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Real world experience with belumosudil for chronic graft versus host disease

Abstract

Background: Hematopoietic stem cell transplantation (HSCT) offers curative potential for hematologic malignancies, but chronic graft-versus-host disease (cGVHD) remains a common and debilitating complication. Belumosudil, recently approved for cGVHD after two or more prior therapies, has shown promise in clinical trials, but real-world data are limited.

Case series: This single-center case series evaluates the real-world tolerability, safety, and accessibility of belumosudil, particularly in combination with other therapies for cGVHD. We reviewed outcomes in 33 patients treated with belumosudil between July 2021 and August 2022. Data on patient demographics, treatment history, adverse effects, drug interactions, and cost/accessibility were collected and analyzed. Belumosudil was generally well tolerated; 45% reported adverse effects, most commonly diarrhea, dizziness, and appetite loss. Less than 10% discontinued due to side effects. Notably, blood glucose fluctuations and elevated sirolimus/tacrolimus levels were observed. Belumosudil was frequently used in combination with other therapies, including ruxolitinib and ibrutinib, with 21% of patients eventually discontinuing all other systemic therapies. The majority of patients had low or no out-of-pocket cost due to secondary payor assistance.

Conclusion: Belumosudil appears to be a well-tolerated, accessible treatment option in real-world settings for patients with cGVHD, including those on combination therapies. Clinicians should monitor for potential drug interactions and metabolic disturbances. Further real-world research is needed to confirm these findings.

Keywords: belumosudil, real-world data, combination therapy, immunosuppressant interactions, drug safety, ruxolitinib, ibrutinib, tacrolimus, sirolimus

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Abbreviations: cGVHD, chronic graft-versus-host disease; HSCT, hematopoietic stem cell transplantation

Introduction

Hematopoietic stem cell transplantation (HSCT) is a treatment modality that can result in long-remissions and a cure for multiple hematologic cancers. However, chronic graft versus host disease (cGVHD) is a complication of an allogeneic HSCT that can affect up to 70% of patients and is a significant cause of morbidity and mortality.[1] Existing therapy options are limited and related to significant short term and long-term toxicities. Belumosudil has gained traction for use in patients with chronic graft-versus-host disease (cGVHD) after two or more prior lines of therapy following the results of the ROCKSTAR trial in March 2022 which demonstrated promising efficacy and a favorable safety profile.[2] Given its recent approval, real-world experience with belumosudil remains limited outside of clinical trials. Recently, Lee et al revealed a correlation between patient reported outcomes to clinical organ responses with belumosudil, demonstrating that belumosudil improves cGVHD symptoms with minimal toxic effects.[3] We aim to further expand on the tolerability of belumosudil in a real-world setting with various combination therapies for cGVHD.

Case series

This real-world single-center, case series describes patient-reported adverse effects, tolerability in combination therapies, and patient access to belumosudil. Between July 2021 and August 2022, 33 patients with cGVHD were treated with belumosudil. The median patient age was 65 years (range, 29-75) and 73% were male. The most common malignancy prompting hematopoietic stem cell transplant was acute myeloid leukemia (AML). Transplants with a matched donor (94%) and/or an unrelated donor (73%) were most common. More patients received a reduced-intensity (55%) versus myeloablative (45%) conditioning regimen. The most common GVHD prophylaxis regimen was tacrolimus and methotrexate (73%). At the time of belumosudil initiation, 79% of patients had severe cGVHD per the National Institutes of Health, with skin (88%), ocular (73%), and oral (67%) being the most affected organs as seen in Figure 1 & 2. Patients were heavily pretreated with 97% of patients having received at least three lines of prior therapy (range 2 -6) including ruxolitinib (73%) or ibrutinib (45%). One patient utilized belumosudil off-label as second-line therapy for oral and joint cGVHD after a flare following a prednisone taper.

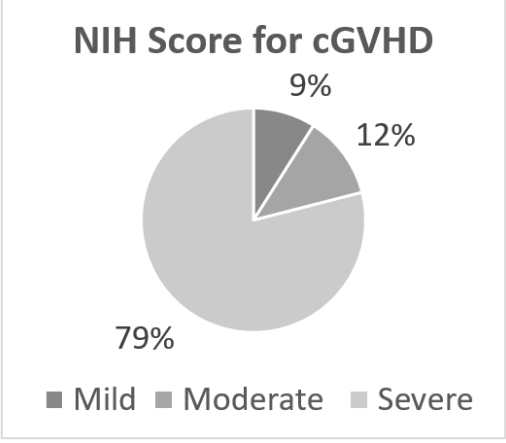

Figure 1 NIH cGVHD scoring at belumosudil initiation.

