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Ivermectin – A Potent Weapon in the Anti-COVID-19 Armamentarium

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ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic has become an earth-shattering menace afflicting the entire globe. With no effective antiviral drugs in sight, the repurposing of many currently available drugs has been considered the mainstay of treatment. One such drug is ivermectin (IVM), a Food and Drug Administration (FDA)-approved antiparasitic agent that has been shown to exhibit antiviral activity against a broad range of viruses. Ivermectin proposes many potential effects to treat a range of diseases, with its antimicrobial, antiviral and anticancer properties as a wonder drug. Several studies have reported antiviral effects of IVM on RNA viruses such as Zika, dengue, yellow fever, West Nile, Hendra, Newcastle, Venezuelan equine encephalitis, chikungunya, Semliki Forest, Sindbis, Avian influenza A, porcine reproductive and respiratory syndrome, human immunodeficiency virus type 1 and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Recent studies have suggested that IVM inhibits the replication of (SARS-CoV-2) *in vitro*, thus suggesting its potential for use against COVID-19. In this review, we describe the mechanism of action, rationale, dosing protocols of IVM in the management and prophylaxis of COVID-19 infection.

Keywords: SARS-CoV-2, antiviral drugs, ivermectin, treatment

Almost 9 months have passed in the search for the "Magic bullet" to kill the novel coronavirus since the first case was detected in Wuhan in late December 2019. The world has come to a standstill, with more than 35 million coronavirus positive cases and 1 million deaths (as on October 4, 2020). People are quickly losing patience and faith in our ability to find a cure. An effective vaccine is at least 6-9 months away. There is a ray of hope in the antiparasitic drug named Ivermectin (IVM).

This 4-decade-old drug is FDA-approved for many other parasitic infections. It has been extensively used in India, given as an oral tablet, once or twice a year, on Anti-Filaria Day, where it has been effective to control filariasis. Can this be replicated for coronavirus disease 2019 (COVID-19) too? For this "wonder drug", Satoshi Omura, a Japanese scientist who discovered it in 1970's and William Campbell who commercialized it in 1981, were awarded the Nobel Prize for Medicine in 2015.[1] In a recent paper by Caly et al, IVM inhibited the replication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) *in vitro* and ~5000-fold reduction in viral RNA was observed at 48 hours.[2] A number of trials, studies and case reports have appeared in literature, covering the entire severity spectrum of COVID-19. During the viremic phase, it has the potential to convert reverse transcription polymerase chain reaction (RT-PCR) positive to negative quickly. In the symptomatic and pulmonary phase, it disrupts the viral propagation and improves survival. In the stage of complications, it has the potential to significantly decrease mortality by preventing clot formation and reversing happy hypoxia with higher IVM doses. Such encouraging results obtained with the use of IVM alone or in combination with other medications have appeared in literature. All in all, IVM decreases severity, duration and community spread of infection.

IVERMECTIN – A MULTIFACETED "WONDER" DRUG

Ivermectin – a drug derived from avermectin, has an extraordinary history. It is a semisynthetic analog of the

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natural product avermectin B1a, a lipophilic macrolide isolated from *Streptomyces avermitilis*. It was initially developed as insecticide for crop management and later used as an antihelminthic. William C Campbell and Satoshi Ōmura were awarded the Nobel Prize in Physiology or Medicine in 2015, for discovering avermectin, the derivatives of which have drastically lowered the incidence of river blindness and lymphatic filariasis. The plethora of evidence from publications on IVM has surprised us with new indications appearing ever so often, from antihelminthic to antibacterial to anticancer and now antiviral effects. It has been found to be effective against certain flavivirus (dengue fever, Japanese encephalitis and tick-borne encephalitis virus) and chikungunya. In a recent *in vitro* study by Caly and his team at Monash University's Biomedicine Discovery Institute (BDI) and the Peter Doherty Institute of Infection and Immunity, it was found that the exposure of Vero/hSLAM (human signalling lymphocyte-activation molecule) cells infected with the SARS-CoV-2 or COVID-19 virus, to 5 μM IVM, kills SARS-CoV-2 virus in the lab, with 93% reduction in viral RNA in 24 hours and 99.8% in 48 hours, i.e., a 5,000-fold reduction in viral RNA load (killing almost all the viruses). This indicated that IVM could form the basis of a COVID-19 treatment protocol, given that it has proven successful in *in vitro* tests against the viruses.[2] Ivermectin is an old molecule with proven safety. It is FDA-approved for treatment of parasitic infections. Ivermectin is widely available due to its inclusion on the World Health Organization (WHO) model list of essential medicines. It has been used in India in the mass drug administration program under the Ministry of Health and Family Welfare (MoHFW), for eradication of lymphatic filariasis.[3] Human studies will be required to test its efficacy against the coronavirus, which has a potential for repurposing.

