

Axatilimab in Combination With Ruxolitinib in Patients With Newly Diagnosed Chronic Graft-Versus-Host Disease: Interim Safety Analysis of a Randomized, Phase 2 Study

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Introduction

- Chronic graft-versus-host disease (cGVHD) is a leading cause of morbidity and nonrelapse mortality in patients who undergo allogeneic hematopoietic stem cell transplantation^{1,2}
- Pathogenesis of cGVHD involves activation of colony-stimulating factor 1 receptor (CSF-1R)–dependent monocytes and macrophages, which contribute to multiorgan inflammation and fibrosis, as well as T-cell activation, cytokine signaling, and inflammation mediated by Janus kinase (JAK)1/JAK2^{3–7}
- Axatilimab is a high-affinity monoclonal antibody that targets CSF-1R to deplete CSF-1R–dependent monocytes and macrophages^{8,9}
- Ruxolitinib is a potent and selective inhibitor of JAK1/JAK2^{10,11}
- Both axatilimab and ruxolitinib have demonstrated clinically meaningful efficacy and were generally well tolerated as single agents in previously treated cGVHD^{8,10,12,13}
- Due to their distinct mechanisms of action, combining axatilimab and ruxolitinib may improve efficacy without overlapping safety concerns
- An ongoing phase 2 clinical trial (NCT06388564) is evaluating the efficacy and safety of axatilimab 0.3 mg/kg every 2 weeks (Q2W) in combination with ruxolitinib 10 mg twice daily (BID), compared with ruxolitinib alone or corticosteroids alone, in patients with newly diagnosed moderate to severe cGVHD

