Durability of response following retreatment with Descartes-08, an autologous BCMA-directed mRNA CAR-T cell therapy, in generalized myasthenia gravis: a case series with 12-month follow-up

Poster #23

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Key takeaways

- **Retreatment with Descartes-08 was evaluated in participants with gMG who experienced clinical benefit** from an initial treatment course but later experienced recurrence of symptoms (MG-ADL ≥6)
- **Retreatment with Descartes-08 demonstrated improvements in MG severity scores** consistent with or greater than those observed following the initial treatment course
- **The retreatment course remained generally well tolerated, without any new safety signals,** increase in AE severity, or evidence of cumulative toxicity, including CRS or ICANS
- These findings **support the potential for retreatment with Descartes-08**, if needed following recurrence of MG symptoms, with clinical benefit observed and no new safety concerns

Introduction

Myasthenia gravis (MG) is a chronic autoimmune disease characterized by variable muscle weakness and debilitating fatigue. Approximately 85% of patients develop generalized MG (gMG). Despite available therapies, many patients do not achieve sustained disease control and remain reliant on chronic treatment, contributing to substantial treatment burden.[1,2]

B-cell maturation antigen (BCMA) is a cell-surface receptor expressed on later-stage B-lineage cells, including antibody-secreting plasmablasts and plasma cells, which can produce pathogenic autoantibodies that drive MG immunopathogenesis. BCMA is also expressed on activated plasmacytoid dendritic cells (pDCs), which can contribute to inflammatory immune signaling in autoimmune diseases through enhanced type I interferon production.[3-8]

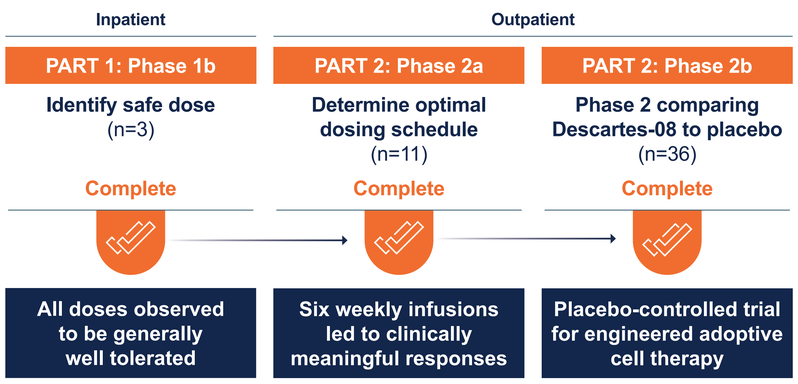
Descartes-08 is an investigational, autologous, nonviral, BCMA-directed mRNA CAR T-cell therapy with transient CAR expression designed to target BCMA+ immune cells. In gMG, it is administered as a course of 6 once-weekly outpatient infusions without lymphodepleting chemotherapy, with the potential for subsequent treatment courses if needed.[3-9]

Retreatment case series: In a pooled case series of 5 participants with gMG from the Phase 2a and Phase 2b MG-001 studies who responded to an initial 6-week course of Descartes-08 and experienced recurrence of symptoms (MG-ADL ≥6), retreatment with Descartes-08 demonstrated improvements in MGC and MG-ADL scores, with benefit sustained through 12 months and no new safety signals observed.[10]

MG-001 Clinical Program Summary

3-Part Phase 1b/2 study of Descartes-08 in MG (NCT04146051)

Across the MG-001 program, Descartes-08 demonstrated clinically meaningful and sustained improvements in MG clinical outcome measures[3,10,11]

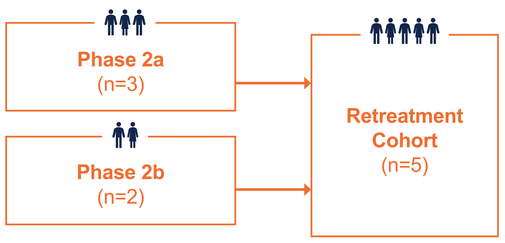


- In **Phase 2a**, clinical effect was observed with 6 once-weekly infusions, which was selected as the preferred treatment regimen
- The **Phase 2b** study demonstrated significant and sustained improvements in MG severity scores through 12 months following a single treatment course
- Descartes-08 was generally **well tolerated without evidence of CRS or ICANS**