IVERMECTIN – MECHANISM OF ACTION

The current COVID-19 pandemic is caused by SARS-CoV-2, a single-stranded positive sense RNA virus that is closely related to SARS-CoV of 2002. There are multiple avenues by which the drug is effective in SARS-CoV-2 infection:

Inhibition of Viral Replication

Ivermectin selectively inhibits host importin $\alpha/\beta1$ transporter protein which decreases translocation (shutting) of SARS-CoV nucleocapsid protein (NCP) from the cytoplasm to the nucleus. Altered NCP distribution disrupts viral propagation and survival. This is a vital step in viral pathogenesis and defense against host immune response.[2]

Blockade of the Entry of the Virus into the Host Cell

Ivermectin also attaches to a spike receptor binding domain attached to angiotensin-converting enzyme 2 (ACE2) receptor, preventing the entry of the virus into the host cell.[4]

Action as an Ionophore Molecule

Ivermectin binds to metal cations like zinc and forms lipid-soluble complexes that facilitate their transport across cellular membranes, and deregulate osmosis and direct cytotoxic effects killing the cell. This is achieved at concentrations that are easily reachable clinically.[5,6]

Prevention of Microvascular Thrombosis

Ivermectin normalizes the microvascular abnormalities by alleviation of CD147-mediated "catch and clump mechanism", which is responsible for silent hypoxia. The CD147 receptors on red blood cells (RBCs) are a key to adhesion for the SARS-CoV-2 virus, which gets blocked by IVM. This prevents microvascular thrombosis and alleviates intravascular clumping and agglutination. However, this process is dependent on the IVM concentration.[7]

Sequestration in the Pulmonary Tissue

Ivermectin has been found to selectively concentrate in the pulmonary tissue, around 3 times the plasma concentration and is sequestered in the pulmonary tissue with a long residence time.[8]

SYNERGISTIC EFFECT WITH OTHER ANTI-COVID DRUGS

Ivermectin can be used with other drugs with synergistic effect.

- Ivermectin-Doxycycline-Zinc triple drug therapy: The miraculous antiviral effect of IVM-zinc-doxycycline combination in COVID-19 patients is possibly due to the following actions:[9]
  - Inhibition of spike-ACE2 and thereby blocking the virus entry
  - Chelation of the zinc and immunomodulatory property
  - Inhibition of viral RNA replication within the host cell.

- Ivermectin and hydroxychloroquine (HCQ) combination therapy: It has also been hypothesized that combination therapy using HCQ and IVM may exert a synergistic inhibitory effect where both block ACE2 receptors,[10] whereas IVM further enhances the antiviral activity by inhibiting viral replication.[11]

DOSING AND PHARMACOKINETICS

Ivermectin has a wide therapeutic index and is widely used in humans for treatment of parasitic diseases at single or repeated doses. It has a proven safety profile when taken orally as a tablet. Recommended safe dose is 150-200 μg/kg body weight per day and a weight-based dosing chart is depicted in Table 1. The IVM dose and duration can be tailored to the severity of disease based on various clinical studies.

