Updated exposure–safety analysis of emapalumab in patients with macrophage activation syndrome (MAS)

Rafael T. Krmar,[1] Brian Jamieson,[2] Fabrizio De Benedetti,[3] Alexei A. Grom,[4] Axel Facius,[5] Patrick Brossard[6]
[1]Sobi, Sweden; [2]Sobi, Inc., Waltham, MA, USA; [3]Division of Rheumatology, Ospedale Pediatrico Bambino Gesu, IRCCS, Rome, Italy;
[4]Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA; [5]thinkQ2 AG, Baar, Switzerland; [6]Sobi, Basel, Switzerland

CONCLUSIONS

- Increasing emapalumab exposure among patients with MAS in Still's disease or systemic lupus erythematosus (SLE) was not associated with an increased risk of moderate or severe, serious, nor infection treatment-emergent adverse events (TEAEs)
- This analysis confirms that repeated administration and/or increasing doses of emapalumab are well tolerated by patients with MAS in Still's disease or SLE[1–4]
- The correlation between high emapalumab exposure (area under the emapalumab–time curve [AUC_T]) and a lower prevalence of infections suggests a beneficial effect of emapalumab treatment that improved disease control, allowing tapering of generalized immunosuppression (e.g., glucocorticoids)

INTRODUCTION

- Emapalumab, an anti–interferon-gamma (IFNγ) antibody, has demonstrated efficacy and safety in clinical trials in patients with primary hemophagocytic lymphohistiocytosis (pHLH) and patients with MAS in Still's disease or SLE[1–3,5,6]
- No increased risk of TEAEs, including infections, has been observed in previous exposure–safety analyses of patients with pHLH or MAS in Still's disease administered emapalumab[4,5,7]

OBJECTIVE

- To evaluate the relationship between emapalumab exposure and the predicted risk of TEAEs, including infections, in an expanded population of patients with MAS in Still's disease or SLE

STUDY METHODS

- Data were pooled from 47 patients, including:
  - 39 patients with MAS in Still's disease who had an inadequate response to high-dose glucocorticoids during two open-label, single-arm interventional studies (NI-0501-06 [NCT03311854], n=14; NI-0501-14 [EMERALD] Cohort 1 [NCT05001737], n= 25)
  - Eight patients with MAS in SLE (EMERALD Cohort 2 [NCT05001737])
- Three patients from EMERALD (Cohort 1, n=1; Cohort 2, n=2) were excluded due to the absence of pharmacokinetic data