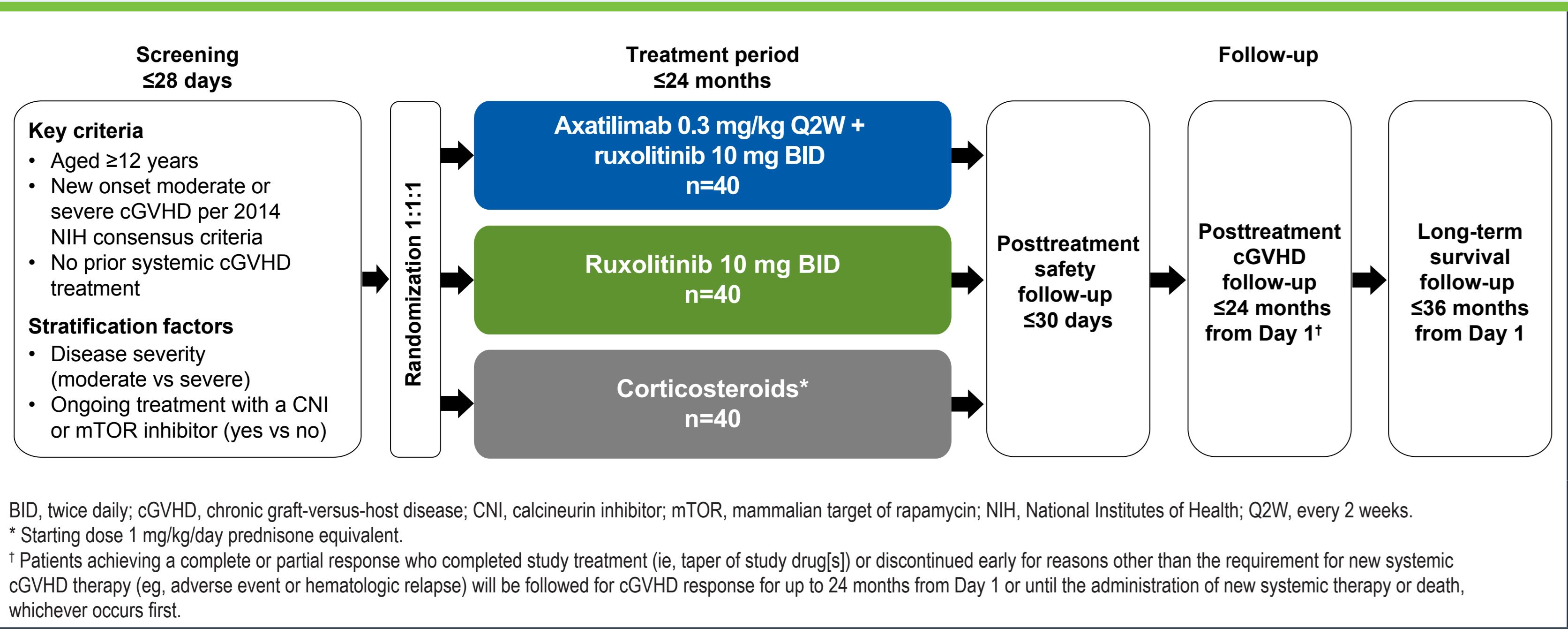
Objective

- To report a prespecified interim safety analysis of axatilimab in combination with ruxolitinib in patients with newly diagnosed cGVHD

Methods

- In this ongoing, randomized, open-label, multicenter, phase 2 study, patients were randomized 1:1:1 to receive axatilimab 0.3 mg/kg Q2W in combination with ruxolitinib 10 mg BID, ruxolitinib 10 mg BID alone, or corticosteroids alone for up to 24 months (**Figure 1**)
 - Study treatment was considered completed if a patient achieves a complete or partial response and completes the study treatment taper

Figure 1. Study Design



- The primary endpoint is overall response at 6 months, defined as complete or partial response per NIH 2014 consensus criteria¹⁴ in the absence of a new systemic cGVHD therapy
- Safety and tolerability evaluations include the frequency and severity of treatment-emergent adverse events (TEAEs), physical examinations, and laboratory assessments
- A prespecified interim safety analysis was planned to occur after approximately 30 patients (10 patients in each group) received ≥1 cycle of study treatment
- Safety data were summarized using descriptive statistics

Results

Patients

- As of the interim analysis, 44 patients have enrolled, and 43 patients have received study treatment (**Table 1**)

Table 1. Baseline Patient Demographics and Clinical Characteristics

	Axatilimab 0.3 mg/kg Q2W + ruxolitinib 10 mg BID (n=15)	Ruxolitinib 10 mg BID (n=15)	Corticosteroids (n=14)
Characteristic			
Age, median (range), y	64.0 (19–77)	69.0 (43–76)	66.5 (49–75)
≥18–64 y, n (%)	8 (53.3)	6 (40.0)	6 (42.9)
≥65 y, n (%)	7 (46.7)	9 (60.0)	8 (57.1)
Male, n (%)	7 (46.7)	7 (46.7)	9 (64.3)
Ethnicity, n (%)			
Non-Hispanic/Latino	10 (66.7)	13 (86.7)	14 (100)
Hispanic or Latino	5 (33.3)	2 (13.3)	0
Time from transplant to cGVHD diagnosis, median (range), mo	14.0 (4.4–49.5)	11.0 (4.6–26.7)	6.4 (3.4–72.3)
Severity of cGVHD at study entry, n (%)			
Moderate	6 (40.0)	7 (46.7)	7 (50.0)
Severe	9 (60.0)	8 (53.3)	7 (50.0)
Stem cell source, n (%)			
PBSC	14 (93.3)	14 (93.3)	13 (92.9)
Bone marrow	1 (6.7)	1 (6.7)	1 (7.1)
Donor source, n (%)			
Unrelated	7 (46.7)	13 (86.7)	8 (57.1)
Sibling	7 (46.7)	0	4 (28.6)
Related (non-sibling)	1 (6.7)	2 (13.3)	2 (14.3)
Underlying disease, n (%)			
Acute myeloid leukemia	6 (40.0)	6 (40.0)	7 (50.0)
Myelodysplastic syndrome	3 (20.0)	6 (40.0)	2 (14.3)
Other malignant disease	6 (40.0)	3 (20.0)	5 (35.7)

BID, twice daily; cGVHD, chronic graft-versus-host disease; PBSC, peripheral blood stem cells; Q2W, every 2 weeks.

