JCI The Journal of Clinical Investigation

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J Clin Invest. 2020. https://doi.org/10.1172/JCI144186.

Viewpoint In-Press Preview

In the quest to provide treatment for COVID-19 patients, available therapies that have been approved for other indications but have insufficient evidence of safety and efficacy for use against COVID-19 have been considered. One of the unintended consequences of this approach is the potential creation of shortages, depriving existing patients who are benefiting from products based on their proven indications. Here, a pharmaceutical company outlines their ethical decision-making framework to guide decision-making and ensure equity of access to products.

Drugs of unproven benefit for COVID-19: a pharma perspective on ethical allocation of available therapies

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COI statements:

Joanne Waldstreicher is a Johnson & Johnson employee and owner of Johnson & Johnson stock.

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Arthur Caplan serves as the unpaid chair of the Compassionate Use Advisory Committees (CompAC), independent panels of internationally recognized medical experts, bioethicists, and patient representatives formed by NYU School of Medicine (SOM) in collaboration with Janssen. CompAC advises Janssen about requests for compassionate use of its investigational medicines. NYU receives administrative funding from Janssen to facilitate the CompAC committees. Dr. Caplan is on the scientific advisory board of WIRB/WCG and gives lectures on research ethics topics to WIRB/WCG staff and visiting fellows. The Division of Medical Ethics that Dr. Caplan directs also has a grant from WIRB/WCG to provide education as part of an annual international research ethics fellows educational program held at NYU SOM.
Dr. Caplan consulted in 2017-2019 for CSL, Glaxo, Abeona, member of a Genae/Cardialen-DSMB, Cabaletta Bio and Moderna (unpaid). Dr. Caplan gave a lecture sponsored by Pfizer as a Zoom webinar open to the public.

The current COVID-19 outbreak has led to global efforts to care for those affected, contain the current outbreak, and develop vaccines and therapeutic approaches to prevent and treat COVID-19. In the absence of definitive clinical trial data, clinicians and public health authorities may consider offering available therapies which have been approved for other indications but have insufficient preclinical or clinical evidence of safety and efficacy for use against COVID-19. One of the unintended consequences of this approach is the potential creation of shortages, depriving existing patients who are benefiting from products based on their proven indications. To manage these allocation challenges, the development of evidence-based international consensus guidelines as well as consideration of supply issues is critical. Manufacturers play a key, if little-recognized, role in responding to requests for supply.

A need for therapies for a new threat

Since the beginning of the COVID-19 pandemic, a number of therapies already approved for other uses have been considered, studied, and/or used as potential treatments for COVID-19 prior to the availability of peer-reviewed data from randomized controlled clinical trials. This includes hydroxychloroquine and chloroquine (1) (including in combination with azithromycin), IL6 inhibitors, TNF inhibitors (2), various HIV antivirals (3,4,5), among others. Their use has been based on limited data and experience from preclinical in vitro data, biologic hypotheses, and uncontrolled clinical experience data.

While urgent collaborative efforts are underway on a variety of fronts to develop robust preclinical and clinical data on the use of these and many other drugs, none has yet identified a safe and effective treatment supported by high-quality clinical evidence, with the exception of initial results on remdesivir (6,7) and dexamethasone (8). However, under the current global pandemic conditions there may be an increase in demand for some of these products, and companies may be faced with supply issues related to COVID-19 as well as fulfilling supply needs for the currently approved uses. Anticipating the potential increase in demand for products that may be effective against COVID-19 but are as yet unproven, Johnson & Johnson set up a working group to develop an ethical decision-making framework which would guide decision-making and ensure equity of access to products within its operating companies' portfolios. This framework was reviewed with the New York University Langone's Compassionate Use Advisory Committee – an independent body (including independent ethicists, physicians, and patient representatives) that provides guidance to the Janssen pharmaceutical businesses of Johnson & Johnson on the ethical allocation of drugs in development in the context of Pre-Approval Access or Compassionate Use (9).