Despite the enterohepatic circulation, its effect is short-lived (6-11 days). Previous studies have shown doses up to 2,000 μg/kg (i.e., 10 times the US FDA approved dose) are well-tolerated and safe.[12] Ivermectin is extensively metabolized *in vitro* by liver microsomal cytochrome P450 3A4 to hydroxylated and demethylated metabolites. The mean half-life of IVM, when administered orally, ranges from about 15 to 20 hours. It is eliminated mainly in the feces, with minimal urinary excretion (≤1% of the administered dose). From past 25 years of experience, no resistance to this novel drug has been reported in humans for tropical diseases.[13] Bioavailability of IVM increases about 2.5 times when administered with a high fat meal.[14] Ivermectin should be taken at least 2 hours after the meal. Further, citrus juice, milk and alcohol should be avoided.[15]

ADVERSE REACTIONS

Ivermectin is generally well-tolerated. Adverse effects, which are mild and transient in nature, include diarrhea, muscle or joint pain, dizziness, fever, headache, fast heartbeat, skin rash and itching. A very serious allergic reaction to this drug is rare. Ivermectin should not be given to patients with chronic liver disease with cytochrome P450 disorder and seizure disorder.[16]

Table 1. A Weight-based Dosing Regimen for Ivermectin Use in COVID-19 Infection

Body weight	Dose
Below 2 years & <15 kg	Not allowed
15-30 kg	6 mg/day
31-60 kg	12 mg/day
61-90 kg	18 mg/day
>90 kg	24 mg/day

SPECIAL POPULATIONS[17]

Pregnancy

Ivermectin has not shown any teratogenic effect during pregnancy. There is; however, scarcity of adequate and well-controlled studies in pregnant women. Ivermectin should not be used during pregnancy since safety in pregnancy has not been established.

Nursing Mothers

Ivermectin is excreted in human milk in low concentrations. Treatment of mothers who wish to breastfeed should be undertaken only when the risk of delayed treatment to the mother outweighs the possible risk to the neonates.

Pediatric Use

Safety and effectiveness in pediatric patients weighing less than 15 kg are not known.

Geriatric Use

Clinical studies of the drug did not include sufficient numbers of subjects aged 80 and above to determine if they respond differently from younger subjects. Other reported clinical experience has not shown differences in responses between the elderly and younger patients.

Miscellaneous

Need caution in prescribing IVM to patients with seizures and liver disease.

INDICATIONS IN COVID-19

It is indicated in a broad range of COVID patients, ranging from those who are asymptomatic, mildly symptomatic, to those with moderate-to-severe COVID-19 disease. Latest trial results show that it works very well in protecting close contacts and family members of COVID-positive patients. While waiting for an effective vaccine, it can be used as a prophylactic in healthcare workers and COVID warriors. It is to be mentioned here that more than 500 doctors have lost their lives in the war against COVID-19. It is a big loss for us, including medical fraternity, community and country at large. Understanding COVID-19 infection and its impact on health workers is crucial not only for

characterizing the transmission pattern of the virus but also as a means of prevention of the infection amongst the providers of healthcare who have a key role in saving the world from this pandemic.[18] Mass treatment with IVM is an underutilized public health strategy today.

PROPHYLAXIS

The suggested prophylaxis regimens with the drug are summarized below (Fig. 1):

- For contacts of COVID-19 positive patients: 200 μg/kg body weight per day doses on Day 1 and 7.
- COVID warriors, including healthcare workers: 200 μg/kg body weight per day doses on Day 1, 7, & 30 and monthly thereafter for 6 months.

IVERMECTIN FOR COVID-19 IN INDIA

A total of 10 trials are underway as listed in in the Clinical Trials Registry - India (CTRI), but recruitment of patients is very slow. Their results are awaited. Recently, a white paper has been published on IVM by Indian experts and this is a proud moment for us that the paper is reflected on WHO website.[19,20]

Uttar Pradesh Model[21]

The health department of the government of Uttar Pradesh issued an order to replace HCQ with IVM and doxycycline to treat:

- COVID-19 patients
- Close contacts
- As a prophylaxis for healthcare workers.