- All patients received prior treatment for cGVHD prophylaxis
- As of the data cutoff, 34 patients were continuing to receive treatment, 2 have completed treatment, and 8 have discontinued (**Table 2**)
 - The median (range) number of cycles of study treatment received was 2 (1–6), 3 (1–9), and 2 (1–4) for axatilimab combined with ruxolitinib, ruxolitinib alone, and corticosteroids alone, respectively; these data reflect that most patients continue to receive study treatment as of the interim analysis

Table 2. Patient Disposition

	Axatilimab 0.3 mg/kg Q2W + ruxolitinib 10 mg BID (n=15)	Ruxolitinib 10 mg BID (n=15)	Corticosteroids (n=14)
Treatment status, n (%)			
Ongoing	14 (93.3)	14 (93.3)	6 (42.9)
Completed*	0	0	2 (14.3)
Discontinued	1 (6.7)	1 (6.7)	6 (42.9)
New systemic cGVHD therapy [†]	0	0	5 (35.7)
Death	0	1 (6.7) [‡]	0
Patient withdrawal	0	0	1 (7.1) [§]
Relapse or progression of underlying hematologic disease	1 (6.7) [¶]	0	0

BID, twice daily; cGVHD, chronic graft-versus-host disease; Q2W, every 2 weeks.
* Treatment is considered complete if a patient achieves a complete or partial response and completes the study treatment taper (ie, ruxolitinib and axatilimab taper for the combination treatment group, ruxolitinib taper for the ruxolitinib monotherapy group, and corticosteroid taper for the corticosteroids alone treatment group).
[†] Patient received new systemic therapy owing to insufficient response to treatment.
[‡] Death due to bronchospastic crisis and considered unrelated to treatment.
[§] One patient withdrew prior to receiving the first dose; withdrawal occurred because the patient preferred not to receive corticosteroids.
[¶] Relapse considered unrelated to treatment; patient was deemed to be at high risk of relapse.

Safety

- Among all treated patients, 32 patients experienced TEAEs, and 5 patients experienced grade ≥3 TEAEs (**Table 3**)

Table 3. Summary of TEAEs

	Axatilimab 0.3 mg/kg Q2W + ruxolitinib 10 mg BID (n=15)	Ruxolitinib 10 mg BID (n=15)	Corticosteroids (n=13)
n (%)			
TEAEs (all grade)	11 (73.3)	12 (80.0)	9 (69.2)
TEAEs (grade ≥3)	2 (13.3)	2 (13.3)	1 (7.7)
Most frequent TEAEs*			
Amylase increased	2 (13.3)	3 (20.0)	0
Constipation	1 (6.7)	1 (6.7)	3 (23.1)
Anemia	1 (6.7)	3 (20.0)	0
Diarrhea	2 (13.3)	2 (13.3)	0
Fatigue	2 (13.3)	2 (13.3)	0
Upper respiratory tract infection	1 (6.7)	3 (20.0)	0
Blood alkaline phosphatase increased	1 (6.7)	2 (13.3)	0
Hyperkalemia	2 (13.3)	1 (6.7)	0
Insomnia	0	0	3 (23.1)
Neutrophil count decreased	2 (13.3)	1 (6.7)	0
Edema peripheral	0	2 (13.3)	0
Pollakiuria	0	2 (13.3)	0
Vertigo	0	2 (13.3)	0
TEAEs leading to dose reduction			
Amylase increased	0	1 (6.7)	0
Anemia	1 (6.7) [†]	0	0
Creatinine renal clearance decreased	1 (6.7) [†]	0	0
Insomnia	0	0	1 (7.7)
Platelet count decreased	0	1 (6.7)	0
Staphylococcal sepsis	0	1 (6.7)	0
TEAEs leading to study drug discontinuation			
Anxiety	1 (6.7) [‡]	0	0
Fatigue	1 (6.7) [‡]	0	0

BID, twice daily; TEAE, treatment-emergent adverse event; Q2W, every 2 weeks.
Safety population includes all patients who received ≥1 treatment dose.
* Occurring in ≥2 patients in a treatment group.
[†] TEAE led to dose reduction of ruxolitinib only.
[‡] TEAE led to discontinuation of both axatilimab and ruxolitinib.

Conclusions

- In this interim analysis of a randomized phase 2 trial, the combination of axatilimab + ruxolitinib was well tolerated and had a similar safety profile to ruxolitinib alone, with no evidence of additive toxicity

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