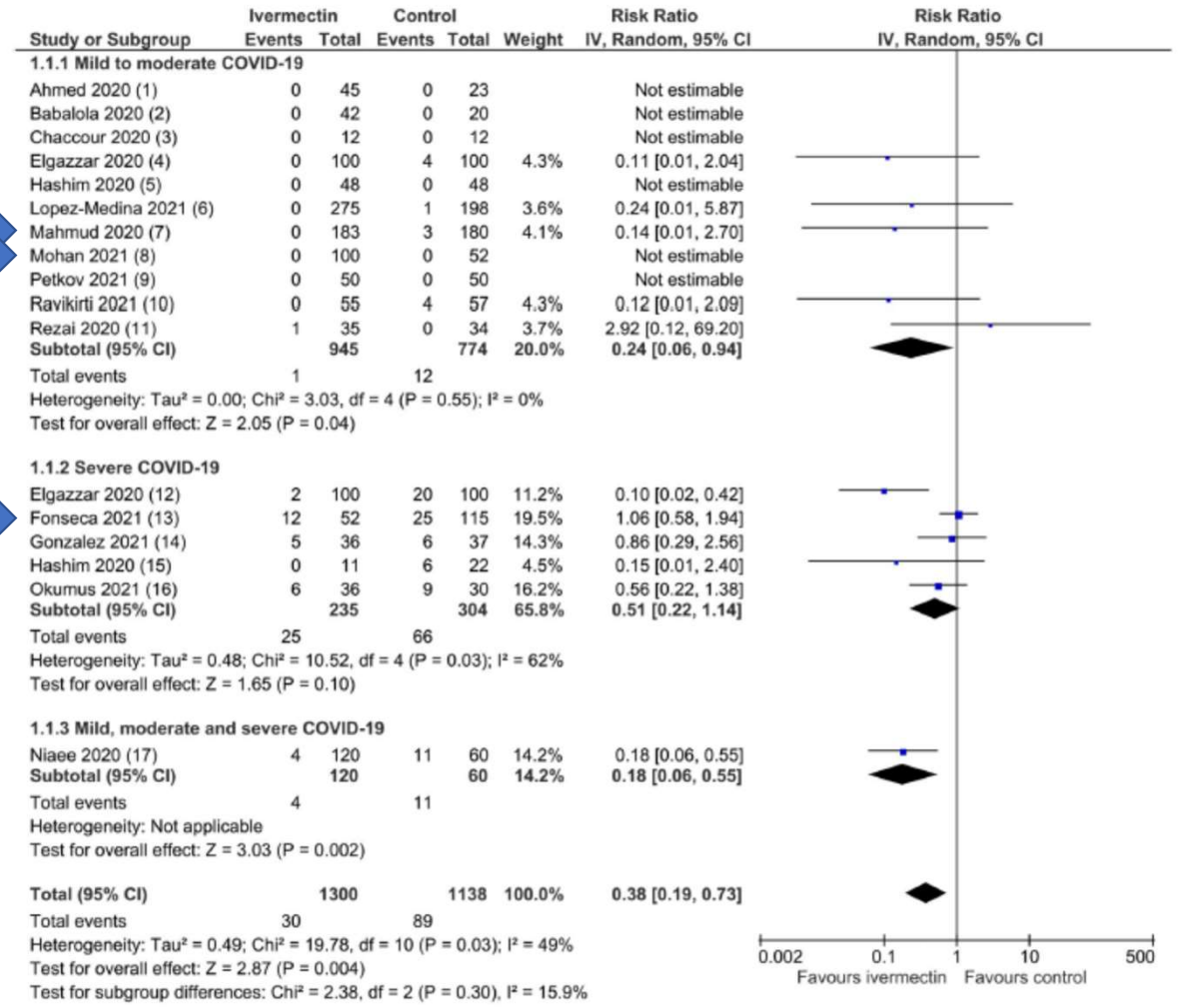
Andrew Bryant, MSc,[1]* Theresa A. Lawrie, MBBCh, PhD,[2] Therese Dowswell, PhD,[2] Edmund J. Fordham, PhD,[2] Scott Mitchell, MBChB, MRCS,[3] Sarah R. Hill, PhD,[1] and Tony C. Tham, MD, FRCP[4]

