Annals of Hematology (2025) 104:1241–1247
https://doi.org/10.1007/s00277-024-06128-6

RESEARCH

Belumosudil in pediatric patients with chronic graft-versus-host disease after failed multi-line therapy: a case series

Wenting Chen[1,2,3] · Zhi Wang[2] · Zhouyang Liu[4] · Bin Fu[5] · Tingting Xing[2] · Jianhua You[2,6] · Jiong Hu[6]

Received: 29 September 2024 / Accepted: 26 November 2024 / Published online: 11 December 2024

Abstract

Belumosudil is a selective small molecule inhibitor of Rho-associated coiled-coil kinase 2 (ROCK2) indicated for patients with glucocorticoid-refractory chronic graft-versus-host disease (cGVHD). Despite its approval for ages 12–18, there is limited pediatric data available. This case series presents three 12-year-old patients with severe cGVHD who had failed multiple lines of therapy. Case #1 received treatment for 210 days with belumosudil, prednisone, cyclosporine A, mycophenolate mofetil, and ruxolitinib. Initial assessments showed skin and joint fascia involvement (National Institutes of Health score 3), along with oral cavity, ocular, and pulmonary involvement (score 2). Following treatment, all affected organs demonstrated at least a partial response (PR), with an overall assessment of PR. Case #2 was treated for 205 days with belumosudil, tacrolimus, and ruxolitinib. Baseline assessments indicated involvement of the skin and joint fascia (score 3), and the oral cavity and eyes (score 2). Most organs achieved PR or complete response (CR), resulting in an overall PR. Case #3 underwent 121 days of therapy with belumosudil, prednisone, and tacrolimus, showing similar baseline organ involvement as Case #2. The treatment resulted in an overall PR, with improvement noted in the skin, oral cavity, eyes, and joint fascia. The Lee cGVHD symptom scale scores improved meaningfully for all patients over time. There was no recurrence of the primary disease or any fatalities. Adverse events were limited to grade 1–2 severity. This case series indicates that belumosudil may be effective in 12-year-old pediatric patients with severe, multi-organ cGVHD refractory to multiple treatments. The findings suggest that belumosudil-based regimens can be feasible and well-tolerated in this population, providing preliminary evidence for its potential therapeutic effects in clinical management.

Keywords Belumosudil · Pediatric · Refractory · Chronic graft-versus-host disease

Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) offers a potentially curative option for various hematological malignancies and disorders. In 2019, pediatric patients made up 37.5% of all allo-HSCT recipients in China, compared to only about 10.1% in the United States [1, 2]. Chronic graft-versus-host disease (cGVHD) is a common and serious complication following transplantation, significantly contributing to late morbidity and mortality [3]. Its incidence varies widely, ranging from 30 to 70%, and affects approximately 50% of pediatric recipients [4, 5]. cGVHD can involve a single organ or multiple systems, resembling autoimmune or immunologic diseases [6–8], with a wide range of severity that can greatly impact patients' quality of life [7, 9]. A key feature of cGVHD is fibrosis, which involves the thickening and scarring of connective tissue in affected organs. This fibrotic process,

Wenting Chen and Zhi Wang contributed equally to this work.

✉ Jianhua You
yjhxm722@163.com

✉ Jiong Hu
hj10709@rjh.com.cn

1 Hainan General Hospital, Haikou, China

2 Hainan Hospital of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Qionghai, China

3 School of Biomedical Engineering, Hainan University, Haikou, China

4 Beijing Jingdu Children's Hospital, Beijing, China

5 Department of Hematology, Xiangya Hospital of Central South University, Changsha, China

6 Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

driven by chronic inflammation, can lead to organ dysfunction, complicating clinical management [10].

The current first-line treatment for cGVHD is glucocorticoids (GCs), with or without calcineurin inhibitors (CNIs), regardless of patient age [5, 8, 11]. However, long-term GC therapy in pediatric patients can lead to significant adverse effects, including growth retardation, osteoporosis, metabolic disturbances, and a higher risk of infections [12]. Efforts to improve the efficacy of first-line GC therapy by adding agents such as mycophenolate mofetil (MMF) or cyclosporine A (CSA) have not consistently resulted in substantial benefits [13]. As a result, approximately 70% of patients require second-line therapy.