This drug should not be given to pregnant women and children below 2 years of age.

New Delhi's Lok Nayak Hospital has added IVM and remdesivir to the management protocol for COVID-19 patients.[22] The Tata Main Hospital, Jamshedpur has also included IVM and doxycycline combination in their armamentarium to fight against COVID-19.[23] The Assam state government has also included IVM in their protocol to treat mild-to-moderate COVID cases.[24]

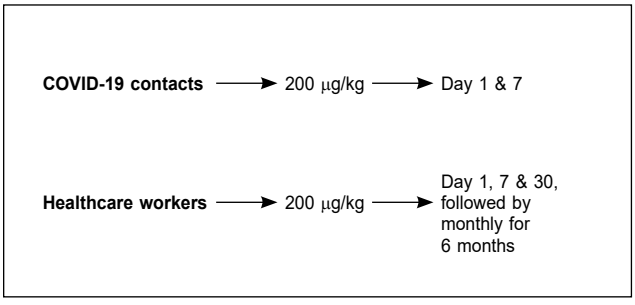

Figure 1. Prophylaxis regimens for ivermectin according to clinical scenarios in COVID-19 infection.

Cost and Availability of Ivermectin in India

Ivermectin therapy costs less than Rs. 1000 (15 USD) for the complete course (at a dose of 12 mg BID for 3-7 days). Ivermectin is easily available at retail stores throughout India at the price of INR 20-35 approximately per 12 mg tablet. In short, IVM can justify the abbreviation "I-SEE" i.e., Ivermectin is Safe, Effective and Economical. This is an easily available and affordable therapeutic option.[8]

INTERNATIONAL STATUS

Latin American Scenario

In mid-April 2020, just after the publication of the Monash study, physicians in the Dominican Republic were compelled to use IVM in mild-to-moderate COVID-19 cases due to unavailability of HCQ. They treated 150 cases successfully without any mortality. Encouraged by the astounding results, doctors in Peru voluntarily administered IVM to a large population. Peru became the epicenter of the movement for off-label use of IVM. Backed by sufficient evidence, the government accepted it as a therapeutic option.[25] In Beni, a district of Bolivia, the government handed out 3,50,000 doses of this drug for mildly symptomatic patients.[26] Brazil, Colombia and Argentina followed the trend.

Bangladesh

Several studies and a trial have been completed and published in Bangladesh. They used IVM and doxycycline to reduce COVID-19 symptoms in patients in just 3 days. They also tested RT-PCR negative in the next 4 days. Trial showed nearly 100% success without any mortality. Treating COVID-19 cases early saves patients from severe, critical disease and decreases mortality by 20%.[27,28]

Australia

To combat the Australian COVID-19 crisis, triple drug combination of IVM, doxycycline and zinc is being promoted. These three medicines are already approved and are listed in Australian Therapeutic Goods Administration.

United States of America

Two observational studies have been completed with favorable results of IVM in the treatment of COVID-19

patients. A dynamic research organization in Ventura, California, named Progenabiome, LLC is set to start a Phase 2 clinical trial titled "A Phase II Double-blind Randomized Placebo-controlled Trial of Combination Therapy to Treat COVID-19 Infection." The intervention arm includes IVM as well as the antibiotic doxycycline, zinc, vitamin D3 and vitamin C.[29]

Global Clinical Trials and Observational Studies on Ivermectin

There are around 50 clinical trials currently going on globally. Of these, 3 trials have been completed, and their results are being evaluated.

Efficacy of ivermectin as add-on therapy in COVID-19 patients

This pilot clinical trial was conducted among hospitalized adult patients with mild-to-moderate COVID-19 diagnosed in line with the WHO interim guidance. Sixteen patients were administered a single dose of IVM 200 μg/kg on admission as add-on therapy to HCQ and azithromycin (AZT) and were compared with 71 controls who were given HCQ and AZT, matched in age, gender, clinical features and comorbidities.

