Emapalumab Treatment for Patients with Differing Presentations of Macrophage Activation Syndrome (MAS) Secondary to Still's Disease: Results from a Pooled Analysis of Two Prospective Trials

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*At time of study conduct

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Disclosures

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- Research grants/contracts: National Institutes of Health (NIH), Novartis, Sobi, Systemic Juvenile Idiopathic Arthritis (sJIA) Foundation
- Royalties: Up-To-Date

Background

- MAS is a life-threatening complication of Still's disease, and is characterized by IFNγ-driven macrophage activation and systemic hyperinflammation[1–4]
- Patients with Still's disease may present with MAS at any disease stage, including at the time of initial diagnosis of Still's disease
- Some patients may have chronic relapsing MAS, which may be difficult to treat[1]

IFNγ, interferon gamma; MAS, macrophage activation syndrome.

1. Fautrel B, et al. *Ann Rheum Dis* 2024;83:1614–1627; 2 Jacqmin P, et al. *Br J Clin Pharmacol* 2022;88:2128–2139; 3. Fajgenbaum DC, June CH. *N Engl J Med* 2020;383:2255–2273; 4. De Benedetti F, et al. *Nat Rev Rheumatol* 2021;17:678–691.

Emapalumab in MAS

- Emapalumab, an anti-IFNγ antibody, binds free and receptor-bound IFNγ, providing rapid and targeted neutralization of IFNγ,[1] and is the only targeted therapy that has demonstrated sustained control of MAS in clinical trials (NCT03311854, NCT05001737)[2,3]

- Emapalumab has been recently approved by the FDA for adult and pediatric (newborn and older) patients with MAS in known or suspected Still's disease with an inadequate response or intolerance to GCs, or with recurrent MAS[4]

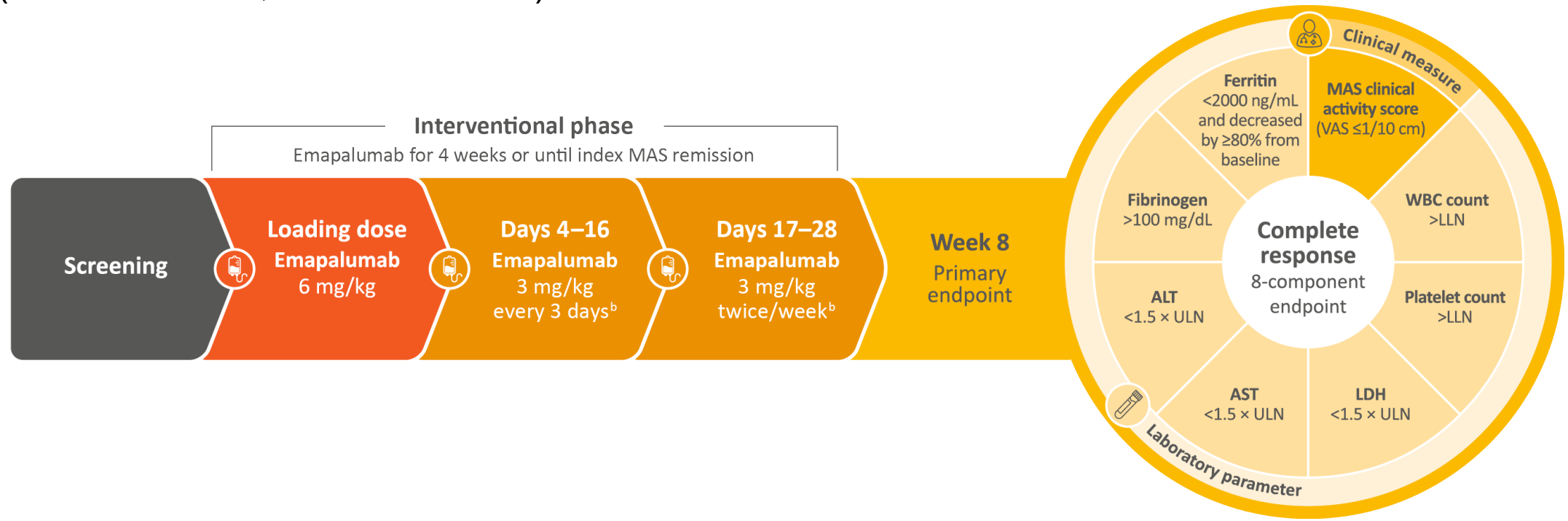
- This analysis presents data by MAS presentation from a population of patients treated with emapalumab for MAS in Still's disease

