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Letter to the Editor

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Is G-CSF Dangerous in COVID-19: Why Not Use GM-CSF?

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We recently published an article in *Acta Haematologica* (DOI: 10.1159/000510352) [1] wherein we compared safety and efficacy of G-CSF and GM-CSF therapy in persons with acute respiratory distress syndrome (ARDS) such as that associated with infection with severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) and attendant coronavirus disease-2019 (COVID-19). We discussed differences between the drugs and suggested that in persons with lung infection and/or ARDS, GM-CSF may be safer than G-CSF because of its pleiotropic effects. There are now 2 publications emphasizing the potential danger of giving G-CSF to persons with COVID-19-related ARDS [2, 3]. Nawar and colleagues [2] reported 3 persons with ARDS in the setting of COVID-19 with rapid deterioration of lung function after receiving G-CSF. They attribute this finding to an influx of granulocytes into the inflamed lung concluding: In the setting of COVID-19 illness, further rapid rise in neutrophilia with NLR (neutrophil lymphocyte ratio) >5 may portend respiratory deterioration to the point of mechanical ventilation within the next 72 h, especially in those patients who are older than age 50 and have comorbid medical conditions. Taha and colleagues [3] report similar rapid deterioration in someone with COVID-19-related ARDS receiving G-CSF concluding: This rapid neutropenia recovery and the robust inflammatory response in COVID-19 raise concerns about G-CSF safety in patients with COVID-19.

We ended our article noting: In persons with lung infection and/or ARDS, GM-CSF may be a safer drug than G-CSF. Whether this is so can only be definitively answered in a randomized comparative trial. Unfortunately, such a trial is unlikely to be done and we may have to rely on indirect evidence of safety and efficacy, perhaps to the chagrin of North et al. [4], who advocate enhancing enrollment to clinical trials, especially during the pandemic. The articles we cite on use of G-CSF in this setting are perhaps a warning and the kind of indirect evidence needed.

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Conflict of Interest Statement

H.M.L. has been a consultant for Partner Therapeutics, Jazz Pharmaceuticals, Seattle Genetics, AstraZeneca, Celgene/Bristol-Myers Squibb, and Actinium Pharmaceuticals. R.P.G. is consultant to: BeiGene Ltd., Kite Pharma Inc., Fusion Pharma LLC, LaJolla NanoMedical Inc., Mingsight Parmaceuticals Inc., and CStone Pharmaceuticals. Medical Director: FFF Enterprises Inc. Partner: Neopharm Ltd, AZACA Inc. Board of Directors: RakFond Foundation for Cancer Research Support. Scientific Advisory Board: Antegene Biotech LLC, StemRad Ltd.

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3 Taha M, Sharma A, Soubani A. Clinical deterioration during neutropenia recovery after G-CSF therapy in patient with COVID-19. Respir Med Case Rep. 2020;31:101231.

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