Retreatment case series

MG-001 participants previously treated with Descartes-08

All participants had 12-month follow-ups for both initial treatment and retreatment



- The case series analyzed the efficacy, safety, and durability of response to Descartes-08 retreatment in participants with gMG who previously received a full treatment course in the Phase 2 portion of the MG-001 study and experienced recurrence of symptoms (MG-ADL ≥6)
- Retreatment consisted of 6 once-weekly Descartes-08 infusions
- Clinical outcomes were assessed by mean change in MGC and MG-ADL scores from baseline through Month 12 and compared with outcomes following the initial treatment course. Safety and tolerability were assessed across treatment courses

Descartes-08 is an investigational product candidate and has not been approved for use by the FDA or any other regulatory authority.

Abbreviations: AChR, acetylcholine receptor; AE, adverse event; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CI, confidence interval; CRS, cytokine release syndrome; FDA, Food and Drug Administration; gMG, generalized myasthenia gravis; ICANS, immune effector cell-associated neurotoxicity syndrome; IVIG, intravenous immunoglobulin; MC, myasthenic crisis; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MGC, Myasthenia Gravis Composite; MMF, mycophenolate mofetil; MSE, minimal symptom expression; mRNA, messenger ribonucleic acid; MTX, methotrexate; pDC, plasmacytoid dendritic cell; PLEX, plasma exchange; SAE, serious adverse event; SD, standard deviation.

References: 1. Tannemaat MR, Verschuuren JJGM. *Neuromuscul Disord*. 2020;30(2):111-119. 2. Feng X, et al. *Front Neurol*. 2021;1:12:725700. 3. Vu T, et al. *Nat Med*. 2026;32(3):1131-1141. 4. Zografou C, et al. *Front Immunol*. 2021;12:686466. 5. Jin W, et al. *Cell Discov*. 2021;7:85. 6. Song Y, *et al. Neuroimmunomodulation*. 2023;30:69-80. 7. Ye Y, et al. *Clin Transl Immunology*. 2020;9:e1139. 8. Khodadadi L, *et al. Front Immunol*. 2019;10;721. 9. Fedak RR, et al. *Nat Med*. 2026;32(3):1118-1130. 10. Chahin N, *et al. Ann Clin Transl Neurol*. 2025;12(11):2358-2366. 11. Granit V, et al. *Lancet Neurol*. 2023;22(7):578-590.

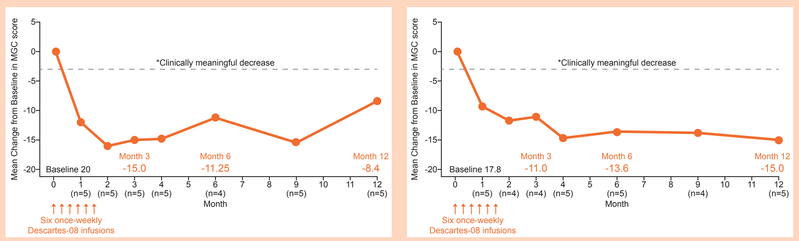
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For further information on the data presented, scan the QR code

Retreatment case series: participant baseline characteristics

Characteristic	Participants (n=5)
Age, mean (SD)	58 (12) years
Age range	49–79
Women, n (%)	4 (80%)
AChR+ gMG, n (%)	4 (80%)
MG-ADL at baseline before initial treatment, mean (SD)	9.2 (3.1)
MG-ADL at baseline before retreatment, mean (SD)	9.6 (3.4)
Median interval between end of initial treatment course and first retreatment infusion	16.6 months (range 11.7–22.6)

