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# Long-Term Treatment Duration and Safety of Axatilimab Among Patients With Chronic Graft-Versus-Host Disease in AGAVE-201

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## Introduction

- Chronic graft-versus-host disease (cGVHD) is a major cause of morbidity and nonrelapse mortality among patients who undergo allogeneic hematopoietic stem cell transplantation[1,2]
- In patients with cGVHD, colony-stimulating factor 1 receptor (CSF-1R)–dependent monocytes and macrophages potentiate inflammation and fibrosis, which contribute to multiorgan damage[3,4]
- Treatment with axatilimab, a high-affinity monoclonal antibody targeting CSF-1R, depletes CSF-1R–dependent monocytes and macrophages[5]
- Axatilimab 0.3 mg/kg every 2 weeks (Q2W) was approved by the US Food and Drug Administration (FDA) for the treatment of cGVHD after failure of ≥2 prior lines of therapy based on findings from the pivotal, phase 2 AGAVE-201 study (NCT04710576)[6]
- In AGAVE-201, an overall response was achieved in 74% (95% CI, 63%–83%) of patients receiving axatilimab 0.3 mg/kg Q2W in the first 6 treatment cycles, and axatilimab was generally well tolerated, with 6% of patients receiving axatilimab 0.3 mg/kg Q2W experiencing treatment-emergent adverse events (TEAEs) leading to treatment discontinuation[7]

## Objective

- To report long-term treatment duration and safety among patients with cGVHD enrolled in AGAVE-201

## Methods

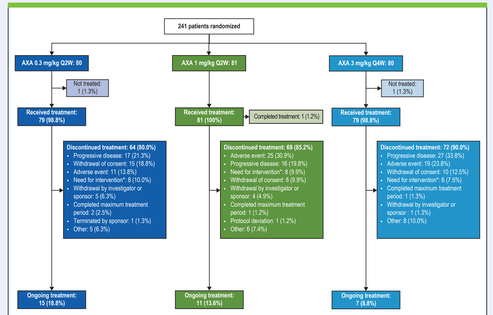
- Patients aged ≥2 years with refractory or recurrent cGVHD after ≥2 prior lines of systemic therapy were randomized 1:1:1 to intravenous axatilimab 0.3 mg/kg Q2W, 1 mg/kg Q2W, or 3 mg/kg every 4 weeks (Q4W)
- Treatment could continue if the patient was deriving clinical benefit per investigator assessment and if the patient reported clinically meaningful symptomatic improvement, up to a maximum of 2 years
- Based on independent data monitoring committee recommendations after Cycle 7 Day 1 (C7D1), patients randomized to the 3 mg/kg Q4W cohort had their dose reduced to 0.6 mg/kg Q4W, and patients randomized to 1 mg/kg Q2W cohort could continue at their current dose or transition to 0.3 mg/kg Q2W per investigator discretion
- Patients enrolled into Q2W dosing cohorts could switch to a 0.6 mg/kg Q4W dosing regimen if they were able to sustain a partial or complete response for 20 weeks or did not have disease progression per the study protocol and investigator discretion
- The safety follow-up period was 90 days after the last dose of axatilimab; survival data were collected for 5 years after the safety follow-up period
- Long-term overall survival (OS), safety, and duration of treatment were assessed, with a focus on the 0.3 mg/kg Q2W cohort as well as the full study population
- The data cutoff for this analysis was March 30, 2025

## Results

### *Overall Efficacy and Safety*

- Of 241 patients enrolled in AGAVE-201, 239 received axatilimab (0.3 mg/kg Q2W, n=79; 1 mg/kg Q2W, n=81; 3 mg/kg Q4W, n=79)
- As of March 30, 2025, 205 patients discontinued treatment, 33 patients remained on treatment, and 1 patient completed treatment (**Figure 1**)

**Figure 1. Patient Disposition (ITT Population)**




AXA, axatilimab; ITT, intent to treat; Q2W, every 2 weeks; Q4W, every 4 weeks.
* Need for intervention or therapy determined by the investigator to be medically necessary and was precluded by protocol.

- No new safety signals were observed during long-term follow-up.
- Incidences of fatigue (26.8% in the long-term analysis vs 23.0% in the primary analysis[7]), COVID-19 (22.2% vs 17.6%), and diarrhea (20.9% vs 15.9%) were similar in the long-term and primary analyses
- Incidences of laboratory enzyme elevations were similar in the long-term and primary analyses (aspartate aminotransferase [AST] increased, 38.1% in the long-term analysis vs 35.6% in the primary analysis; alanine aminotransferase [ALT] increased, 26.8% vs 24.7%; creatine phosphokinase [CPK] increased, 38.9% vs 35.1%)
- Incidences of dose interruptions due to laboratory enzyme elevations were generally similar between the primary and long-term analyses (CPK increased, 2.9% in the long-term analysis vs 2.1% in the primary analysis; AST increased, 2.5% in both; ALT increased, 2.1% in both)
- Incidences of dose reductions due to laboratory enzyme elevations were also generally similar in the primary and long-term analyses (CPK increased, 1.3% in the long-term analysis vs 1.7% in the primary analysis; AST increased, 0.8% vs 0.4%; ALT increased, 0.8% in both)
- Across all doses in the long-term analysis, 1 patient discontinued owing to increased CPK, and 2 patients discontinued owing to increased gamma-glutamyl transferase; no patients in the 0.3 mg/kg Q2W cohort discontinued owing to laboratory enzyme elevations
- The overall incidence of periorbital edema was stable (18.4% in both analyses)
- The incidence of TEAEs among all treated patients generally decreased after C7D1; the safety profile after C7D1 is summarized in **Table 1**