FDA, US Food and Drug Administration; GC, glucocorticoids; IFNγ, interferon gamma; MAS, macrophage activation syndrome.

1. Jacqmin P, et al. *Br J Clin Pharmacol* 2022;88:2128–2139; 2. De Benedetti F, et al. *Ann Rheum Dis* 2023;82:857–865; 3. Grom A. et al. *Arthritis Rheumatol* 2024;76(suppl 9):LB19;
4. GAMIFANT® (emapalumab-lzsg). US prescribing information. June 2025 Available at: https://www.gamifant.com/sites/default/files/2025-07/Full-Prescribing-Information.pdf. Accessed October 2025.

Study Design

Design of the two prospective, open-label, single-arm, interventional studies of emapalumab in patients with MAS in Still's disease with an inadequate response to high-dose IV GCs[a] (NCT03311854, NCT05001737)



[a]Eligible patients had high presumption or confirmed diagnosis of MAS (ACR/EULAR criteria). High-dose GC dosing was defined as ≥2 mg/kg/day of prednisolone-equivalent in two divided doses, or at least 60 mg/day in patients weighing ≥30 kg, including but not limited to pulses up to 30 mg/kg/day for at least 3 consecutive days; [b]Dose adjustment (decrease in dose interval or increase in dose up to a maximum of 10 mg/kg every 3 days), or treatment extended beyond 4 weeks, was allowed if an investigator observed an inadequate improvement in key MAS parameters after initiating treatment.
ACR, American College of Rheumatology; ALT, alanine aminotransferase; AST, aspartate aminotransferase; EULAR, European Alliance of Associations for Rheumatology; GC, glucocorticoid; IV, intravenous; LDH, lactate dehydrogenase; LLN, lower limit of normal; MAS, macrophage activation syndrome; ULN, upper limit of normal; VAS, visual analog scale; WBC, white blood cell.

Objective: To evaluate response status at week 8 after treatment initiation **by MAS Subgroup**

Methods:

Data were pooled from two prospective, open-label, single-arm interventional studies[a]. Responses were analyzed in relation to MAS presentation

8-component composite endpoint

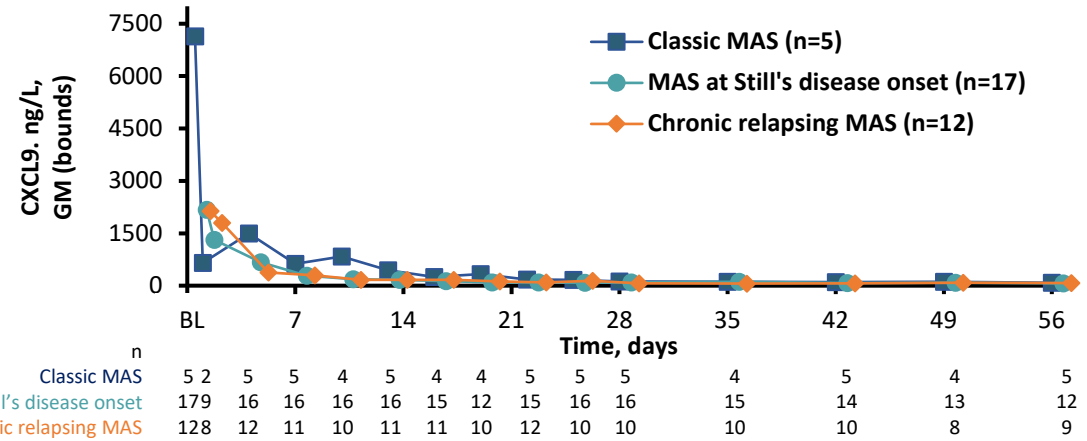
Complete response:

- Absence of MAS clinical signs and symptoms (VAS ≤1 cm)
- Normalization of 7 lab parameters

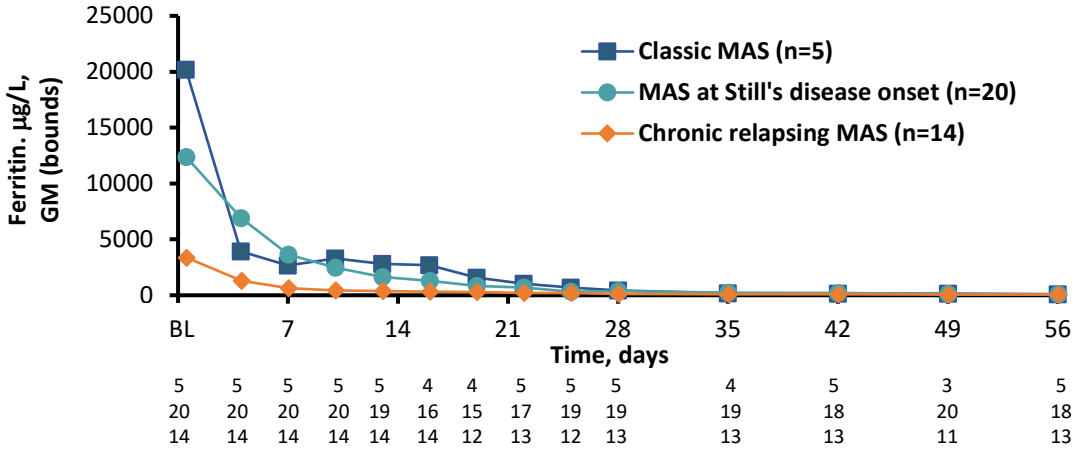
- MAS occurring during the course of Still's disease (classic MAS)
- MAS at Still's disease onset
- Chronic relapsing MAS

[a]NI-0501-06 (NCT03311854) and NI-0501-14 (EMERALD; NCT05001737);
CXCL9, chemokine C-X-C motif ligand 9; MAS, macrophage activation syndrome; PD, pharmacodynamic; sCD25, soluble CD25; VAS, visual analog scale.

Results – Baseline and Evolution of PD Inflammatory Markers



n															
Classic MAS	5	2	5	5	4	5	4	4	5	5	5	4	5	4	5
MAS at Still's disease onset	17	9	16	16	16	16	15	12	15	16	16	15	14	13	12
Chronic relapsing MAS	12	8	12	11	10	11	11	10	12	10	10	10	10	8	9



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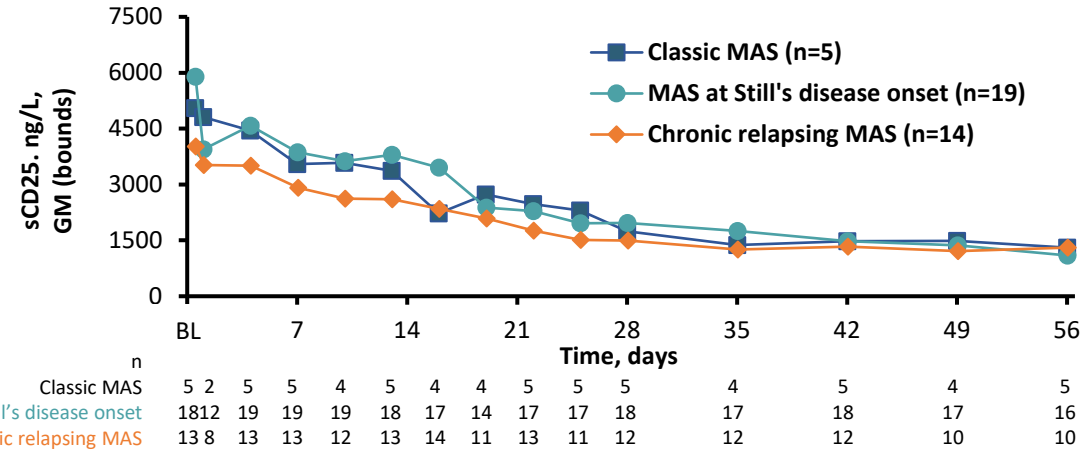
Classic MAS	5	5	5	5	5	4	4	5	5	5	4	5	4	5	3	5
MAS at Still's disease onset	20	20	20	20	19	16	15	17	19	19	19	18	20	18		
Chronic relapsing MAS	14	14	14	14	14	14	12	13	12	13	13	13	11	13		