Belumosudil, a small molecule inhibitor of Rho-associated coiled-coil kinase 2 (ROCK2) [14–16], is approved for the treatment of steroid-refractory (SR-cGVHD) and steroid-dependent (SD-cGVHD) cases. This agent helps restore immune balance and may reduce or even reverse fibrosis [17]. It is the first targeted drug approved in China for cGVHD after inadequate response to frontline therapy. Although belumosudil is indicated for pediatric patients aged 12–18 years [14, 18], data on this population remain limited, with only one reported case involving a 16-year-old [19]. Therefore, more treatment data on pediatric patients are needed to guide clinical practice. This case series describes three 12-year-old Chinese patients with cGVHD who were treated with belumosudil after failing multiple lines of systemic therapy.

Case reports

Case 1

A 12-year-old male patient, weighing 32 kg with a body mass index (BMI) of 15.4 kg/m², underwent matched unrelated donor transplantation in December 2017 due to chronic active Epstein-Barr virus infection. His conditioning regimen prior to stem cell infusion included etoposide, cytarabine, total body irradiation (TBI), busulfan (BU), cyclophosphamide (CTX), and fludarabine (FLU). For GVHD prophylaxis, he received anti-thymocyte globulin, CSA, and MMF. The patient had no history of acute GVHD (aGVHD).

In July 2018, he was diagnosed with severe cGVHD according to the 2014 National Institutes of Health (NIH) cGVHD consensus criteria, involving the skin, joints, liver, and lungs. The patient subsequently underwent six lines of systemic treatment, including mesenchymal stem cells (MSC), ruxolitinib, infliximab, methotrexate (MTX), cord blood regulatory T cell infusion, CTX, basiliximab, and CSA, but did not achieve a durable response. Disease progression occurred after the last treatment regimen in August 2023. Given the patient's age, lung cGVHD was assessed based on symptoms rather than forced expiratory volume in one second (FEV1). Reassessment of cGVHD severity indicated NIH scores of 3 for skin and joint fascia involvement, 2 for the oral cavity, eyes, and lungs, and 1 for the esophagus, gastrointestinal (GI) tract, and liver, confirming severe cGVHD (Table 1). The Photographic Range of Motion (P-ROM) score was 9 at baseline. On August 23, 2023, the patient began treatment with belumosudil, along with other immunosuppressants (Table 2). After 10 days, the prednisone dosage was reduced. By day 56, the patient showed an initial partial response (PR) according to the 2014 NIH consensus criteria [20], with improvements in the oral cavity, GI tract, and eyes (Table 1). The lung score decreased from 2 to 1 by day 114. By day 183, the skin score declined from 3 to 1, and the P-ROM score improved from 9 at baseline to 11. PR or complete response (CR) was observed in all affected organs, with an overall response maintained as PR (Table 3). Additionally, the Lee cGVHD Symptom Scale (LSS) score decreased from 62 before treatment to 34 after 183 days, indicating a clinically meaningful improvement (Table 1).

The patient was followed for up to 210 days, during which treatment with belumosudil, MMF, and ruxolitinib continued, while prednisone was tapered (Table 2). He maintained PR without exacerbation of symptoms. Seven days after starting belumosudil, the patient experienced moderate adverse events (AEs), including grade 2 hypertension, liver enzyme elevation, creatine kinase elevation, stomach upset, nausea, and skin itching, as per Common Terminology Criteria for Adverse Events (CTCAE) 5.0. Symptomatic treatment was provided, and liver tests gradually returned to normal after 58 days of belumosudil treatment. Given that the AEs were manageable, the dosage of belumosudil remained unchanged (Table 2). There was no recurrence of the primary disease during the treatment period.

Case 2

The second patient was a 12-year-old male, weighing 20 kg with a BMI of 9.9 kg/m², who underwent matched-related donor (MRD) transplantation in March 2019 for chronic granulomatous disease. His conditioning regimen included BU, FLU, and CTX. For GVHD prophylaxis, he received CSA and MMF. One month after transplantation, he developed grade II aGVHD affecting the skin and liver, which was effectively managed with methylprednisolone (MP), MTX, and tacrolimus (FK506).

