Emapalumab induces rapid, durable responses and reliable bridging to curative HSCT in patients with primary HLH: Pooled analysis of prospective trials NI-0501-04, NI-0501-05 and NI-0501-09

A037

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*At time of analysis completion

CONCLUSIONS

- **This pooled post-hoc analysis confirms that in patients with primary hemophagocytic lymphohistiocytosis (pHLH), emapalumab, through IFNγ-activity neutralization, delivers rapid and durable responses, enabling HSCT or ≥3 months survival without HSCT in 78% of patients and enabling glucocorticoid (GC) tapering.**
- **These findings reinforce and extend previously published evidence of emapalumab's efficacy and clinical utility as a well-tolerated bridge to curative HSCT in a difficult-to-treat population with high rates of mortality.**

INTRODUCTION

- pHLH is a life-threatening, genetically driven, IFNγ-mediated hyperinflammatory disorder.[1]
- Emapalumab, a fully human immunoglobulin-G1 anti-IFNγ monoclonal antibody that binds both free and receptor-bound IFNγ, neutralizing its biological activity,
- is approved by the US Food and Drug Administration (FDA) for adults and children with pHLH with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy.[2]
- The pivotal NI-0501-04 study first showed, and the NI-0501-09 study later confirmed, that emapalumab rapidly controls hyperinflammation and enables successful HSCT in patients with pHLH.[3,4]
- This post-hoc analysis evaluates the response rates of patients treated with emapalumab based on the investigator's global assessment to closely emulate the real-world clinical practice.

OBJECTIVE

- To quantify (i) investigator-assessed overall response (OR=complete response [CR] + partial response [PR]), (ii) bridging-success survival (patients alive at HSCT and patients alive without HSCT ≥3 months), and (iii) GC-sparing effects of emapalumab, via a pooled analysis of three prospective trials.

METHODS

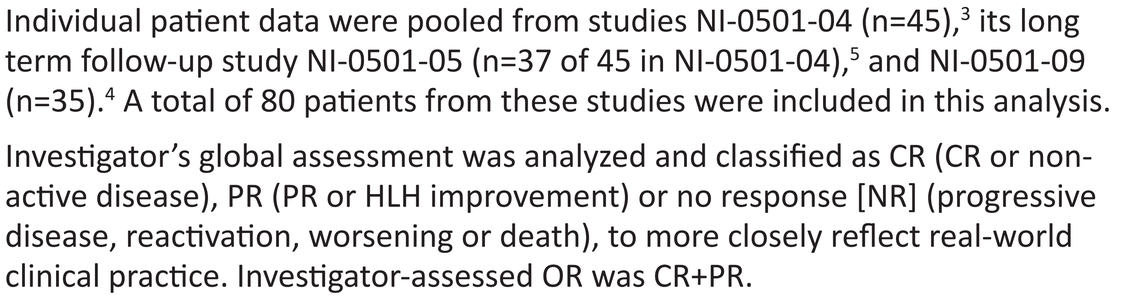
- Individual patient data were pooled from studies NI-0501-04 (n=45),[3] its long term follow-up study NI-0501-05 (n=37 of 45 in NI-0501-04),[5] and NI-0501-09 (n=35).[4] A total of 80 patients from these studies were included in this analysis.
- Investigator's global assessment was analyzed and classified as CR (CR or non-active disease), PR (PR or HLH improvement) or no response [NR] (progressive disease, reactivation, worsening or death), to more closely reflect real-world clinical practice. Investigator-assessed OR was CR+PR.
- Patients who received ≥3 emapalumab doses with investigator assessments made up the response-evaluable set at week 8 or end of treatment (EOT) (n=62) and the best-response (time from study start to investigator assessment of best response up to Week 8) set (n=71); bridging-success survival set comprised of patients alive at HSCT and patients alive without HSCT ≥3 months.
- Steroid-sparing effect of emapalumab was analyzed as the proportion of patients achieving at least 25% reduction in GC dose from baseline by day 14 and EOT.