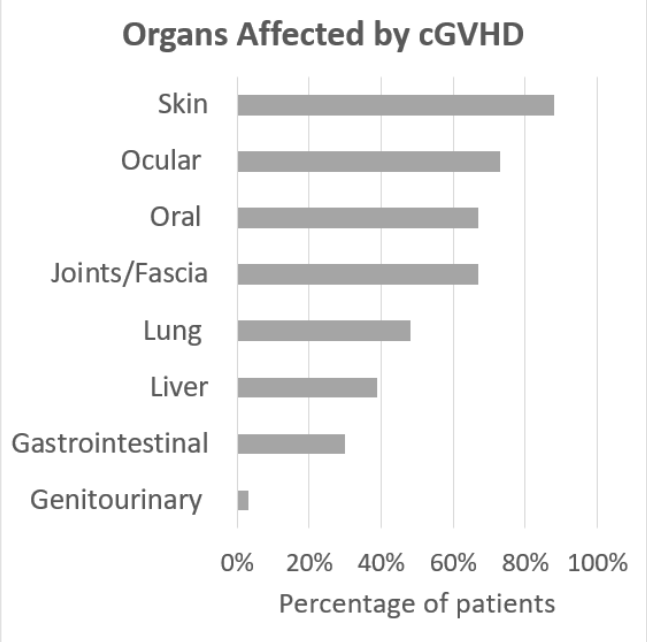

Figure 2 Organs affected by cGVHD at belumosudil initiation.

In this review, 15 patients (45%) reported adverse effects following initiation of belumosudil including diarrhea (15%), dizziness (12%), and decreased appetite (9%). Less than 10% of patients discontinued treatment due to adverse effects. Interestingly, blood glucose and immunosuppression trough abnormalities were observed shortly following initiation of belumosudil, neither of which are described in the package insert.[3,4] Of the 12 diabetic patients, blood glucose abnormalities were observed in five (42%), which included hyperglycemia in four patients and hypoglycemia in one patient. Two patients with blood glucose abnormalities were on prednisone, however, no dose changes to steroids occurred during belumosudil initiation. Adverse effects resulted in the discontinuation of therapy for two patients (6%), due to transaminitis resulting in hospitalization (n=1) and cardiac dysfunction complicated by fluid overload (n=1). Treatment related adverse events are reported in Table 1.

Table 1 Toxicity during belumosudil treatment

Adverse effects, n (%)	15 (45)
Diarrhea	5 (15)
Dizziness	4 (12)
Decreased appetite	3 (9)
Elevated blood pressure	2 (6)
Nausea	2 (6)
Abdominal pain	2 (6)
Infection, n (%)	
Upper respiratory infection	8 (24)
Pneumonia	4 (12)
Skin/soft tissue infection	3 (9)
Gastrointestinal infection	2 (6)
Bacteremia	2 (6)
COVID	2 (6)
Laboratory abnormalities, n (%)	
Any Grade transaminitis	6 (18)
Grade 3-4 transaminitis	4 (12)
Blood sugar abnormalities	5 (15)
Increased immunosuppression levels	3 (9)
Action, n (%)	
Treatment held	6 (18)
Treatment discontinued	2 (6)

Ten patients (30%) were on tacrolimus or sirolimus at belumosudil initiation. An increase in trough levels was observed in three patients (tacrolimus, n=1; sirolimus, n=2). A tacrolimus trough increased from 5.1 mg/dL to 16.4 mg/dL, 40 days after initiating belumosudil. Sirolimus troughs increased from 3.8 mg/dL to 13.7 mg/dL, 27 days after initiation and 2.6 mg/dL to 10.5 mg/dL, 12 days after initiation. In all cases, patients were stable on their immunosuppression prior to initiation of belumosudil. A recent retrospective review of 30 patients similarly noted supratherapeutic levels of immunosuppression on patients initiated on belumosudil, with tacrolimus levels increasing by 25% and sirolimus levels increasing by 62%.[5] The authors proposed a pre-emptive dose reduction of 25% when starting patients on belumosudil. As evidence for drug interactions continues to evolve, practitioners should be wary of increased exposure to immunosuppressants.