In August 2020, the patient showed symptoms of lung cGVHD, which improved with FK506 and MP. By February 2021, he had severe cGVHD affecting six organs: skin,

Table 1 Effectiveness assessment

	Date	NIH Severity Score							P-ROM score				LSS score	Overall response assessment
		Skin	Oral cavity	Eye	Esophagus	GI tract	Liver	Lung	Joint fascia	Shoulder	Elbow	Wrist/ fingers	Ankle		
Case 1	Baseline	3	2	2	1	1	1	2	3	2	4	2	1	62	/
	Day 56	3	1	1	1	0	1	2	3	2	4	3	1	47	PR
	Day 114	3	1	1	1	0	1	1	3	2	4	3	2	36	PR
	Day 183	1	0	1	0	0	0	1	3	2	4	3	2	34	PR
Case 2	Baseline	3	2	2	1	1	0	1	3	3	3	1	2	69	/
	Day 48	2	1	1	1	1	0	1	3	3	3	1	2	46	PR
	Day 118	2	1	1	1	0	0	1	3	4	4	1	2	33	PR
	Day 145	2	0	1	0	0	0	1	3	4	4	1	2	29	PR
	Day 197	1	1	1	0	0	0	0	3	4	4	1	2	21	PR
Case 3	Baseline	3	2	2	1	1	0	1	3	4	4	6	2	66	/
	Day 31	2	2	1	1	1	0	1	2	4	4	6	3	51	PR
	Day 60	2	1	1	1	1	0	1	2	4	4	6	3	45	PR
	Day 121	2	1	1	1	1	0	1	3	4	4	6	2	46	PR

NIH: National Institutes of Health; P-ROM: Photographic Range of Motion; LSS: Lee cGVHD symptom scale score; GI: gastrointestinal

oral cavity, eyes, GI tract, lungs, and joint fascia. Despite various systemic therapies, including GCs, MSC, infliximab, ruxolitinib, FK506, CSA, MTX, tofacitinib, pomalidomide, ibrutinib, dupilumab, and abatacept, no satisfactory response was achieved.

Reassessment in August 2023, prior to beginning belumosudil treatment, revealed severe involvement of the skin and joint fascia (score 3), moderate involvement of the oral cavity and eyes (score 2), and mild involvement of the esophagus, GI tract, and lungs (score 1), confirming severe cGVHD (Table 1). The patient's LSS score was 69, and the P-ROM score was 9 at baseline. On August 23, 2023 (day 0), treatment with belumosudil commenced, along with other immunosuppressants (Table 2). By day 48, the patient achieved an overall PR, particularly noted in the oral cavity and eyes. Reductions in GI tract and esophagus scores were observed at days 118 and 145, respectively. The lung score decreased to 0 by day 197. Significant improvements were also noted in the skin score, which decreased from 3 to 1, and the P-ROM score, which improved from 9 at baseline to 11. The patient achieved an overall PR, with CR in the esophagus, GI tract, and lungs, and PR in other affected organs (Table 3). The LSS score decreased to 21, indicating substantial symptom relief (Table 1). Throughout treatment, the patient experienced mild AEs, including grade 1 skin itching, nausea, insomnia, and joint pain, which were managed symptomatically. No dose modifications of belumosudil were required (Table 2), and no recurrence of the primary disease was observed during this period.

Case 3

The third patient was a 12-year-old female weighing 22.2 kg with a BMI of 13.8 kg/m², who underwent MRD transplantation for thalassemia on October 21, 2021. Her conditioning regimen included FLU, BU, and CTX, followed by a short course of MTX and intravenous immunoglobulin (IVIG) for GVHD prophylaxis. The patient had no history of aGVHD.

In February 2022, she developed cGVHD with severe involvement of the skin and liver. Despite undergoing five lines of systemic therapies, including MP, ruxolitinib, FK506, MMF, a recombinant humanized anti-CD25 monoclonal antibody, MSC, rituximab, CTX, and imatinib, her cGVHD progressed, with new organ involvement in the lungs and joint fascia. After the last treatment on January 4, 2024, with MP, FK506, imatinib, and rituximab, there was no organ response.

