



## Positive Quality Intervention: Use of Belumosudil (Rezurock®) for the Treatment of Chronic Graft-Versus-Host Disease

**Description:** The purpose of this PQI is to discuss the use of belumosudil (Rezurock®) in the management of chronic graft-versus-host disease (cGVHD) after allogeneic hematopoietic cell transplantation. Belumosudil was approved by the United States Food & Drug Administration (FDA) in 2021 with indication for use in patients  $\geq 12$  years of age with cGVHD after two or more prior systemic therapies.

**Background:** cGVHD affects 35% to 50% of patients following allogeneic hematopoietic cell transplantation (HCT) and significantly impairs quality of life, increases morbidity, and is a leading cause of non-relapse mortality.<sup>1</sup> Corticosteroid therapy is typically the first-line approach to treatment of cGVHD; however, less than 20% of patients who initiate corticosteroid therapy achieve a complete or partial response at one year thus requiring treatment with additional agents.<sup>2</sup> Traditionally, many agents have been used in the second-line setting based on limited data with low response rates overall and a “trial-and-error” approach was recommended by clinical practice guidelines.<sup>3</sup> In 2017, ibrutinib (Imbruvica®) became the first agent to be FDA approved for steroid-refractory cGVHD demonstrating an overall cGVHD response of 67% with 71% of responders demonstrating a sustained response for  $\geq 20$  weeks.<sup>4</sup> Despite the approval of ibrutinib for cGVHD, an unmet need remains for additional agents that may be effective in the treatment of cGVHD. The rho-associated coiled-coil-containing protein kinase-2 (ROCK2) signaling pathway has been of interest in recent years as this pathway is involved in regulation of the Th17/regulatory T cell balance and control of profibrotic pathways. The utilization of the selective ROCK2 inhibitor belumosudil (Rezurock®) was further investigated in the phase II, randomized, multicenter ROCKstar trial.<sup>5</sup> This study included 132 patients with cGVHD who had received 2 to 5 prior lines of therapy with a median of 3 prior lines, although 23% had received 5 or more prior therapies. Sixty-six patients were randomized to receive 200 mg by mouth once daily while the remaining 66 patients received 200 mg by mouth twice daily. The primary endpoint for the ROCKstar study evaluated overall response rate which was demonstrated in 74% of patients in the 200 mg daily cohort and 77% in the 200 mg twice daily cohort with median duration of response of 54 weeks.<sup>5</sup> Time to response was 1.8 months (95% CI, 1.0 – 1.9). High response rates were observed among all subtypes evaluated and responses were observed among all organ types affected. Belumosudil was well-tolerated overall with only 9% of patients requiring a dose reduction. Other meaningful results included a 2-year overall survival rate of 82% and association with a corticosteroid-sparing effect with 20% of patients able to discontinue corticosteroid therapy while undergoing treatment with belumosudil. Adverse events (AEs) observed were consistent with expected events in the patient cohort. Results from this trial ultimately led to FDA approval for cGVHD after failure of two or more lines of therapy on July 16, 2021.<sup>6</sup>

### PQI Process:<sup>7</sup>

- Belumosudil should be considered for patients  $\geq 12$  years of age with cGVHD refractory to two or more prior lines of therapy and may be added to the patient’s current regimen as long as the patient has been on stable doses of other systemic agents for cGVHD for at least 2 weeks
- Contact information for authorized specialty pharmacies/distributors available through [Kadmon ASSIST](#)
- Dosing
  - The recommended initial dosing is 200 mg by mouth once daily
  - Concomitant use with CYP3A4 inducers or proton pump inhibitors: 200 mg by mouth twice daily
  - No dose adjustments for renal or liver dysfunction are currently recommended, although limited data are available in these patient populations
  - Monitor total bilirubin and transaminases monitored at least monthly while on therapy

**IMPORTANT NOTICE:** NCODA has developed this Positive Quality Intervention platform. This platform is intended as an educational aid, does not provide individual medical advice, and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication. The materials contained in this platform do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA. NCODA does not ensure the accuracy of the information presented and assumes no liability relating to its accuracy. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. It is the individual’s sole responsibility to seek guidance from a qualified healthcare professional. *Updated 9.29.23*

- Dose modifications are recommended for Grade  $\geq 3$  hepatotoxicity and any Grade  $\geq 3$  AE that is felt to be related to belumosudil
- Pregnancy status should also be verified prior to initiation in females of childbearing potential
- Of note, no cases of cytomegalovirus reactivation or infection were reported in the study population

### Patient-Centered Activities:<sup>7</sup>

- Provide [Oral Chemotherapy Education Sheet](#)
- Discuss the most common ( $\geq 20\%$ ) AEs: upper respiratory infection (53%), diarrhea (35%), nausea (42%), dyspnea (33%), headache (21%), peripheral edema (27%), cough (30%), and hypertension (21%)
- Serious AEs occurred in 43% of patients and included dyspnea (7%), lung infection (6%), hypoxia (4%), and influenza-like illness (4%) \*a low rate of Grade  $\geq 3$  cytopenias was observed occurring in only two patients which also coincided with relapse of underlying malignancy
- Belumosudil is supplied as a 200 mg tablet which should be swallowed whole with food and a glass of water at approximately the same time(s) each day
- Patient Assistance: [NCODA Financial Assistance Tool](#)

### References:

1. Sarantopoulos S, Cardones AR, Sullivan KM. How I treat refractory chronic graft-versus-host disease. *Blood*. 2019;133(11): 1191-1200.
2. Martin PJ, Storer BR, Inamoto Y, et al. An endpoint associated with clinical benefit after initial treatment of chronic graft-versus-host disease. *Blood*. 2017;130(3): 360-367.
3. Wolff D, Schleuning M, von Harsdorf S, et al. Consensus conference on clinical practice in chronic GVHD: Second-line treatment of chronic graft-versus-host disease. *Biol Blood Marrow Transplant*. 2011;17: 1-17.
4. Miklos D, Cutler CS, Arora M, et al. Ibrutinib for chronic graft-versus-host disease after failure of prior therapy. *Blood*. 2017;130(21): 2243-2250.
5. Cutler CS, Lee SJ, Arai S, et al. Belumosudil for chronic graft-versus-host disease (cGVHD) after 2 or more prior lines of therapy: The ROCKstar study. *Blood*. 2021;blood.2021012021. doi: 10.1182/blood.2021012021. Online ahead of print.
6. FDA approves belumosudil for chronic graft-versus-host disease. Available at: <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-belumosudil-chronic-graft-versus-host-disease>.
7. [Rezurock® \(belumosudil\) \[package insert\]. Warendale, PA: Kadmon Pharmaceuticals, LLC; 2021.](#)