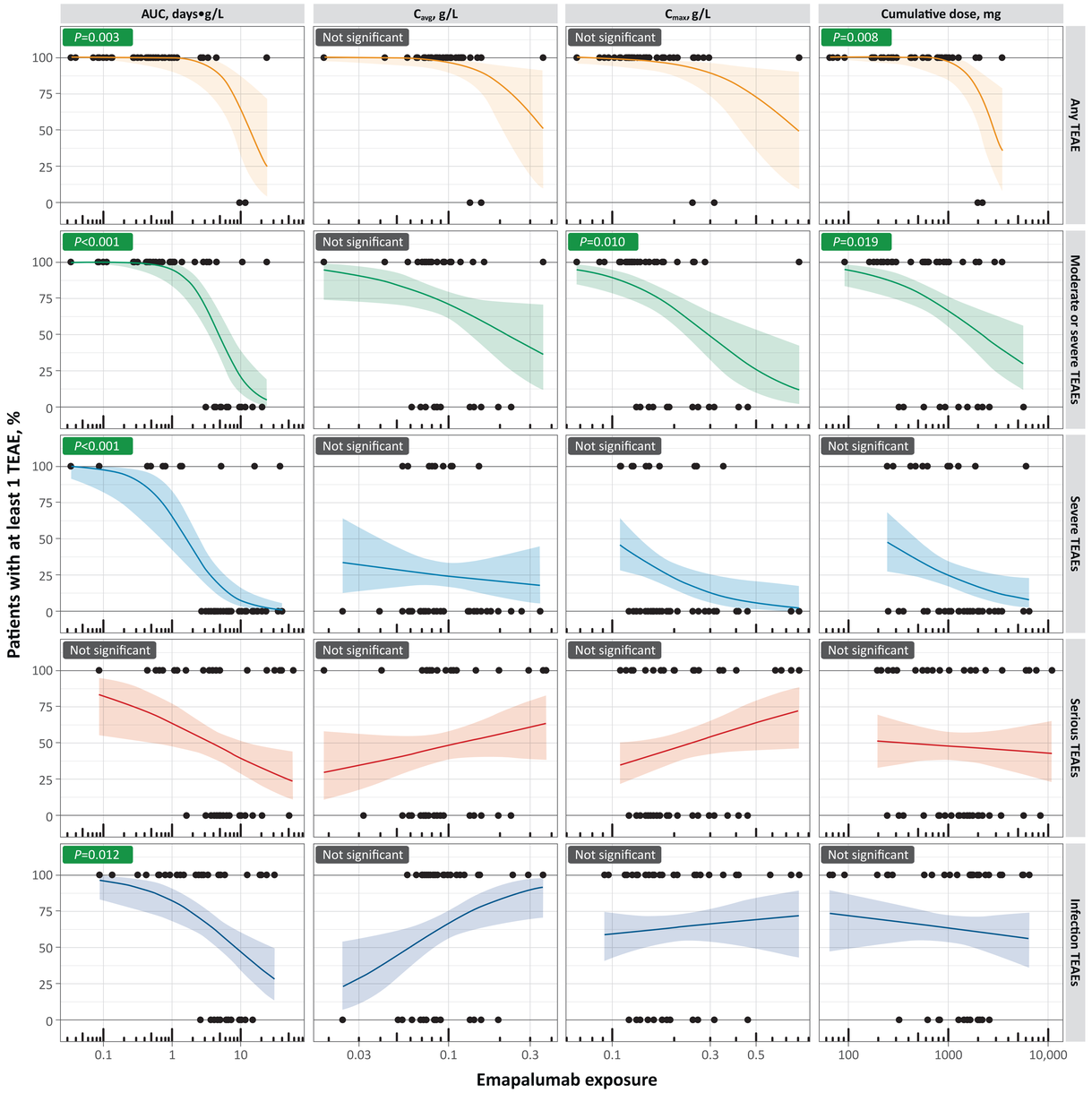
SAFETY–EXPOSURE ANALYSIS

- The relationship between safety outcomes and cumulative AUC_T, average emapalumab concentration ($C_{avg,T}$), and maximum emapalumab concentration ($C_{max,T}$) during the time between administering the first dose of emapalumab and time (T) of the first event (or up to 45 days after the last dose) was quantified using logistic regression
- The relationship between each safety category and total cumulative emapalumab dose was also analyzed

RESULTS

- This analysis was performed using data from 44 patients:
  - 38 patients (14 patients from Study 06 and 24 patients from EMERALD Cohort 1) with MAS in Still's disease
  - 6 patients with MAS in SLE from EMERALD Cohort 2
- The frequency of any TEAE was close to 100% in this population (42 out of 44 patients analyzed), even with very low emapalumab exposure, creating a ceiling effect that limits interpretation of this endpoint
- Moderate or severe TEAEs, severe TEAEs, and infection TEAEs were all significantly less frequent in patients with increasing emapalumab AUC_T (P<0.001, <0.001 and 0.012, respectively; **Figure**)
- Higher C_{max} was associated with a significantly lower risk of moderate or severe TEAEs (P=0.010; **Figure**)
- A higher cumulative dose of emapalumab was also associated with a lower risk of moderate or severe TEAEs (P=0.019; **Figure**)
- No statistically significant relationship was observed between any exposure parameter and serious TEAEs (**Figure**)

Figure: Exposure–safety analysis for patients with MAS in Still's disease and SLE administered emapalumab (N=44)



P values from an analysis of deviance.
AUC_T, area under the emapalumab–time curve; C_{avg}, average emapalumab concentration; C_{max}, maximum emapalumab concentration; MAS, macrophage activation syndrome; SLE, systemic lupus erythematosus; TEAE, treatment-emergent adverse event.

Disclosures

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References

1. De Benedetti F, et al. *Ann Rheum Dis* 2023;82:857–865.
2. Grom A, et al. *Ann Rheum Dis* 2025;84(Suppl 1):172–173.
3. Grom A, et al. *Arthritis Rheumatol* 2026;78(Suppl 3):Abstract 010.
4. Krmar R, et al. *Ann Rheum Dis* 2025;84(Suppl 1):1154–1155.
5. Jacqmin P, et al. *Br J Clin Pharmacol* 2022;88:2128–2139.
6. Locatelli F, et al. *N Engl J Med* 2020; 382:1811–1822.
7. Jordan MB, Locatelli F. *Pediatr Blood Cancer* 2024;71:e30778.

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