**Table 1. TEAEs After C7D1 Among All Treated Patients**

| n (%) | Axatilimab 0.3 mg/kg Q2W (n=79) | Axatilimab all doses (n=239) |
|---|---|---|
| Patients with TEAE | 52 (65.8) | 131 (54.8) |
| Grade ≥3 | 33 (41.8) | 81 (33.9) |
| Patients with treatment-related TEAE | 33 (41.8) | 86 (36.0) |
| Grade ≥3 | 6 (7.6) | 24 (10.0) |
| Patients with serious TEAE | 27 (34.2) | 63 (26.4) |
| Patients with TEAE leading to dose interruption | 22 (27.8) | 51 (21.3) |
| Patients with TEAE leading to dose reduction | 3 (3.8) | 11 (4.6) |
| Patients with TEAE leading to discontinuation | 5 (6.3) | 20 (8.4) |
| Most common TEAEs (any grade)* | | |
| Upper respiratory tract infection | 15 (19.0) | 26 (10.9) |
| Diarrhea | 14 (17.7) | 27 (11.3) |
| Cough | 12 (15.2) | 28 (11.7) |
| Nausea | 11 (13.9) | 17 (7.1) |
| COVID-19 | 10 (12.7) | 19 (7.9) |
| Fatigue | 10 (12.7) | 22 (9.2) |
| Pyrexia | 10 (12.7) | 16 (6.7) |
| ALT increased | 9 (11.4) | 27 (11.3) |
| CPK increased | 9 (11.4) | 31 (13.0) |
| Dyspnea | 9 (11.4) | 15 (6.3) |
| AST increased | 8 (10.1) | 24 (10.0) |
| Vomiting | 8 (10.1) | 13 (5.4) |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; C7D1, Cycle 7 Day 1; CPK, creatine phosphokinase; Q2W, every 2 weeks; TEAE, treatment-emergent adverse event.
* As reported in ≥10% of patients in the 0.3 mg/kg Q2W cohort.

### *Patients Remaining on Treatment*

- Among the 33 patients who remained on treatment, the median (range) treatment duration was 33.1 (31–41) months for the 0.3 mg/kg Q2W group and 34.0 (31–41) months across all doses
- Clinical characteristics of patients who remained on treatment (**Table 2**) were generally similar to those of the overall randomized population[7]

**Table 2. Baseline Demographics and Clinical Characteristics of Patients Remaining on Treatment**

| | Axatilimab 0.3 mg/kg Q2W (n=15)* | Axatilimab all doses (n=33)† |
|---|---|---|
| Age, median (range), y | 49.0 (7–76) | 53.0 (7–76) |
| Male, n (%) | 10 (66.7) | 24 (72.7) |
| Race, n (%) | | |
| White | 13 (86.7) | 28 (84.8) |
| Asian | 1 (6.7) | 3 (9.1) |
| Not reported/other | 1 (6.7) | 2 (6.1) |
| Time from cGVHD diagnosis to randomization, median (range), y | 4.9 (2.9–8.2) | 5.0 (1.1–12.6) |
| Number of organs involved at baseline, median (range), y | 4.0 (1–8) | 4.0 (1–8) |
| Severe disease, n (%) | 12 (80.0) | 26 (78.8) |
| Prior FDA-approved therapy for cGVHD, n (%) | 15 (100) | 29 (87.9) |
| Ruxolitinib | 13 (86.7) | 25 (75.8) |
| Ibrutinib | 5 (33.3) | 12 (36.4) |
| Belumosudil | 3 (20.0) | 6 (18.2) |

cGVHD, chronic graft-versus-host disease; FDA, US Food and Drug Administration; Q2W, every 2 weeks.
* At the analysis cutoff, dosing schedules for axatilimab among patients in the 0.3 mg/kg Q2W cohort were 0.2 mg/kg Q2W (n=1), 0.3 mg/kg Q2W (n=2), 0.3 mg/kg Q4W (n=1), and 0.6 mg/kg Q4W (n=11).
† At the analysis cutoff, dosing schedules for axatilimab among all patients remaining on treatment were 0.2 mg/kg Q2W (n=1), 0.3 mg/kg Q2W (n=2), 0.3 mg/kg Q4W (n=2), 0.6 mg/kg Q4W (n=27), and 1 mg/kg Q2W (n=1).