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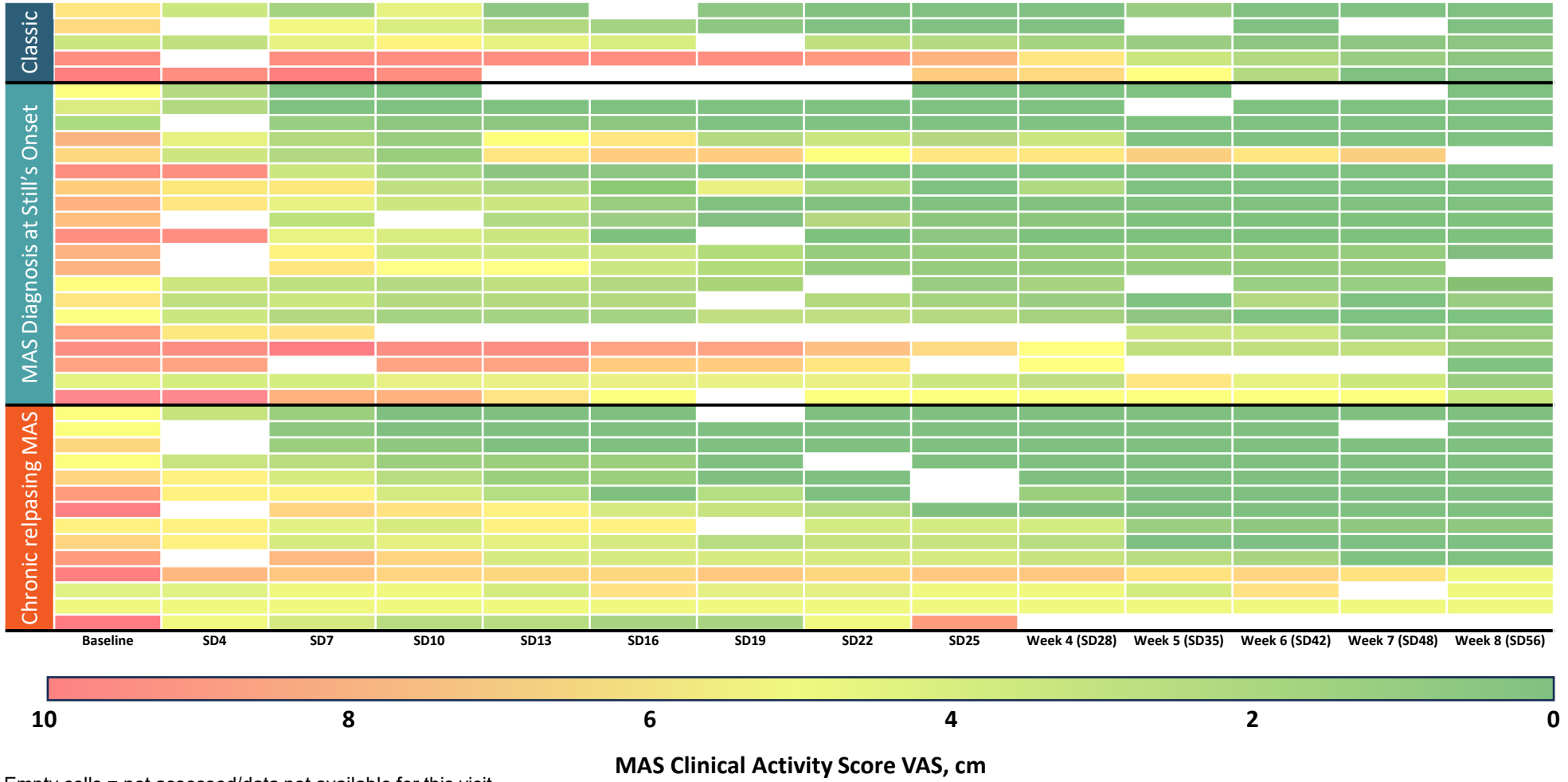
Classic MAS	5	2	5	5	4	5	4	4	5	5	5	4	5	4	5
MAS at Still's disease onset	18	12	19	19	19	18	17	14	17	17	18	17	18	17	16
Chronic relapsing MAS	13	8	13	13	12	13	14	11	13	11	12	12	12	10	10