RESULTS

Patient Demographics and Baseline Characteristics

- Key patient demographics and baseline characteristics are presented in **Figure 1.**

Figure 1: Baseline characteristics of patients included in the pooled analysis

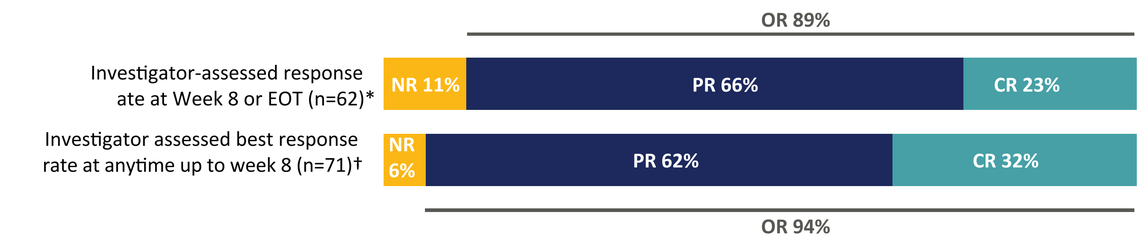


Pooled data for NI-0501-04, NI-0501-05, and NI-0501-09 studies. Total N=80.
CNS, central nervous system; DM, data missing; HLH, hemophagocytic lymphohistiocytosis.

Investigator-assessed Response Rate

- At Week 8, the majority of evaluable patients achieved OR **(Figure 2)**, including CR, which was achieved in 23% of the patients.
- Considering best response up to Week 8, a higher proportion of patients responded and attained CR **(Figure 2)**.

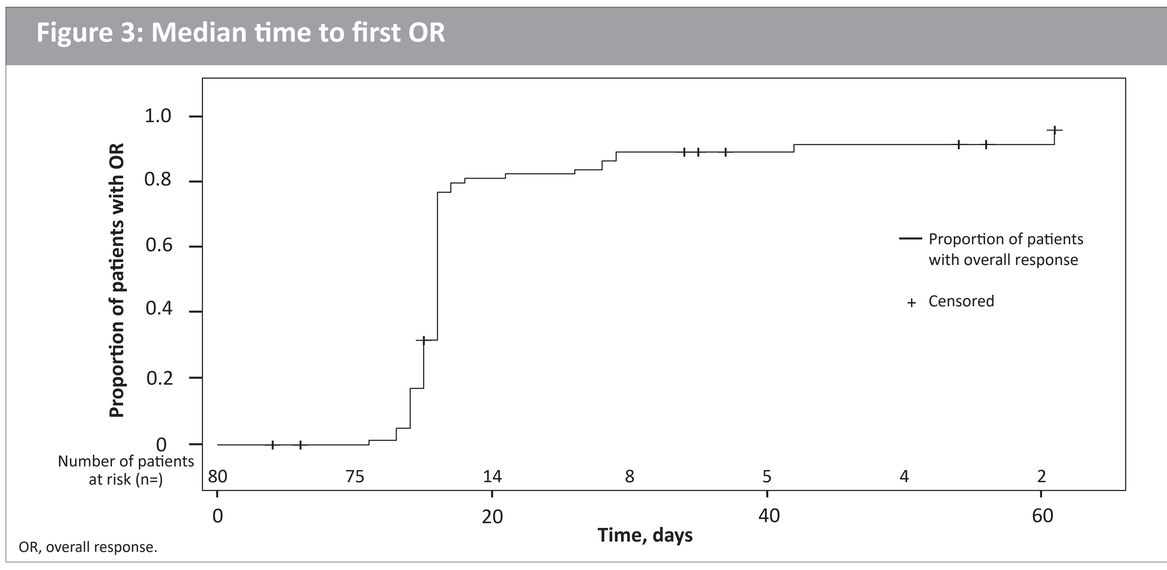
Figure 2: Investigator-assessed response shows a high rate of responders to emapalumab



*Evaluable patients: 5 patients received <3 doses of emapalumab, 2 were protocol violations, and 11 did not have recorded investigator assessment response at Week 8.
†Evaluable patients: 5 patients received <3 doses of emapalumab, 2 were protocol violations, and 2 did not have recorded investigator assessment response at any time.
CR, complete response; EOT, end of treatment; NR, no response; OR, overall response; PR, partial response.

- Median time to first OR was 16 days **(Figure 3)**, while median time to first CR was not evaluable.