Variation of dose, duration and combination

(1) IVM 12mg x 5 days (24 pts) or IVM 12 mg + doxy x 5 days (24 pts)
(2) IVM 6mg-12mg every 84 hrs for 2 wks; vs lopinavir/ritonavir
(3) IVM 0.4mg/kg single dose
(4) IVM up to 24 mg daily for 4 days vs HCQ
(5) IVM 0.2mg/kg x 2-3 days + Doxy 100 mg BID x 10 days
(6) IVM 0.3mg/kg solution for 5 days vs placebo solution
(7) IVM 6mg once + Doxy 100 mg x 5 days
(8) IVM 12mg or 24 mg single dose
(9) IVM 0.4mg/kg x 3 days
(10) IVM 12 mg x 2 days
(11) IVM 0.2mg/kg single dose
(12) IVM up to 24 mg daily for 4 days vs HCQ
(13) IVM 14 mg x 3 days vs HCQ x 5 days or CQ x 5 days
(14) IVM single dose 12mg or 18mg depending on weight
(15) IVM 0.2mg/kg x 2-3 days + Doxy 100 mg BID x 10 days
(16) IVM 0.2mg/kg x 5 days (both arms received HCQ, favipiravir, azithromycin)
(17) IVM 0.2mg/kg to 400 µgm/kg (1 to 3 doses) vs HCQ







Manu studies in criteria Some Concerns and High Risk of Bias

Cochrane Method for Risk of Bias v2 (RoB-2)
Suggested overall risk of bias judgement

Domain 1	Domain 2	Domain 3	Domain 4	Domain 5		Overall
Low	Low	Low	Low	Low	→	Low
Low	SC	Low	Low	SC	→	SC
Low	Low	High	Low	Low	→	High
High	Low	SC	High	High	→	High
SC	SC	SC	Low	SC	→	High

Clinical Infectious Diseases

ACCEPTED MANUSCRIPT

Ivermectin for the treatment of COVID-19: A systematic review and meta-analysis of randomized controlled trials

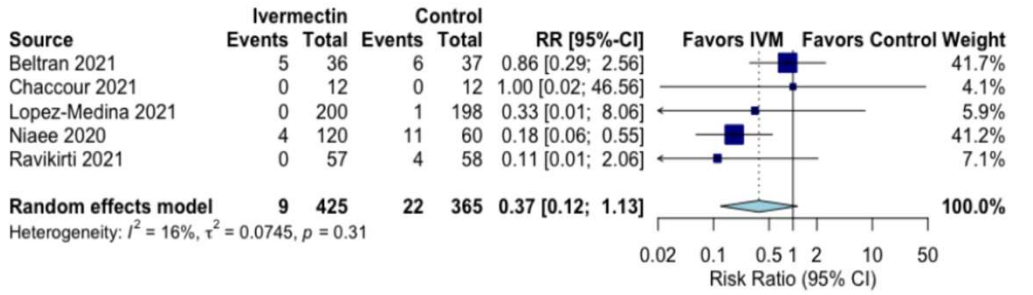
Yuani M Roman, MD, MPH, Paula Alejandra Burela, BSc, Vinay Pasupuleti, MD, PhD, Alejandro Piscoya, MD, Jose E Vidal, MD, PhD, Adrian V Hernandez, MD, PhD

Clinical Infectious Diseases, ciab591, https://doi.org/10.1093/cid/ciab591

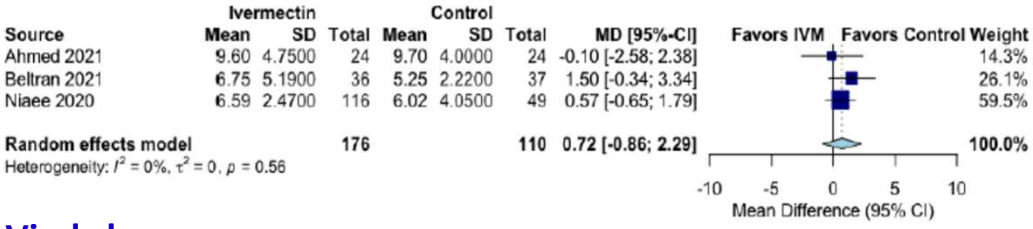
Published: 28 June 2021 **Article history**