- At baseline:
  - CXCL9 and ferritin levels were highest in Classic MAS
  - Chronic relapsing patients generally presented with lower CXCL9 and ferritin levels
  - No differences in sCD25 levels across MAS subtypes
- Emapalumab induces rapid and robust PD marker improvements across all MAS subtypes

BL, baseline; CXCL9, chemokine C-X-C motif ligand 9; GM, geometric mean; MAS macrophage activation syndrome; sCD25, soluble CD25 (also known as soluble interleukin-2 receptor α).

Results – Individual MAS Clinical Activity Score VAS



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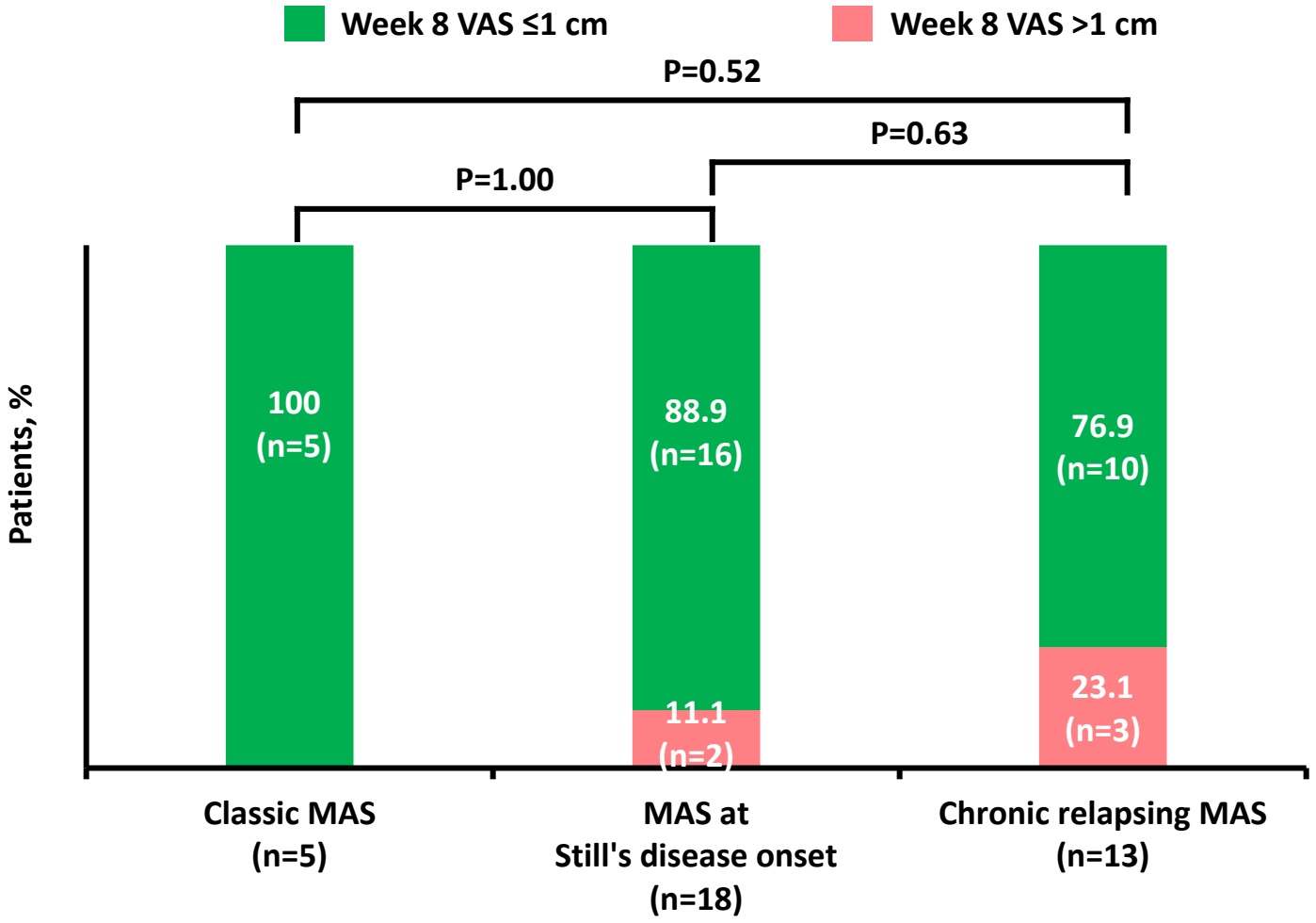
MAS, macrophage activation syndrome; SD, study day; VAS, visual analog scale.