Framework for allocating therapies during the pandemic

Recognizing that other companies may experience a similar situation with requests for their medicines, we are sharing the guiding principles (10) developed for the allocation of supply of approved medicines for prevention or treatment of COVID-19 in the absence of definitive confirmatory data. These guiding principles are currently being

leveraged within Johnson & Johnson as part of its pandemic response management and planning.

In the absence of definitive data on efficacy and safety in COVID-19, we believe that the primary obligation is to do what is best to assure supply for patients who currently rely on products for approved uses. Therefore, we set up an internal control mechanism within our supply chain to flag new or unusually high orders. These are then assessed by a working group for evaluation. Orders for the treatment of current or newly diagnosed patients under the approved indication are given priority, and their supply prioritized.

In the absence of robust clinical trial data in COVID-19 patients, the next priority is supply for well-designed randomized, controlled clinical trials (RCTs) conducted according to Good Clinical Practice (GCP) standards with a commitment to rapid and transparent sharing of the results, which can provide important safety and efficacy data to inform clinical practice.

The next priority is to supply certain additional studies or registries that are not designed as RCTs but will collect and share additional valuable information on the efficacy and safety of medicines.

If there is further supply available after allocation is given to the groups above, it should be allocated as fairly as possible and in accordance with local laws and regulations, while also recognizing that there may be a variety of manufacturers or sources available for any one medicine and there may also be other similar medicines to choose from within the same class. National and international health authorities and regulatory bodies can perform an important role in assessing and guiding study and supply allocation efforts at both a local and global level. In the absence of such allocation guidance, we are guided by this ethical framework and draw upon an internal team of medical, ethical, and epidemiological experts to recommend an allocation plan which is based on the best current epidemiologic information about the pandemic, with the aim to save as many lives as possible.

Other requests, including requests from non-affected areas to ‘stock up’ for a future epidemic scenario, should be accorded lower priority or denied in the absence of clinical evidence supporting the use of a medicine for treatment of COVID-19.

Given the likelihood of continued requests for approved medicines and the prospect of similar future events, we are sharing our approach with the goal of advancing the dialog around how best to manage drug supply in a global epidemic.

References

1. Ibáñez S, Martínez O, Valenzuela F, Silva F, Valenzuela O. Hydroxychloroquine and chloroquine in COVID-19: should they be used as standard therapy?. *Clin. Rheumatol.* 2020;39(8):2461–2465.

2. Feldmann M et al. Trials of anti-tumour necrosis factor therapy for COVID-19 are urgently needed. *Lancet* 2020;395(10234):1407–1409.

3. De Meyer S et al. Lack of Antiviral Activity of Darunavir against SARS-CoV-2 [Internet]. *Infectious Diseases (except HIV/AIDS)* 2020; doi:10.1101/2020.04.03.20052548

4. Wang Y et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet* 2020;395(10236):1569–1578.

5. Cao B et al. A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. *N. Engl. J. Med.* 2020;382(19):1787–1799.

6. Goldman JD et al. Remdesivir for 5 or 10 days in patients with severe Covid-19 [Internet]. *N. Engl. J. Med.* [published online ahead of print: 2020];https://www.nejm.org/doi/full/10.1056/NEJMoa2015301. cited May 27, 2020

7. Beigel JH et al. Remdesivir for the Treatment of Covid-19 — Preliminary Report [Internet]. *New England Journal of Medicine* 2020; doi:10.1056/nejmoa2007764

8. Horby P et al. Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report [Internet] doi:10.1101/2020.06.22.20137273

9. Division of Medical Ethics Compassionate Use Advisory Committees [Internet]https://med.nyu.edu/departments-institutes/population-health/divisions-sections-centers/medical-ethics/research/compassionate-use-advisory-committees. cited August 24, 2020

10. Johnson & Johnson. Johnson & Johnson Establishes Ethical Framework to Guide Our Decisions During the COVID-19 Pandemic [Internet]. *Johnson & Johnson* 2020;https://www.jnj.com/our-company/johnson-johnson-establishes-ethical-framework-to-guide-our-decisions-during-the-covid-19-pandemic. cited August 24, 2020