At belumosudil initiation, 30 (90%) patients were receiving concomitant therapy for cGVHD. Furthermore, 15 patients (45%) at our institution received belumosudil in combination with ruxolitinib or ibrutinib. In contrast to the ROCKSTAR trial, which featured one patient (2%) who received ruxolitinib in combination with belumosudil (2%). The ROCKSTAR trial did not allow concomitant ibrutinib. At initiation, 36% (n = 12) were on two concomitant therapies and 18% (n = 6) were on three concomitant cGVHD therapies. Chin et. al similarly evaluated 26 patients using belumosudil in combination therapies for refractory cGVHD and demonstrated safety when used in 3-4 drug combinations which aligns with our findings. [6] Belumosudil was not only well tolerated in combination therapy, but also allowed for 21% of patients to discontinue all concomitant cGVHD therapies and 48% to discontinue at least one cGVHD systemic therapy. Table 2 contrasts the cGVHD treatment of each patient at belumosudil initiation and at data cutoff.

Table 2 cGVHD therapy changes following belumosudil initiation

Patient	cGVHD therapy at belumosudil initiation	cGVHD therapy with belumosudil at data cutoff
1	None	monotherapy
2	None	monotherapy
3	None	monotherapy
4	ruxolitinib, prednisone	monotherapy
5	ruxolitinib, prednisone	monotherapy
6	ruxolitinib, prednisone	monotherapy
7	ruxolitinib	monotherapy
8	ibrutinib	monotherapy
9	ibrutinib, tacrolimus, prednisone	monotherapy
10	tacrolimus	monotherapy
11	ruxolitinib, tacrolimus	tacrolimus
12	ruxolitinib, ECP	ECP
13	ruxolitinib, ECP	ECP
14	imatinib, ECP	ECP
15	rituximab, ECP	ECP
16	ruxolitinib, prednisone, ECP	ECP
17	ruxolitinib, prednisone, ECP	ECP, prednisone
18	ibrutinib, prednisone, ECP	prednisone

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Table 2 Continued....

19	rituximab, ruxolitinib, prednisone	rituximab
20	ruxolitinib	ruxolitinib
21	prednisone	prednisone
22	prednisone	prednisone
23	prednisone	prednisone
24	tacrolimus	tacrolimus
25	tacrolimus	tacrolimus
26	sirolimus	sirolimus
27	sirolimus, ECP	sirolimus, ECP
28	ECP	ECP
29	ECP	ECP
30	ruxolitinib, sirolimus, prednisone	ruxolitinib, sirolimus, prednisone
31	prednisone, tacrolimus	prednisone, tacrolimus
32	prednisone, sirolimus	prednisone, sirolimus
33	prednisone, MMF	prednisone, MMF

Abbreviations: ECP, extracorporeal photopheresis; MMF, mycophenolate mofetil.

Conclusion

Lastly, belumosudil proved to be an accessible option for patients with a median copay for a 30-day supply being $0 (range $0-38), although the majority of prescriptions (57%) received additional reimbursement by secondary payors or grants.

While the major limitation is the inability to assess efficacy outcomes, our review demonstrates that belumosudil is affordable, well tolerated in combination therapies, and may allow patients to taper off concomitant systemic therapies. Despite being well tolerated, side effects of special interest include elevated sirolimus and tacrolimus serum trough levels as well as changes in blood glucose. More real-world studies are needed to better characterize belumosudil efficacy, adverse effects, and use in combination therapies.

Acknowledgments

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

1. Amanam I, Otoukesh S, Malki M, et al. Chronic GVHD: review advances in prevention, novel endpoints, and targeted strategies. *Hematology Am Soc Hematol Educ Program.* 2023:2023(1):164–170.
2. Cutler C, Lee SJ, Arai S, et al. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar study. *Blood*. 2021;138(22):2278–2289.
3. Lee SJ, Cutler C, Blazar BR, et al. Correlation of patient-reported outcomes with clinical organ responses: data from the belumosudil chronic graft-versus-host disease studies. *Transplant Cell Ther.* 2022;28(10):700.e1–700.e6.
4. Belumosudil. Bridgewater, NJ: Kadmon pharmaceuticals, LLC. 2024.
5. Daly P. Belumosudil significantly affects IST serum concentrations. HOPA. *64th ASH annual meeting and exposition*. 2022.
6. Chin M, Shizuru J, Muffly L. Belumosudil combination therapy in refractory chronic graft-versus-host disease. *Blood*. 2022;140(Suppl 1):4788–4789.

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