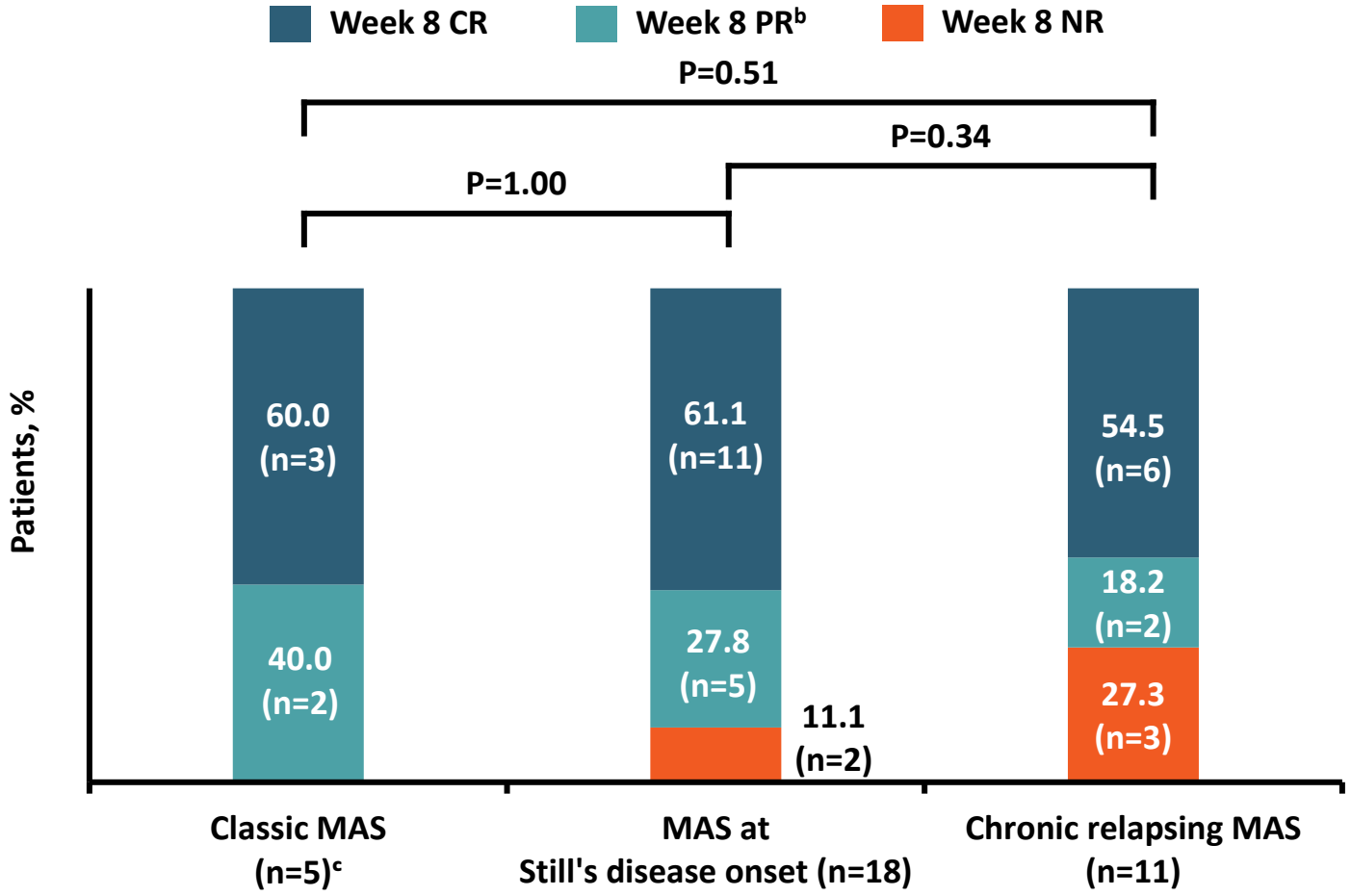
Results – MAS Clinical Activity Score VAS ≤1 cm[a]