Reevaluation in January 2024 showed severe involvement of the skin and joint fascia (score 3 each), moderate involvement of the oral cavity and eyes (score 2 each), and mild involvement of the esophagus, GI tract, and lungs (score 1

Table 2 Dosing of immunosuppressants during belumosudil treatment

	Date	Belumosudil	Prednisone	Cyclosporine A	Mycophenolate mofetil	Ruxolitinib	Tacrolimus (FK506)
Case 1	Baseline	200 mg qd	20 mg tid	25 mg bid	125 mg qd	2.5 mg qd	/
	Day 56	200 mg qd	10 mg bid	25 mg bid	125 mg qd	2.5 mg qd	/
	Day 114	200 mg qd	5 mg bid	25 mg bid	125 mg qd	2.5 mg qd	/
	Day 183	200 mg qd	0	25 mg bid	125 mg qd	2.5 mg qd	/
Case 2	Baseline	200 mg qd	/	/	/	2.5 mg bid	0.15 mg bid
	Day 48	200 mg qd	/	/	/	2.5 mg bid	0.15 mg bid
	Day 118	200 mg qd	/	/	/	2.5 mg bid	0.15 mg bid
	Day 145	200 mg qd	/	/	/	2.5 mg bid	0.15 mg bid
	Day 197	200 mg qod	/	/	/	2.5 mg bid	0.15 mg bid
Case 3	Baseline	200 mg qd	10 mg qd	50 mg bid	/	/	1 mg bid
	Day 31	200 mg qd	5 mg qd	0	/	/	1 mg bid
	Day 60	200 mg qd	2.5 mg qod	0	/	5 mg bid	1.5 mg qd
	Day 86	200 mg qod	0	0	/	5 mg bid	0
	Day 121	200 mg qod	10 mg qd	0	/	5 mg bid	1 mg bid

Qd, once daily; tid, thrice daily; bid, twice daily; qod, every other day. The dose of '0' indicates that the patient discontinued the corresponding medication at that follow-up point. The '/' indicates that the patient did not use the corresponding medication throughout the entire follow-up period

Table 3 Response status of each organ at latest evaluation

No.	Skin	Oral cavity	Eyes	Esophagus	GI tract	Liver	Lung	Joint fascia	Overall response assessment
Case 1	PR	CR	PR	CR	CR	CR	PR	PR	PR
Case 2	PR	CR	PR	CR	CR	NE	UN	PR	PR
Case 3	PR	PR	PR	UN	UN	NE	UN	UN	PR

GI: gastrointestinal; CR: complete response; PR: partial response; UN: unchanged

each), confirming the severity of her condition (Table 1). On January 20, 2024 (day 0), the patient began treatment with belumosudil and other immunosuppressants (Table 2). By day 31, scores for the skin and joint fascia decreased from 3 to 2, and the score for the eyes improved from 2 to 1, resulting in an overall PR. By day 60, she maintained improved NIH scores, with a decrease from 2 to 1 in the oral cavity, further supporting the overall PR. The LSS score improved from 66 at baseline to 45 by day 60 (Table 1). Based on the improvement in her organ conditions, the medication regimen was adjusted (Table 2). However, due to persistent joint symptoms, ruxolitinib was added without significant improvement. After day 86, the dose of belumosudil was reduced to every other day based on the family's preference (Table 2). By day 121, following this reduction, the patient experienced worsening joint and skin symptoms, including decreased joint mobility, increased pain, skin edema, and hardness. The treatment regimen was subsequently modified again (Table 2). Throughout the follow-up to day 121, the patient experienced mild AEs, such as grade 1 liver enzyme elevation and nausea, none of which required a modification of belumosudil (Table 2). Importantly, there was no recurrence of the primary disease during this period.

Discussion

Belumosudil is approved for treating SR and SD cGVHD in patients aged 12 years and older, but data on its use in the 12–18 age group are limited. In a phase II trial with Chinese patients and the pivotal ROCKstar trial, the youngest participants were 29.5 years old and 21 years old, respectively [14, 15]. A prior case report from Poland described a 16-year-old patient with refractory cGVHD who showed gradual improvement in lung, skin, and joint symptoms, achieving an overall PR after 12 months of follow-up [19]. This case series presents three 12-year-old patients with severe cGVHD affecting multiple organs who had failed multiple lines of treatment and received combination therapy with belumosudil and other immunosuppressants. All three patients achieved an initial PR at the first evaluation (6 weeks after starting belumosudil), with many affected organs showing either CR or PR after ongoing treatment. Only grade 1–2 AEs were reported during treatment. These findings suggest that belumosudil may be a feasible and tolerable option for 12-year-old patients with severe cGVHD that is resistant to multiple therapies.