- The overall safety profile among patients who remained on treatment (**Table 3**) was mostly similar to that of all treated patients over the course of the study

**Table 3. Long-Term Safety in Patients Remaining on Treatment**

| n (%) | Axatilimab 0.3 mg/kg Q2W (n=15)* | Axatilimab all doses (n=33)† |
|---|---|---|
| Patients with TEAE | 15 (100) | 33 (100) |
| Grade ≥3 | 9 (60.0) | 22 (66.7) |
| Patients with treatment-related TEAE | 12 (80.0) | 29 (87.9) |
| Grade ≥3 | 4 (26.7) | 12 (36.4) |
| Patients with serious TEAE | 8 (53.3) | 16 (48.5) |
| Patients with TEAE leading to dose interruption | 9 (60.0) | 19 (57.6) |
| Patients with TEAE leading to dose reduction | 2 (13.3) | 8 (24.2) |
| Most common TEAEs (any grade)‡ | | |
| Upper respiratory tract infection | 8 (53.3) | 14 (42.4) |
| COVID-19 | 6 (40.0) | 9 (27.3) |
| Headache | 6 (40.0) | 15 (45.5) |
| Influenza | 5 (33.3) | 6 (18.2) |
| Respiratory tract infection | 5 (33.3) | 6 (18.2) |
| Arthralgia | 4 (26.7) | 10 (30.3) |
| AST increased | 4 (26.7) | 12 (36.4) |
| Back pain | 4 (26.7) | 6 (18.2) |
| CPK increased | 4 (26.7) | 14 (42.4) |
| Pyrexia | 4 (26.7) | 7 (21.2) |
| ALT increased | 3 (20.0) | 9 (27.3) |
| Cough | 3 (20.0) | 8 (24.2) |
| Fatigue | 3 (20.0) | 8 (24.2) |
| Hyperkalemia | 3 (20.0) | 4 (12.1) |
| Nausea | 3 (20.0) | 7 (21.2) |
| Parainfluenza virus infection | 3 (20.0) | 3 (9.1) |
| Rash | 3 (20.0) | 4 (12.1) |
| Rhinorrhea | 3 (20.0) | 4 (12.1) |

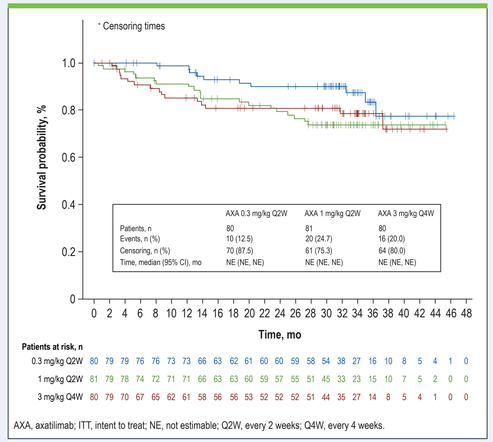
ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; Q2W, every 2 weeks; TEAE, treatment-emergent adverse event.
* At the analysis cutoff, dosing schedules for axatilimab among patients in the 0.3 mg/kg Q2W cohort were 0.2 mg/kg Q2W (n=1), 0.3 mg/kg Q2W (n=2), 0.3 mg/kg Q4W (n=1), and 0.6 mg/kg Q4W (n=11).
† At the analysis cutoff, dosing schedules for axatilimab among all patients remaining on treatment were 0.2 mg/kg Q2W (n=1), 0.3 mg/kg Q2W (n=2), 0.3 mg/kg Q4W (n=2), 0.6 mg/kg Q4W (n=27), and 1 mg/kg Q2W (n=1).
‡ As reported in ≥20% of patients in the 0.3 mg/kg Q2W cohort.

- Serious TEAEs of any grade observed in ≥1 patient were pneumonia (n=4, 12.1%) and COVID-19 and respiratory tract infection (n=2 each, 6.1%)
- Patients who remained on treatment had more dose interruptions due to TEAEs, which may be attributable to the longer duration of therapy for these patients
- The most common TEAEs leading to dose interruption were pneumonia and respiratory tract infection (n=4 each, 12.1%) and COVID-19 and pyrexia (n=3 each, 9.1%)

### *Overall Survival*

- Among the patients enrolled in AGAVE-201, median OS was not reached in any treatment cohort (**Figure 2**)
  - The 46-month OS rate (95% CI) was 77.6% (57.8%–89.0%) among the 0.3 mg/kg Q2W cohort and 74.1% (64.8%–81.3%) across all doses, with median (range) follow-up of 31.7 (0–46.5) and 31.2 (0–46.5) months, respectively

**Figure 2. Kaplan-Meier Estimate of Overall Survival (ITT Population)**




AXA, axatilimab; ITT, intent to treat; NE, not estimable; Q2W, every 2 weeks; Q4W, every 4 weeks.

## Conclusions

- **Initial data from the AGAVE-201 study showed a promising overall response rate and safety profile for axatilimab in patients with cGVHD**
- **Long-term safety follow-up showed a continued tolerable safety profile, as TEAEs generally did not accumulate with a prolonged duration of exposure**
- **Of 239 patients who received axatilimab, 33 (13.8%) have continued on treatment, with a median duration of therapy of 34 months across all doses, suggesting long-term safety and clinical benefit from treatment**
- **In patients with long-standing cGVHD with multiorgan involvement, prolonged therapy with axatilimab can be considered to optimize clinical outcomes**

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