Study ID	Experimental	Comparator	Outcome	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall
Chaccour 2021	IVM	Placebo	PCR positivity at day 7 post treatment	Low	Low	Low	Low	Low	Low
Lopez-Medina 2021	IVM	Placebo	Resolution of symptoms (days)	Low	High	Some concerns	Low	Some concerns	High
Podder 2020	IVM	Standard of care	Resolution of symptoms (days)	Some concerns	High	High	High	Some concerns	High
Ahmed 2021	IVM	Placebo	Time to virological clearence (days)	Some concerns	Low	Low	Low	High	High
Chachar 2020	IVM	Standard of care	Asymptomatic at day 7	Some concerns	Low	Low	High	Low	High
Krolewiecki 2020	IVM	Standard of care	Viral load at day 5	Low	Low	High	Low	Low	High
Niaee 2020	IVM	Standard of care	Mortality at 45 days	Low	Low	Low	High	High	High
Ravikirti 2021	IVM	Placebo	Negative PCR at day 6	Low	Low	High	Low	Low	High
Beltran 2021	IVM	Placebo	Hospital discharge	Some concerns	Low	Low	Low	Low	Some concerns
Karamat 2021	IVM	Standard of care	Viral clearence at day 14	Low	High	High	Some concerns	Low	High

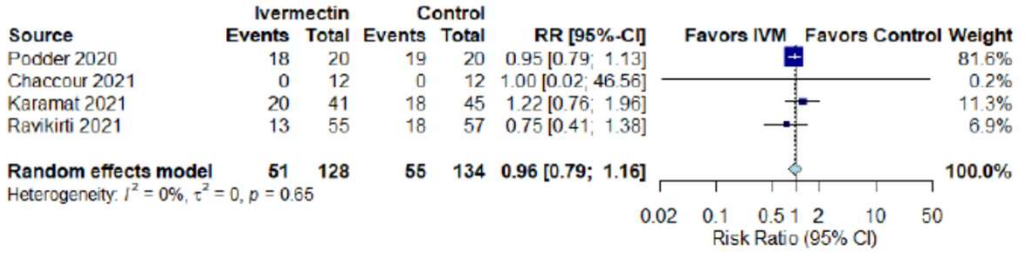
All cause mortality



Length of stay



Viral clearance



Retracted COVID-19 papers

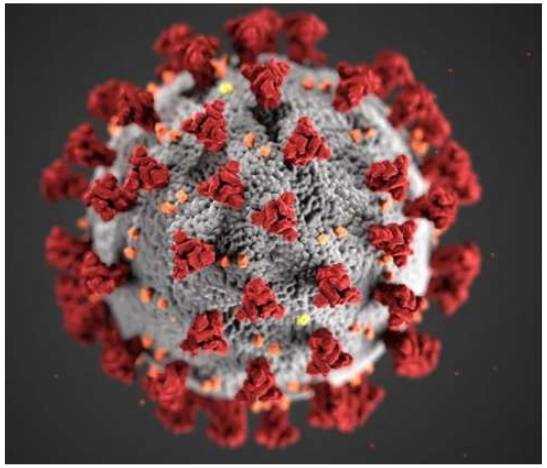
frontiers

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

Pierre Kory, MD[1]*, G. Umberto Meduri, MD[2]†, Jose Iglesias, DO[3], Joseph Varon, MD[4], Keith Berkowitz, MD[5], Howard Kornfeld, MD[6], Eivind Vinjevoll, MD[7], Scott Mitchell, MBChB[8], Fred Wagshul, MD[9], Paul E. Marik, MD[10]

1 Front-Line Covid-19 Critical Care Alliance.
2 Memphis VA Medical Center - Univ. of Tennessee Health Science Center, Memphis, TN.
3 Hackensack School of Medicine, Seton Hall, NJ.
4 University of Texas Health Science Center, Houston, TX.

