

Guiding Principles from the American College of Rheumatology for Scarce Resource Allocation During the COVID-19 Pandemic: The Case of IL-1 and IL-6 and JAK Antagonists

Background

Ethical principles must be balanced when making decisions about scarce resource allocation. In extreme circumstances, like the COVID-19 pandemic caused by the SARS-CoV-2 virus, the focus of medical care “shifts from the needs of the individual (ethical principle of autonomy) to the needs of the community as a whole (ethical principle of distributive justice)” (1) with the goal of achieving the greatest good for the greatest number of people.

Biologic therapies that inhibit interleukin (IL)-1 (anakinra, canakinumab), IL-6 (tocilizumab, sarilumab) and small molecule inhibitors of janus kinase (JAK) signaling pathways (tofacitinib, upadacitinib, baricitinib) are routinely used by rheumatologists and rheumatology health professionals in the treatment of a variety of rheumatologic conditions including rheumatoid arthritis, giant cell arteritis, juvenile idiopathic arthritis (JIA) and others. These therapies are critical for patients who often have failed numerous other treatments. For children with systemic JIA, anti-IL-1 and anti-IL-6 therapies are the most effective treatments (2-4). For adults with GCA, anti-IL-6 therapy is the only treatment proven to reduce the need for glucocorticoids (5). For many patients on these drugs, loss of access to treatment could be life-threatening.

Some patients with severe forms of COVID-19 appear to display a “cytokine storm” syndrome similar to that seen in secondary hemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS) (6, 7). Secondary HLH/MAS is a hyperinflammatory syndrome that can be triggered by autoimmune diseases such as systemic lupus erythematosus and systemic JIA. This has led to interest in antagonists of IL-1, IL-6 and JAK signaling pathways, therapies that have been used to treat systemic JIA and secondary HLH/MAS, as potential treatments for patients with severe COVID-19. Experience with these drugs and protocols for their use are being reported (8, 9) and controlled clinical trials in the US and abroad are underway (10-15).

On 17 March 2020, in response to concerns about potential future drug shortages, Genentech began allocation of IV formulations of tocilizumab. Genentech currently reports no supply shortages. Genentech has pledged to provide 10,000 vials of tocilizumab to the U.S. Strategic National Stockpile for potential future use at the direction of the US Department of Health and Human Services. On 23 March 2020 Genentech announced that the US Food and Drug Administration had approved a randomized, double-blind, placebo-controlled Phase III clinical trial in collaboration with the Biomedical Advanced Research and Development Authority to evaluate the safety

and efficacy of intravenous tocilizumab in hospitalized adults with severe COVID-19 pneumonia.

We offer the following recommendations regarding the allocation of IL-1 and IL-6 and JAK antagonists during the COVID-19 pandemic. Clinical guidance from the American College of Rheumatology for the treatment of rheumatology patients during the COVID-19 pandemic are available [here](#). All recommendations are based on current knowledge and are subject to revision as circumstances evolve.

Recommendations

- Every effort must be made to ensure an adequate supply of IL-1 and IL-6 and JAK antagonists for all patients who need them. Efforts to increase production and distribution of IL-1 and IL-6 and JAK antagonists for rheumatology patients, as well as patients with COVID-19 if indicated, should be supported. Protections on the supply of IL-1 and IL-6 and JAK antagonists should include all aspects of the supply chain from manufacturer to wholesaler, wholesaler to pharmacy, and final distribution to patients.
- Adequate supplies of IL-1 and IL-6 and JAK antagonists should be allocated for patients with rheumatologic conditions, especially those in whom even brief drug holidays would be reasonably expected to cause a flare of their disease or require a switch to an alternative regimen with less efficacy and/or safety.
- In the case of COVID-19, allocation of IL-1 and IL-6 and JAK antagonists should be prioritized (but not limited) to support clinical trials designed to test the efficacy of IL-1 and IL-6 and JAK antagonists as therapy for severe cases of COVID-19.
- The potential therapeutic benefits of IL-1 and IL-6 and JAK antagonists in COVID-19, and the urgent need for effective therapy against SARS-CoV-2, justifies expedited controlled trials in humans. Such trials should be carried out by experienced investigators equipped to generate and interpret reliable results while safeguarding patient safety and informed consent.
- Decisions about allocation of IL-1 and IL-6 and JAK antagonists should be made locally, with input from experts, based on local conditions and calibrated over time as circumstances evolve. Decisions around allocation should not be made *ad hoc* by individual dispensing pharmacies acting in isolation.
- Decisions about allocation of IL-1 and IL-6 and JAK antagonists, whenever possible, should incorporate recommendations from rheumatologists and rheumatology health professionals who are expert in the management of these medicines and the rheumatologic conditions for which they are prescribed.
- Rheumatologists and rheumatology health professionals, in shared decision making with a patient, may reasonably pursue IL-1 and IL-6 and JAK antagonist dose reductions and extend dosing intervals tailored to an individual patient's needs when faced with shortages.

- During drug shortages we urge insurers to exempt rheumatology patients from prior authorization, step therapy protocols, and other utilization management practices so that they may more readily gain access to appropriate alternatives as determined by their rheumatologist or rheumatology health professional.

To Be Avoided

- Pharmacy-level restrictions on new starts of IL-1 and IL-6 and JAK antagonists for patients with appropriate rheumatologic conditions are inappropriate.
- Predatory price increases or cost-sharing requirements, especially during the COVID-19 pandemic, should be vigorously opposed by regulatory bodies.

References:

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