Although this case series included only three patients, all achieved an overall PR with belumosudil-based treatment. Each patient showed a meaningful improvement in symptoms, as indicated by a reduction of at least 7 points on the

LSS, similar to findings from the ROCKstar study of belumosudil [15]. Notably, Case #1 maintained PR even after reducing prednisone and CSA. In contrast, reducing the steroid dosage in Case #3 may have worsened her cGVHD, but increasing the dosage again still resulted in a satisfactory response. This suggests that any reduction or discontinuation of steroids should be tailored to the individual patient's condition. Patients with cGVHD treated with frontline GCs often achieve an ORR of about 50%, but they may experience steroid withdrawal symptoms and recurrent disease, including the reappearance of cGVHD and temporary worsening of affected organs. Additionally, rapid tapering of belumosudil after achieving an initial response may lead to accelerated progression of cGVHD, indicating that dose reductions should only occur in the context of a sustained response.

In our series, all three patients had involvement of the oral cavity, eyes, lungs, and joint fascia. While treatment with belumosudil resulted in a rapid response, improvements in lung and joint fascia symptoms were slower. Lung cGVHD is concerning due to its severity and poor prognosis, and it often requires complex management without a standardized approach [21]. Previous studies have shown that the ORR for lung cGVHD is low, ranging from 9 to 17% with treatments like rituximab, ruxolitinib, abatacept, and interleukin-2 (IL-2) [22]. In our case series, significant improvements were observed in lung symptoms for Cases #1 and #2 after treatment with belumosudil, noted at days 114 and 197, respectively. This therapeutic effect aligns with findings by DeFilipp et al. [23], who reported a lung-specific ORR of 37% (23% PR, 14% CR) in 65 patients with bronchiolitis obliterans syndrome treated with belumosudil.

All three patients in this case series presented with severe involvement of the skin and joint fascia, which are commonly affected in cGVHD. This highlights the extent of fibrosis and the need for prolonged treatment to achieve better outcomes. Notably, all patients achieved a PR in joint fascia at different time points (day 56, day 118, and day 31), reflecting significant improvements in a challenging area. This observation aligns with findings from the ROCKstar study, which reported an organ-specific ORR of 71% in the joint fascia [15]. Severe symptoms in this area can have long-term effects on the physical health and growth of children and adolescents, potentially impacting musculoskeletal development and leading to disability. Early diagnosis and treatment are crucial for better recovery. While the results of this case series suggest that belumosudil may be a promising option for managing severe cGVHD in pediatric patients, larger studies are needed to confirm these findings.

The most common AEs associated with belumosudil in patients with cGVHD include infection (53%), fatigue (46%), nausea (42%), and diarrhea (35%) [17]. Grade 3 or 4 AEs included pneumonia (8%), hypertension (6%), and hyperglycemia (5%) [15]. In this case series, AEs were limited to grade 1–2 severity, consistent with the known safety profile of belumosudil and not introducing new safety concerns [17]. Interestingly, the body weights of the three patients were lower than those in clinical trials [14, 15, 17], yet they tolerated the 200 mg daily dose well, indicating good safety and tolerability of belumosudil in pediatric patients with low body weight. In contrast, long-term treatment with other immunosuppressants and steroids in pediatric patients often leads to significant adverse effects, including growth retardation, osteoporosis, increased infection risk, and metabolic disturbances [12]. Targeted agents like ruxolitinib and ibrutinib also raise safety concerns, particularly related to infections and hematologic toxicities, which are critical issues in this population [24]. The mild to moderate AEs observed in the three pediatric patients treated with belumosudil were consistent with those reported in adults, suggesting a favorable safety profile.

However, several limitations must be acknowledged in this case series. First, the findings are based on only three low-weight pediatric patients, so the effectiveness of belumosudil requires validation through studies with larger sample sizes. Furthermore, the pharmacokinetics and pharmacodynamics of belumosudil may differ in children with low body weight, making it crucial to determine an optimal dosing regimen that considers variations in body composition, growth, and development to maximize therapeutic effectiveness while minimizing adverse effects. Second, all patients in this case series were 12 years old. Future studies should include a broader age range to develop safe and effective treatment protocols tailored to the unique physiological characteristics of younger children. Lastly, all patients had previously failed multiple lines of treatment before starting belumosudil. Therefore, it remains to be explored whether early intervention with belumosudil leads to improved prognosis. These considerations highlight the need for further investigation to better understand the potential of belumosudil in pediatric patients with cGVHD.