Retracted coronavirus (COVID-19) papers



via CDC

[Retracted coronavirus (COVID-19) papers – Retraction Watch]

Ivermectin in COVID-19: Living guidelines with GRADE

Outcome (timeframe)	Study results and measurements	Absolute effect estimates		Certainty of the Evidence	Plain text summary
		Standard care	Ivermectin	Quality of evidence	
All-cause mortality Within 28 days of commencing treatment	**RR=0.41 (CI 95% 0.19 - 0.92)** Based on data from 1079 patients in 6 studies	53 per 1000	22 per 1000	**Low**	Ivermectin may decrease death slightly (38 events).
		Difference: 31 fewer per 1000 (CI 95% 43 fewer - 4 fewer)		Due to serious risk of bias and serious imprecision	
Invasive mechanical ventilation End of follow-up	**RR=0.75 (CI 95% 0.23 - 2.43)** Based on data from 497 patients in 4 studies	40 per 1000	30 per 1000	**Low**	Ivermectin may have little or no difference on invasive mechanical ventilation
		Difference: 10 fewer per 1000 (CI 95% 31 fewer - 57 more)		Due to serious imprecision	
Supplemental oxygen End of follow-up	**RR=1.08 (CI 95% 0.50 - 2.32)** Based on data from 114 patients in 2 studies	158 per 1000	171 per 1000	**Low**	Uncertain whether ivermectin increases or decreases requirement of supplemental oxygen
		Difference: 13 more per 1000 (CI 95% 79 fewer - 209 more)		Due to serious risk of bias and serious imprecision	

Therapeutics and COVID-19: living guideline (who.int): https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2

Ivermectin in COVID-19: Living guidelines with GRADE

Outcome (timeframe)	Study results and measurements	Absolute effect estimates		Certainty of the Evidence	Plain text summary
		Standard care	Ivermectin	Quality of evidence	
ICU admission End of follow-up	**RR=0.53 (CI 95% 0.11 - 2.51)** Based on data from 143 patients in 2 studies	115 per 1000	61 per 1000	**Low**	Uncertain whether ivermectin increases or decreases admission to ICU
		Difference: 54 fewer per 1000 (CI 95% 102 fewer - 174 more)		Due to serious risk of bias and serious imprecision	
Discharge from Hospital End of follow-up	**RR=1.06 (CI 95% 0.99 - 1.12)** Based on data from 342 patients in 4 studies	868 per 1000	920 per 1000	**Low**	Ivermectin may increase discharge from hospital slightly
		Difference: 52 more per 1000 (CI 95% 9 fewer - 104 more)		Due to serious risk of bias and serious imprecision	
Clinical Improvement End of follow-up	**RR=1.07 (CI 95% 0.94 - 1.22)** Based on data from 125 patients in 1 study	867 per 1000	928 per 1000	**Low**	Uncertain whether ivermectin increases clinical improvement
		Difference: 61 more per1000 (CI 95% 52 fewer - 191 more)		Due to very serious imprecision	

Therapeutics and COVID-19: living guideline (who.int): https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2

Ivermectin in COVID-19: Living guidelines with GRADE

Outcome (timeframe)	Study results and measurements	Absolute effect estimates		Certainty of the Evidence	Plain text summary
		Standard care	Ivermectin	Quality of evidence	
Viral clearance 7-10 days after treatment	**RR=1.30 (CI 95% 0.89 - 1.91)** Based on data from 332 patients in 4 studies	539 per 1000	701 per 1000 Difference: 162 more per 1000 (CI 95% 59 fewer - 490 more)	**Very Low** Due to very serious risk of bias and serious imprecision	Uncertain whether ivermectin increases or decreases viral clearance.
Clinical recovery Within 21 days of commencing treatment	**RR=1.04 (CI 95% 0.94 - 1.15)** Based on data from 398 patients in 1 study	788 per 1000	820 per 1000 Difference: 32 more per 1000 (CI 95% 47 fewer - 118 more)	**Low** Due to very serious imprecision	Uncertain whether ivermectin increases or decreases clinical recovery
Serious Adverse Events End of follow-up	**RR=1.12 (CI 95% 0.21 - 5.88)** Based on data from 664 patients in 5 studies	7 per 1000	8 per 1000 Difference: 1 more per 1000 (CI 95% 6 fewer - 34 more)	**Low** Due to serious risk of bias and serious imprecision	Uncertain whether ivermectin increases or decreases serious adverse events

Therapeutics and COVID-19: living guideline (who.int): https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2

WHO Recommendation on Ivermectin

We recommend not to use ivermectin in patients with COVID-19 except in the context of a clinical trial.