Figure 3: Median time to first OR

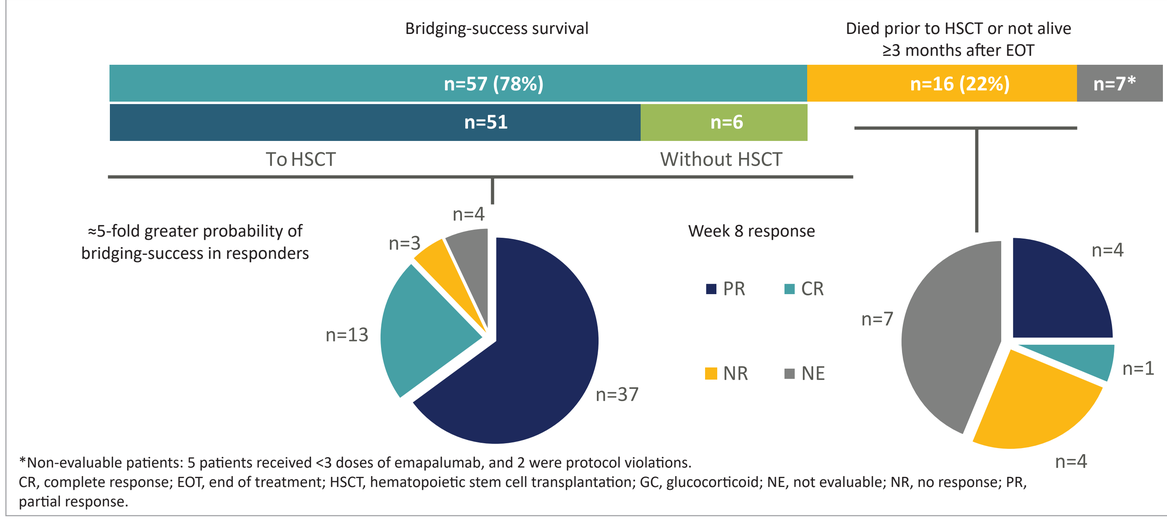


OR, overall response.

Bridging-success Survival

- Bridging-success survival was achieved by 78% (57/73) patients (**Figure 4)**.
  - 51 proceeded to HSCT
  - 6 without HSCT, were alive ≥3 months after EOT (median 358 days; [IQR: 109-380])
- Investigator's assessment of response by Week 8 revealed an approximate 5-fold greater probability of bridging-success in OR vs. NR.

Figure 4: Bridging-success survival analysis shows a clear correlation to investigator-assessed response at week 8

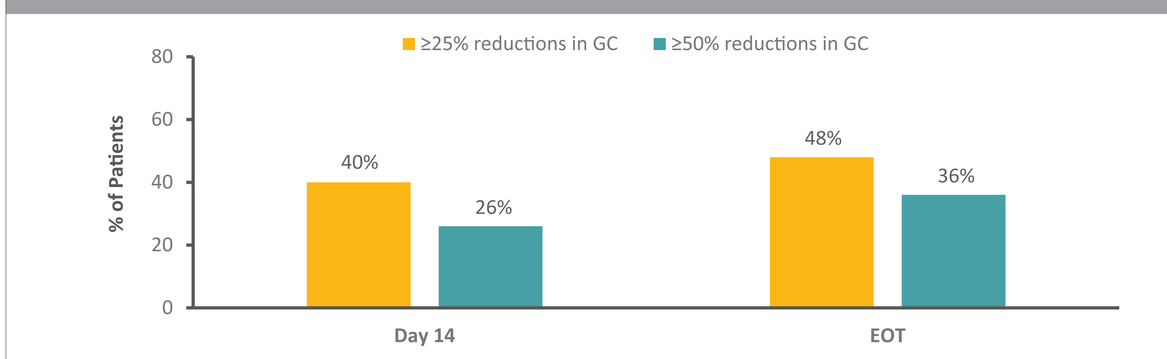


*Non-evaluable patients: 5 patients received <3 doses of emapalumab, and 2 were protocol violations.
CR, complete response; EOT, end of treatment; HSCT, hematopoietic stem cell transplantation; GC, glucocorticoid; NE, not evaluable; NR, no response; PR, partial response.

GC Tapering

- During treatment with emapalumab, GC dose reductions were common. Reductions of ≥25% from baseline were observed by Day 14 and increased by EOT; a subset also achieved ≥50% reductions **(Figure 5)**.

Figure 5: Proportion of patients achieving ≥25% and ≥50% GC dose reductions from baseline at Day 14 and EOT



EOT, end of treatment; GC, glucocorticoid.

Safety

- Safety profile of emapalumab has been documented in the individual trials and reported to be favorable vs. alternative treatment options.[3,4]

References: 1. Jacqmin P, et al. *Br J Clin Pharmacol*. 2022;88(5):2128-2139; 2. GAMIFANT™ (emapalumab-lzsg) injection, for intravenous use initial U.S. Approval: 2018; 3. Locatelli F, et al. *N Engl J Med*. 2020;382(19):1811-1822; 4. Locatelli F, et al. EHA 2025. Milan, Italy; 5. Jordan MB, et al. *Blood*. 2023;142(Supplement 1):1174.

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