MAS clinical activity score VAS ≤1 cm (76.9–100%) rates were similar across MAS subgroups

[a]Patients with a VAS assessment at Week 8.
MAS, macrophage activation syndrome; VAS, visual analog scale.

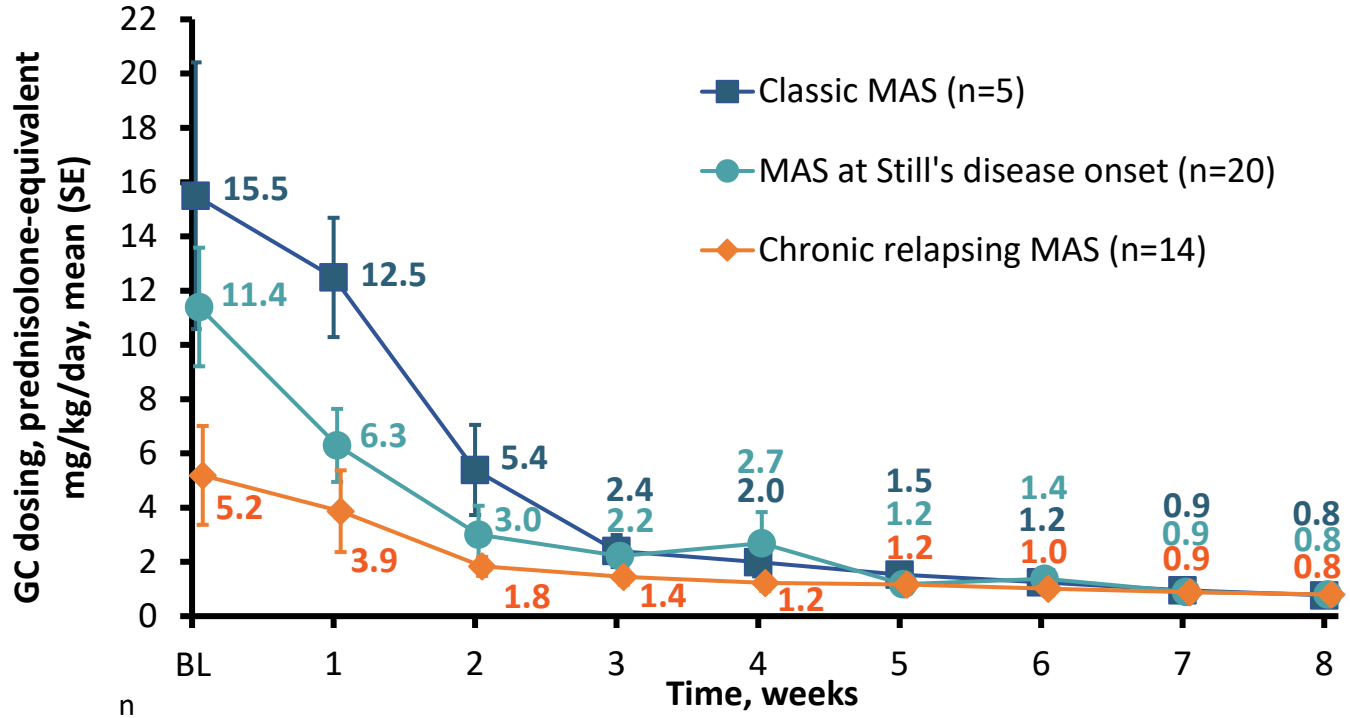
Results – Response Rates[a]