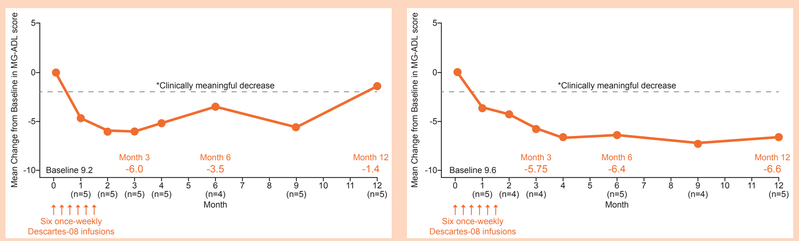
Results: Descartes-08 demonstrated improvement in mean change from baseline in MGC following initial treatment and retreatment



*Clinically meaningful decrease was defined as a ≥3-point change in MGC score

- Retreatment with Descartes-08 led to improvement in mean change from baseline in MGC, with responses sustained through 12 months
- Mean change in MGC from retreatment baseline was -15 points
- The reduction in mean MGC score from baseline following retreatment was consistent with, and potentially greater than, that observed following initial treatment

Results: Descartes-08 demonstrated improvement in mean change from baseline in MG-ADL following initial treatment and retreatment



*Clinically meaningful decrease was defined as a ≥2-point reduction in MG-ADL score

- Retreatment with Descartes-08 led to improvement in mean MG-ADL score from baseline, with responses sustained through 12 months
- Mean change in MG-ADL from retreatment baseline was −6.6 points
- The reduction in mean MG-ADL score from baseline following retreatment was consistent with, and potentially greater than, that observed following initial treatment

Safety summary

Retreatment safety profile was consistent with initial treatment, with no new or cumulative safety signals observed

Initial Treatment vs Retreatment (n=5) Six once-weekly infusions per treatment course		
Safety Event	**Initial Treatment**	**Retreatment**
SAEs*	1	0
Infusion-related reaction (IRR)†	16/30 infusions	17/30 infusions
Grade 1	10	12
Grade 2	6	5
TEAEs in >1 participant		
Tachycardia	1	5‡
CRS	0	0
ICANS	0	0
Cytopenias§	0	0
Hypogammaglobulinemia	0	0

*Participant had an infected port not related to Descartes-08
†IRR is an infusion-related reaction developing within 24 hours and resolving spontaneously or with supportive care within 48 hours of Descartes-08 administration, manifesting as fever, chills, rigors, myalgia, arthralgia, nausea, vomiting, and/or headache
‡All occurred in the same participant with 4 of 5 events ocurring in combination with infusion reaction
§Cytopenia group term defined as anemia, thrombocytopenia, or neutropenia

Conclusion

- Among participants with gMG who initially responded to Descartes-08 and later experienced recurrence of symptoms (MG-ADL ≥6), retreatment with Descartes-08 led to improvements in MG severity scores
- Clinical benefit following retreatment was sustained through Month 12 in multiple participants
- Retreatment was generally well tolerated with a safety profile consistent with initial treatment
  - No new or cumulative safety signals were observed
  - No CRS, ICANS, cytopenias, or hypogammaglobulinemia were observed
- These findings support the potential for retreatment with Descartes-08, if needed following recurrence of MG symptoms, with clinical benefit observed and no new safety concerns
- The ongoing Phase 3 AURORA trial (NCT06799247) is evaluating the efficacy, safety, and durability of Descartes-08 in adults with gMG

Retreatment case profiles

Case #1 (Phase 2a)

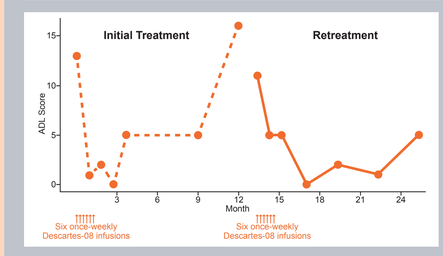
MG History: 52-year-old Caucasian Woman

- 16-year history of AChR+ gMG, MGFA Class IIa at screening
- Prior therapies include prednisone, pyridostigmine, eculizumab, MMF, PLEX, IVIG, thymectomy
- Disease course has been complicated by MC requiring intubation
- Receiving pyridostigmine and azathioprine at time of initial treatment