- Remark: This recommendation applies to patients with any disease severity and any duration of symptoms.
- A recommendation to only use a drug in the setting of clinical trials is appropriate when there is very low certainty evidence and future research has a large potential for reducing uncertainty about the effects of the intervention and for doing so at reasonable cost.

On Going Clinical Trial Ivermectin

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COVID-19 VACCINE INFORMATION | WHAT ARE CLINICAL TRIALS? | I HAVE COVID-19 NOW | I HAD COVID-19 IN THE PAST | I'M A HEALTHCARE PROFESSIONAL | NEWS & MEDIA | TOOLS & RESOURCES

Breaking News: THE U.S. GOVERNMENT IS PAUSING THE DISTRIBUTION OF MONOCLONAL ANTIBODIES BAMLANIVIMAB AND ETESEVIMAB IN HIGH-RISK COVID-19 OUTPATIENTS. THE MONOCLONAL ANTIBODIES HAVE SHOWN TO NOT WORK WELL AGAINST OTHER TYPES OF THE COVID-19 VIRUS. HEALTHCARE PROVIDERS CAN LEARN MORE HERE. LEARN IF YOU OR A LOVED ONE ARE AT A HIGHER RISK FOR COVID-19.

ACTIV-6: A Clinical Research Study

ACTIV-6 is a virtual study. It is testing medicines that are approved for treating health conditions other than COVID-19 to see if these medicines can also be used for treating COVID-19.

Call: 1-833-385-1880 | Chat Now

ACTIV-6

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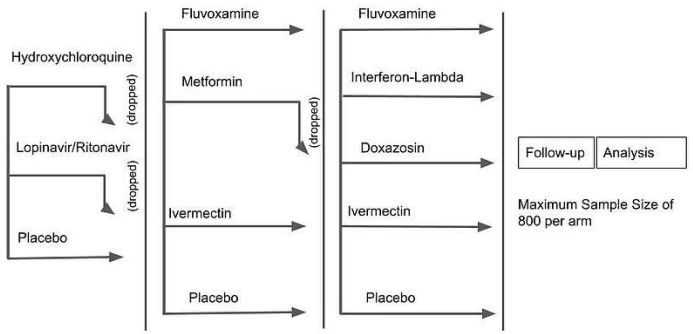

KEMENTRIAN KESEHATAN RI
BADAN LITBANG KESEHATAN
PUSAT PENELITIAN & PENGEMBANGAN SUMBER DAYA DAN PELAYANAN KESEHATAN

30.4 C jakarta Wednesday, 21 July 2021

WASPADA COVID19 | BERANDA | PROFIL | SUMBER DAYA | RISET

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Berita SD - PK

Uji Klinik Obat Ivermectin

By **Eni Yuwarni** - June 24, 2021

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Unproven Interventions in Clinical Practice

In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering.

This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available.

Expanded Access (Compassionate Use)

Expanded access is appropriate when all the following apply:

- Patient has a serious disease or condition, or whose life is immediately threatened by their disease or condition.
- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.
- Patient enrollment in a clinical trial is not possible.
- Potential patient benefit justifies the potential risks of treatment.

Take Home Message

Ivermectin inhibits the replication of SARS-CoV-2 in-vitro study, but based on current pharmacokinetic, the higher dose is need to reach similar concentration in the blood

Meta analysis has been done; the uncertainty due to high risk of bias study is high.

Living guideline base on meta-analysis and GRADE recommendation showed there are low and very low evidences for effectiveness of ivermectin in COVID-19

We recommend not to use ivermectin in patients with COVID-19 except in the context of a clinical trial

The compassionate use to use unproven intervention should be based on risk-benefit, clinical judgment, informed consent and subsequently object of research


THANK
YOU