Primary outcome target: Percentage of cured patients, defined as symptoms free to be discharged from the hospital and 2 consecutive negative PCR tests from nasopharyngeal swabs at least 24 hours apart.

Secondary outcomes target: Time to cure in both groups, assessed by measuring time from admission of the patient to the hospital till discharge.

Among 87 patients, the mean age ± SD (range) of patients in the IVM group was similar to controls (44.87 ± 10.64 [28-60] vs. 45.23 ± 18.47 [8-80] years, p = 0.78). Majority of patients in both the groups were male but it was statistically not significant. All the patients in the IVM group were cured compared with the controls (16 [100%] vs. 69 [97.2%]). The mean time of hospital stay was significantly lower in IVM group compared with the controls (7.62 ± 2.75 vs. 13.22 ± 5.90 days, p = 0.00005, effect size = 0.82). No adverse events were observed.

The study concluded that add-on IVM to HCQ and AZT was associated with better effectiveness, shorter hospital stay, and was relatively safe compared with controls. However, a larger prospective study with longer follow-up may be needed to confirm the findings.

Prophylactic ivermectin in COVID-19 contacts

A randomized controlled trial on prophylactic use of IVM enrolled 304 participants. Albeit 59 out of 101 in the control group that didn't receive IVM prophylaxis developed COVID-19 (58%). Out of 203 in the IVM group, only 15 (7.4%) developed COVID-19. The trial was conducted on family members and close contacts of confirmed COVID-19 cases.

A comparative study on ivermectin and hydroxychloroquine on COVID-19 patients in Bangladesh[30]

The study enrolled 116 patients who were divided randomly into two groups. Ivermectin 200 μgm/kg single dose + doxycycline 100 mg BID for 10 days was given to patients in Group A, and HCQ 400 mg 1st day, followed by 200 mg BID for 9 days + AZT 500 mg daily for 5 days was administered to patients in Group B. All patients in Group A exhibited a negative PCR for SARS-CoV-2, at a mean of 8.93 days, and all attained symptomatic recovery, at a mean of 5.93 days, with 55.10% symptom-free by the 5th day. In Group B, 96.36% patients exhibited a negative PCR at a mean of 6.99 days and were symptom-free at 9.33 days. Ivermectin-Doxycycline combination showed a trend towards superiority to the HCQ-AZT combination therapy in patients with mild-to-moderate COVID-19, though the difference in time to becoming symptom-free and the difference in time to negative PCR was not statistically significant.

Completed Observational Studies

USA: ICON (Ivermectin in COvid Nineteen Ivermectin in COVID-19) study by Rajter et al showed significantly lower mortality rates in those who received IVM compared with usual care (15% vs. 25.2%; p = 0.03). It was a retrospective cohort study (n = 280) in hospitalized patients with confirmed SARS-CoV-2 infection. The mortality rate was also lower among the 75 patients with severe pulmonary disease treated with IVM (38.8% vs. 80.7%; p = 0.001), although the rate of successful extubation did not differ significantly.[31]

Dominican Republic Study: Ivermectin was administered in 1,300 early stage COVID-19 patients. Treatment began with a standard dose of 100-200 μg/kg and escalated to 400 μg/kg. Some of the patients also received AZT. Nearly 99% of them were cured. Average duration of full infection went down from 21 days to 10 days. Ivermectin starts inhibiting the virus within a couple days in humans. Only side effects reported were mild heartburn and diarrhea.[32]