At Retreatment

Timing: 11.7 months after completion of initial treatment course

Ongoing Medications:
- Pyridostigmine
- Azathioprine



Participant experienced a clinically meaningful reduction in MG-ADL through 12 months after retreatment

Case #2 (Phase 2a)

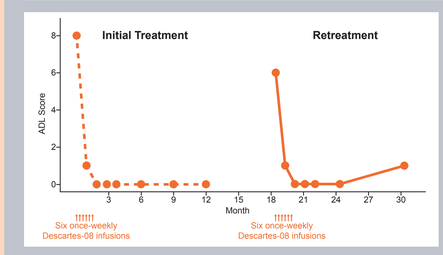
MG History: 67-year-old Caucasian Man

- 10-year history of seronegative gMG, MGFA Class IIa at screening
- Prior therapies include IVIG, PLEX, MMF, prednisone, azathioprine, MTX
- Receiving prednisone and pyridostigmine at time of initial treatment

At Retreatment

Timing: 19.9 months after completion of initial treatment course

Ongoing Medications:
- Prednisone
- Pyridostigmine



Participant experienced a reproducible reduction in MG-ADL with MSE achieved in initial treatment and retreatment

Case #3 (Phase 2a)

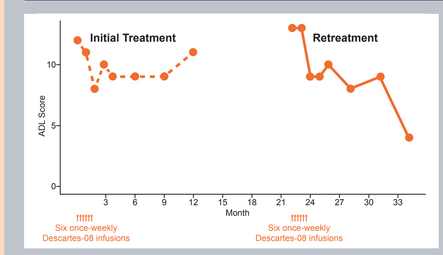
MG History: 49-year-old Caucasian Woman

- 23-year history of AChR+ gMG, MGFA Class IIIa at screening
- Prior therapies include IVIG, PLEX, MMF, pyridostigmine, azathioprine, thymectomy
- Receiving pyridostigmine ER and pyridostigmine at time of initial treatment

At Retreatment

Timing: 22.6 months after completion of initial treatment course

Ongoing Medications:
- Pyridostigmine



Participant experienced a larger reduction in MG-ADL after retreatment, with clinically meaningful improvement

Case #4 (Phase 2b)

MG History: 58-year-old Caucasian Woman

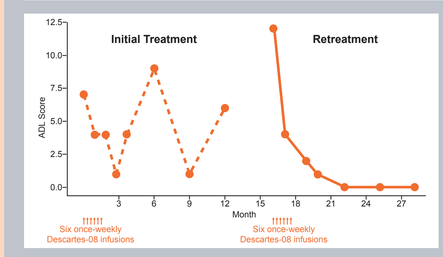
- 13-year history of AChR+ gMG, MGFA Class IIIa at screening
- Prior therapies include azathioprine, pyridostigmine, IVIG, PLEX, cyclosporine, thymectomy
- Receiving pyridostigmine and azathioprine at time of initial treatment

At Retreatment

MGFA Class IIIb

Timing: 14.6 months after completion of initial treatment course

Ongoing Medications:
- Pyridostigmine
- Azathioprine



Participant had improved response with second treatment, with MSE achieved from Month 4 through 12

Case #5 (Phase 2b)

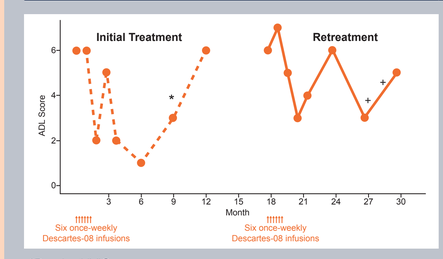
MG History: 79-year-old Caucasian Woman

- 3-year history of AChR+ gMG, MGFA Class IIIa at screening
- Prior therapies include pyridostigmine, prednisone, ALXN2050 IP, Ultomiris, Vyvgart, PLEX
- Receiving zilucoplan at time of initial treatment

At Retreatment

Timing: 16.6 months after completion of initial treatment course

Ongoing Medications:
- None



Highly treatment-resistant participant experienced clinically meaningful response

*Received IVIG
+Received 2 doses of inebilizumab