Conclusion

Belumosudil-based regimens appeared to be effective and well-tolerated in three 12-year-old Chinese children with cGVHD who had previously failed multiple lines of treatment. This case series contributes to the clinical understanding of belumosudil's use in pediatric patients with cGVHD. Although it includes only three patients, the findings suggest potential therapeutic benefits of belumosudil in this population, highlighting the need for further research with larger sample sizes to confirm these results.

Acknowledgements Medical writing support for this manuscript was provided by Dr. Fabao Zhang of Shanghai MedSci Technology Co.Ltd.

Author contributions Wenting Chen: Data curation, Formal analysis, Investigation, Writing - original draft, Writing - review & editing Zhi Wang: Formal analysis, Investigation, Writing - original draft, Writing - review & editing Zhouyang Liu, Bin Fu, Tingting Xing: Data curation, Formal analysis, Writing - review & editing Jianhua You: Conceptualization, Investigation, Methodology, Supervision, Data curation, Formal analysis, Writing - review & editing Jiong Hu: Conceptualization, Investigation, Data curation, Formal analysis, Writing - review & editing.

Funding Not applicable.

Data availability The original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding author.

Declarations

Ethical approval and consent to participate This case series was approved by the Ethics Committee of the Hainan Hospital of Ruijin Hospital affiliated to Shanghai Jiao Tong University School of Medicine (approval number AF-0406;). Written consent to participate in the case series was provided by all patients.

Competing interests The authors declare no competing interests.

References

1. Xu LP, Lu PH, Wu DP, Sun ZM, Liu QF, Han MZ et al (2021) Hematopoietic stem cell transplantation activity in China 2019: a report from the Chinese blood and marrow transplantation Registry Group. Bone Marrow Transpl 56:2940–2947. https://doi.org/10.1038/s41409-021-01431-6
2. Cusatis RLC, Feng Z, Allbee-Johnson M, Shaw BE (2023) Current Uses and Outcomes of Cellular Therapies: CIBMTR Summary Slides. https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fcibmtr.org%2FFiles%2FSummary-Slides--Reports%2FSummary-Slides-2023-website-version.pptx&wdOrigin=BROWSELINK
3. Baumrin E, Loren AW, Falk SJ, Mays JW, Cowen EW (2024) Chronic graft-versus-host disease. Part I: epidemiology, pathogenesis, and clinical manifestations. J Am Acad Dermatol 90:1–16. https://doi.org/10.1016/j.jaad.2022.12.024
4. Xu L, Chen H, Chen J, Han M, Huang H, Lai Y et al (2018) The consensus on indications, conditioning regimen, and donor selectio n of allogeneic hematopoietic cell transplantation for hematological d iseases in China-recommendations from the Chinese Society of Hematolog Y. J Hematol Oncol 11:33. https://doi.org/10.1186/s13045-018-0564-x
5. Haroun E, Agrawal K, Leibovitch J, Kassab J, Zoghbi M, Dutta D et al (2023) Chronic graft-versus-host disease in pediatric patients: differences and challenges. Blood Rev 60:101054. https://doi.org/10.1016/j.blre.2023.101054
6. Jagasia MH, Greinix HT, Arora M, Williams KM, Wolff D, Cowen EW et al (2015) National Institutes of Health Consensus Development Project on Criteria for clinical trials in chronic graft-versus-host disease: I. The 2014 diagnosis and Staging Working Group report. Biol Blood Marrow Transpl 21:389–401e381. https://doi.org/10.1016/j.bbmt.2014.12.001
7. Socie G, Ritz J (2014) Current issues in chronic graft-versus-host disease. Blood 124:374–384. https://doi.org/10.1182/blood-2014-01-514752
8. Hamilton BK (2021) Updates in chronic graft-versus-host disease. Hematol Am Soc Hematol Educ Program 2021:648–654. https://doi.org/10.1182/hematology.2021000301
9. Carpenter PA, Kitko CL, Elad S, Flowers ME, Gea-Banacloche JC, Halter JP et al (2015) National Institutes of Health Consensus Development Project on Criteria for clinical trials in chronic graft-versus-host disease: V. The 2014 Ancillary Therapy and supportive care Working Group Report. Biol Blood Marrow Transpl 21:1167–1187. https://doi.org/10.1016/j.bbmt.2015.03.024
10. Cooke KR, Luznik L, Sarantopoulos S, Hakim FT, Jagasia M, Fowler DH et al (2017) The Biology of Chronic Graft-versus-host disease: a Task Force Report from the National Institutes of Health Consensus Development Project on Criteria for clinical trials in chronic graft-versus-host disease. Biol Blood Marrow Transpl 23:211–234. https://doi.org/10.1016/j.bbmt.2016.09.023
11. Hematopoietic Stem Cell Application Group, Chinese Society of Hematology, Chinese Medical Association; China Association for the Prevention of Hematology Diseases (2021) Chinese consensus on the diagnosis and management of chronic graft-ver sus-host disease (2021). Chin J Hematol 42:265–275. https://doi.org/10.3760/cma.j.issn.0253-2727.2021.04.001
12. Ferrara G, Petrillo MG, Giani T, Marrani E, Filippeschi C, Oranges T et al (2019) Clinical Use and Molecular Action of corticosteroids in the Pediatric Age. Int J Mol Sci 20. https://doi.org/10.3390/ijms20020444
13. Zeiser R (2023) Novel approaches to the treatment of chronic graft-versus-host disease. J Clin Oncol 41:1820–1824. https://doi.org/10.1200/JCO.22.02256
14. Wang Y, Wu D, Zhang X, Li Y, He Y, Liu Q et al (2024) A phase II study of belumosudil for chronic graft-versus-host disease in patients who failed at least one line of systemic therapy in China. BMC Med 22:142. https://doi.org/10.1186/s12916-024-03348-5
15. Cutler C, Lee SJ, Arai S, Rotta M, Zoghi B, Lazaryan A et al (2021) Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. Blood 138:2278–2289. https://doi.org/10.1182/blood.2021012021
16. Salhotra A, Sandhu K, O'Hearn J, Ali H, Nakamura R, Modi BG (2023) A critical review of belumosudil in adult and pediatric patients with chronic graft-versus-host disease. Expert Rev Clin Immunol 19:241–251. https://doi.org/10.1080/1744666X.2023.2152330
17. Blair HA (2021) Belumosudil: first approval. Drugs 81:1677–1682. https://doi.org/10.1007/s40265-021-01593-z
18. Jagasia M, Lazaryan A, Bachier CR, Salhotra A, Weisdorf DJ, Zoghi B et al (2021) ROCK2 inhibition with Belumosudil (KD025) for the treatment of chronic graft-versus-host disease. J Clin Oncol 39:1888–1898. https://doi.org/10.1200/JCO.20.02754

