



Baricitinib: Two Birds with One Stone

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To the Editor

Baricitinib is an oral Janus Kinase 1 and 2 inhibitor approved for the treatment of refractory rheumatoid arthritis [1]. Patients with coronavirus disease 2019 (Covid-19) develop pneumonia associated with immune dysregulation, and unchecked cytokine release, which often involves dysregulation of the Janus Kinase/Signal Transducer and Activator of Transcription (JAK/STAT) pathway. Baricitinib as a single agent or combined with remdesivir reduces cytokine release, viral burden, recovery time, and mortality in patients with moderate to severe covid pneumonia [2]. JAK signaling pathway plays a prominent role in Graft versus host disease (GVHD) occurring in allogeneic hematopoietic stem cell transplant (allo-HCT) recipients, and baricitinib is effective against steroid-refractory chronic GVHD [3]. Here, we present a patient with chronic GVHD and covid-19 pneumonia who was successfully treated with baricitinib.

In December 2020, a sixteen-year-old female patient underwent allo-HCT for high-risk acute lymphoblastic leukemia with human leukocyte antigen (HLA) matched sibling donor. The conditioning was myeloablative with fludarabine-busulfan, and GVHD prophylaxis was with cyclosporine. Six months post-transplant, her disease remained in remission with 98% donor chimerism. She developed chronic GVHD involving eyes, gut, skin, oral cavity, and liver with a National Institute of Health (NIH) chronic GVHD score of 11. After the initial response to

prednisolone, her GVHD started progressing. On day + 152, she developed upper respiratory tract symptoms, and RT-PCR for Covid-19 was positive. She developed moderately severe covid pneumonia with a CT severity score of 19, requiring high flow oxygen by face mask. Given the co-existence of steroid-refractory GVHD and covid-19 infection, she was started on oral baricitinib at a dose of 2 mg per day. She also received prednisolone and remdesivir.

She tolerated baricitinib without any significant toxicities. Low-grade myalgia alleviated by analgesics was the only patient-reported adverse effect. Seven days after the initiation of baricitinib, the patient's oxygen requirement decreased significantly, and room air saturation normalized. Though, the response of covid-19 pneumonia cannot be ascribed to baricitinib alone, as she was on other supportive medicines, she did have rapid resolution of symptoms. Baricitinib was continued in view of chronic GVHD. After 6 weeks, her chronic GVHD had improved, the NIH score reduced to 2, with the liver involvement remaining stable.

Management of stem cell transplant recipients in the setting of the covid pandemic is challenging. They are at increased risk for covid related complications due to impaired cellular and humoral immunity and immunosuppressive medications. In addition, GVHD can cause pulmonary impairment, thereby promoting covid related ARDS and respiratory failure [4]. Use of the drugs approved for covid like dexamethasone, enoxaparin, and remdesivir may be restricted in transplant recipients due to increased risk for systemic viral infections (like CMV), thrombocytopenia, liver, and renal dysfunction. Moreover, the therapeutic options for steroid-refractory GVHD are limited. JAK-inhibitor ruxolitinib has emerged as an important therapeutic option for GVHD; however, usage is limited by cost [5]. Given the accelerated availability of

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generic versions, thanks to the Covid-pandemic, baricitinib can emerge as a much more economical option than ruxolitinib for the treatment of GVHD in India.

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Declarations

Conflict of interest The authors declare that they have no conflict of interests.

References

1. Genovese MC, Kremer J, Zamani O, Ludivico C, Krogulec M, Xie L et al (2016) Baricitinib in patients with refractory rheumatoid arthritis. *N Engl J Med* 374:1243–1252
2. Kalil AC, Patterson TF, Mehta AK, Tomashek KM, Wolfe CR, Ghazaryan V, et al. (2020) Baricitinib plus remdesivir for hospitalized adults with covid-19. *N Engl J Med* [Internet] 2020 [cited 2021 Jul 4]; Available from: <https://www.nejm.org/doi/https://doi.org/10.1056/NEJMoa2031994>
3. Holtzman NG, Im A, Ostojic A, Curtis LM, Parsons-Wandell L, Nashed J et al (2020) Efficacy and safety of baricitinib in refractory chronic graft-versus-host disease (cGVHD): preliminary analysis results of a phase 1/2 study. *Blood* 136:1–1
4. Lu X, Tang LV, Wang H-F, You Y, Wang Y-D, Hu Y et al (2021) The great challenge of managing recipients of hematopoietic stem cell transplantation combined with COVID-19. *Bone Marrow Transplant* 56:696–700
5. Information NC for B, Pike USNL of M 8600 R, MD B, Usa 20894. Cost Comparison [Internet]. Canadian Agency for Drugs and Technologies in Health; 2019 [cited 2021 Jul 14]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK549721/Table>

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