Bangladesh: A comparative study included 400 COVID-19 positive patients who were divided into two groups - Group A received IVM with doxycycline while Group B received HCQ with AZT. Viral clearance was noted in 66% on Day 5 and 83.5% on Day 6 in Group A. Among them, 16.5% remained PCR positive after 6th day of IVM ingestion in Group A. There was viral clearance in 77% on 11th day and in 81.5% on 12th day of HCQ treatment in Group B. Among them, 18.5% remained PCR positive after 12 days in Group B. The p value was 0.000427 which is significant considering 5th day viral clearance after IVM ingestion and 11th day after HCQ ingestion. Considering 6th day and 12th day, the p-value was 0.59, which was not significant. Ivermectin and doxycycline appear safe and effective combination drug therapy in COVID-19–infected patients; however, further extensive study is needed to find out the scope of application on other groups of patients.[33]

In another study from Bangladesh, a case series of 100 COVID-19 positive patients treated with combination of IVM and doxycycline, combination of IVM and doxycycline was found to be very effective in viral clearance in mild and moderately sick COVID-19 patients.

Ongoing and Promising Trials

University of Tanta, and Mansoura University, Egypt have started two Phase II/III randomized, parallel assigned, five arm study and three arm study, respectively with COVID-19 patients. The primary endpoint is involving the total number of patients with virological cure over a duration of 6-month period.[34]

University of Kentucky (UK) will investigate the effectiveness of azithromycin, IVM and camostat mesylate—drugs that could inhibit replication of SARS-CoV-2. The drugs will be tested either as stand-alone therapies or in combination with the antimalarial drug HCQ. The trial has a "pick-the-winner" design, which will allow researchers to understand what potential therapies appear to be effective, guiding patients to treatments that work and researchers to promising drugs that need added investigation.[35]

Clinica Universidad de Navarra, Spain has initiated the study titled as SARS-CoV-2/COVID-19 Ivermectin Navarra-ISGlobal Trial (SAINT). This is a double-blind, randomized controlled trial with two parallel groups and determines the efficacy of IVM in reducing nasal viral carriage at 7 days after treatment in SARS-CoV-2–infected patients who are at low-risk of progression to severe disease. The trial is currently planned at a single center in Navarra. Primary endpoint is to determine the proportion of patients with a positive SARS-CoV-2 PCR from a nasopharyngeal swab at day 7 post-treatment.[36]

Combined Military Hospital Lahore, Pakistan has designed a randomized, controlled trial to investigate the efficacy of IVM in COVID-19 patients. Patients will be allocated into two groups – one will be given IVM with standard chloroquine regimen, and the other group will be given chloroquine only. The outcomes will be recorded by documenting PCR reports at 48, 96 and 144 hours. The study was initiated on April 15, 2020 and runs till July 2020. It enrolls 100 patients and precludes those with severe conditions or comorbidities such as malignant disease, diabetes, etc.[37]

Laboratorio Elea Phoenix S.A., Argentina: Argentina's Laboratorio Elea Phoenix S.A. (Elea Laboratories) has launched a proof-of-concept clinical trial that involves 45 patients to look into the efficacy of IVM as a treatment for patients infected with SARS-CoV-2. The pharmaceutical company based its decision on the important Monash University lab study and the fact that IVM has been widely in use for decades.[38]

HCQ and IVM: The study seeks to investigate the safety and efficacy of a treatment involving HCQ and IVM for serious COVID-19 infections in non-critical hospitalized patients. Prior to any patient randomization, the investigational team will assess cardiovascular complications determined by the corrected QT interval, related to HCQ intake. For example, if a patient is at high-risk, they will be placed in the IVM group only or allocated to placebo in an independent randomization.[39]

Table 2 summarizes the ongoing and promising ivermectin trials in COVID-19 patients.

CONCLUSION

Indian Council of Medical Research (ICMR) is now reviewing the benefits of IVM and doxycycline as a potential therapy for COVID-19. There is an urgent need for a well-designed randomized controlled trial to assess the efficacy and validate the use of IVM against SARS-CoV-2. Under ideal circumstances, the answer would be yes. But, it's been 6-9 months since the start of the pandemic, and the number of COVID-19 positive cases and the related mortality appears to be out of control. We need to balance "Evidence-based medicine versus loss of human lives" while waiting for 9-12 months for a vaccine or an effective drug.