19. Sobkowiak-Sobierajska A, P118 BELUMOSUDIL FOR SEVERE, REFRACTORY CHRONIC GVHD IN (2024) PEDIATRIC PATIENT: CASE REPORT: 50th EBMT Annual Meeting; https://ebmt2024.abstractserver.com/program/#/details/presentations/1811
20. Lee SJ, Wolff D, Kitko C, Koreth J, Inamoto Y, Jagasia M et al (2015) Measuring therapeutic response in chronic graft-versus-host disease. N ational institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: IV. The 201 4 Response Criteria Working Group report. Biol Blood Marrow Transpl 21:984–999. https://doi.org/10.1016/j.bbmt.2015.02.025
21. Bos S, Murray J, Marchetti M, Cheng G-S, Bergeron A, Wolff D et al (2024) ERS/EBMT clinical practice guidelines on treatment of pulmonary chronic graft-versus-host disease in adults. Eur Respir J 63:2301727. https://doi.org/10.1183/13993003.01727-2023
22. Fatoum H, Zeiser R, Hashmi SK (2024) A personalized, organ-based approach to the treatment of chronic stero id-refractory graft-versus-host disease. Blood rev 63:101142. https://doi.org/10.1016/j.blre.2023.101142
23. DeFilipp Z, Kim HT, Yang Z, Noonan J, Blazar BR, Lee SJ et al (2022) Clinical response to belumosudil in bronchiolitis obliterans syndrome: a combined analysis from 2 prospective trials. Blood Adv 6:6263–6270. https://doi.org/10.1182/bloodadvances.2022008095
24. Andreescu M (2024) Risk of severe infections secondary to the use of targeted therapies in hematological malignancies. Cureus 16:e52050. https://doi.org/10.7759/cureus.52050