- Complete response rates at Week 8 (54.5–61.1%) were similar across MAS subgroups
- Overall response at Week 8 was high (72.7–100%) across all MAS subgroups

[a]Patients with a response assessment at Week 8;
[b]VAS <4 cm and normalization of ≥3 abnormal baseline laboratory parameters included in the composite primary endpoint; [c]MAS occurring during the course of Still's disease.
CR, complete response; MAS, macrophage activation syndrome; NR, no response; PR, partial response; VAS, visual analog scale.

Results – GC tapering



n									
Classic MAS	5	5	5	5	5	5	5	5	5
MAS at Still's disease onset	20	20	20	20	20	20	20	20	20
Chronic relapsing MAS[a]	14	14	14	14	14	13	13	13	13

- Baseline GC dosing differed between patients presenting with classic, diagnosis at onset, or chronic relapsing MAS
- Tapering of GCs dosing from baseline to Week 8 were observed across all the MAS subgroups

[a]One patient with chronic relapsing MAS could not be evaluated from Week 5 after their death.
BL, baseline; GC, glucocorticoid; MAS, macrophage activation syndrome; SE, standard error.

Conclusions

- Emapalumab treatment was associated with consistent complete response rates of approximately 55–60% among patients with different MAS presentations, who had an inadequate response to high-dose GCs, including patients with chronic relapsing disease
- Patients achieving VAS ≤1 cm and GC tapering were also similar across MAS subgroups
- Long-term follow-up of patients from the EMERALD study is ongoing

CR, complete response; GC, glucocorticoid; MAS, macrophage activation syndrome; SE, standard error.

Thank you to the NI-0501-06 and EMERALD investigators

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Economic Burden of Macrophage Activation Syndrome (MAS) in Patients with Still's Disease (Systemic Juvenile Idiopathic Arthritis (sJIA) and Adult-onset Still's Disease (AOSD)): Analysis of a US National Administrative Claims Database

Date: Tuesday, October 28
Session Time: 10:30 AM- 12:30 PM

Session: Poster Session C, (1914–1935) Health Services Research Poster III

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Insight into the **N**atural History and **T**reatment Outcomes of **H**emophagocytic **L**ympho**h**istiocytosis (**HLH**)

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If you have any questions about the INTO-HLH Registry, please contact Dr. Michael Jordan, the Principal Investigator of the INTO-HLH Registry (email: Michael.Jordan@cchmc.org).

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