Table 2. Ongoing and Promising Clinical Trials on the Use of Ivermectin in Patients with COVID-19

Identifier Number	Title	Expected Participants	Starting Date	Completion Date	Length of Treatment	Dose of Ivermectin	Location
NCT 04373824	Max Ivermectin-COVID-19 Study versus Standard of Care Treatment for COVID-19 Cases. A Pilot Study	50	April 25, 2020	July 25, 2020	2 days	200-400 g/kg body weight + standard treatment	India
NCT 04374279	Trial to Promote Recovery from COVID-19 with Ivermectin or Endocrine Therapy	60	November 2020	November 2021	3 days or 6 days	600 g/kg (up to a maximum dose of 60 mg)	USA
NCT 04360356	Ivermectin and Nitazoxanide Combination Therapy for COVID-19	100	May 2020	October 2020	6 days	200 g/kg once orally on empty stomach plus nitazoxanide 500 mg twice daily orally with meal	Egypt
NCT 04343092	Ivermectin Adjuvant to hydroxychloroquine and Azithromycin in COVID-19 Patients	50	April 18, 2020	June 1, 2020	No information	12 mg/week + hydroxy-chloroquine 400 mg/day + azithromycin 500 mg daily	Iraq
NCT 04351347	The Efficacy of Ivermectin and Nitazoxanide in COVID-19 Treatment	60	June 16, 2020	December 1, 2030	No information	Combined with chloroquine (no information about dose)	Egypt
NCT 04374019	Novel Agents for Treatment of High-risk COVID-19 Positive Patients	240	May 1, 2020	May 2021	2 days for ivermectin + 14 days for Hydroxychloro-quine	First 2 days: Weight <75 kg: 4 tablets (12 mg total daily dose). Days 1-2: Weight >75 kg: 5 tablets (15 mg total daily dose) in combination with hydroxychloroquine. Days 1-14: 3 tablets (600 mg total daily dose)	USA
NCT 04345419	A Real-life Experience on Treatment of Patients with COVID-19	120	June 16, 2020	December 2029	No information	As a single dose	Egypt

Under these exceptional circumstances, "Do we have the time?" The cumulative loss of lives and economic loss may be humongous. Ivermectin appears to be the ideal choice as it shows the potential to exactly do that and the 5 A's make it the ideal drug in the scenario as listed in Figure 2. There is always scope of course correction as we learn from the rapidly changing circumstances and ensuing scientific results. Till then, these results raise hope and should be seen as light at the end of the tunnel to successfully manage the coronavirus pandemic till we get a safe and an efficient vaccine or drug against this deadly disease.

Assurance: Ivermectin has a well proven safety profile, with more than a trillion doses consumed every year.

Availability: Ivermectin is readily available; we have many manufacturers in India itself.

Administration: Ivermectin is easy to administer orally, and we already have experience of running a mass drug administration.

Accountability: Ivermectin, owing to its low toxicity and mostly Grade 1 adverse drug events, will not scare the stakeholders.

Affordability: Drug is cheap, which a normal Indian citizen can very well afford.

Figure 2. The Five A's which justify ivermectin as a pivotal drug for fighting coronavirus pandemic.

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FDA to Look at 2 Months of Safety Data Before Considering COVID-19 Vaccine

The US Food and Drug Administration (FDA) has made it clear that it will see 2 months of follow-up data after volunteers are given their second vaccine doses for clinical trials testing potential COVID-19 vaccines.

This is going to make it difficult for any vaccine maker to apply for emergency use authorization by Election Day, as President Trump has suggested, or by the end of October. FDA posted new guidance for manufacturers stating that they need to provide at least 2 months of follow-up safety data following vaccination of volunteers before asking the FDA for emergency use authorization for a vaccine.

The guidance stated that data from Phase 3 studies must include a median follow-up duration of at least 2 months after completion of the full vaccination regimen in order to provide sufficient information for evaluating a vaccine's benefit-risk profile… (*CNN*)