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# POSTER ABSTRACTS

## 203.LYMPHOCYTES AND ACQUIRED OR CONGENITAL IMMUNODEFICIENCY DISORDERS

### Emapalumab, a Fully Human Anti-Interferon Gamma Monoclonal Antibody, in Pediatric Patients with Primary Hemophagocytic Lymphohistiocytosis: Long-Term Follow-up of a Phase 2/3 Study

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**Background:** Primary hemophagocytic lymphohistiocytosis (pHLH) is a rare, life-threatening genetically heterogeneous, autosomal recessive disorder, characterized by immune dysregulation and hyperinflammation. Acute treatment of pHLH has traditionally involved immunochemotherapy with glucocorticoids and etoposide to suppress hyperinflammation and facilitate the patient undergoing allogeneic hematopoietic stem cell transplantation (HSCT), the only potentially curative therapy. Emapalumab, a fully human immunoglobulin G1 anti-interferon-$\gamma$ (IFN$\gamma$) monoclonal antibody, binds free and receptor-bound IFN$\gamma$, neutralizing its biologic activity. Emapalumab has demonstrated efficacy in patients with pHLH and has a favorable safety profile with no increase in the risk of adverse events (AEs), including infections, with increasing drug exposure prior to patients undergoing HSCT.
**Objective:** To monitor the long-term safety and efficacy of emapalumab in patients with pHLH, including the period after undergoing HSCT.
**Methods:** Long-term follow-up study (NCT02069899) of patients with pHLH who had received ≥1 dose of emapalumab in a multicenter, single-arm, open-label phase 2/3 clinical trial who were followed for 1 year after HSCT or last administration of emapalumab in the parent study (NCT01818492). Patients received emapalumab for 4 to 8 weeks in the parent study, which included a 4-week short-term follow-up period, during which patients could have undergone HSCT. Treatment with emapalumab could continue according to the parent study protocol during follow-up, if a favorable benefit/risk assessment was established. Any concomitant treatment ongoing at the time of study entry was continued as considered necessary by the investigators. Endpoints included safety, 1-year survival, and HSCT outcomes.
**Results:** Overall, 37/45 patients who participated in the phase 2/3 study entered long-term follow-up, with 24 patients (64.9%) completing the study; 13 patients (35.1%) withdrew from the study, most commonly because of AEs (6 patients [46.2%]) and withdrawal of informed consent (2 patients [15.4%]). All patients had ≥1 concomitant medications including systemic corticosteroids and ≥1 systemic antimicrobial. Emapalumab treatment continued during long-term follow-up for 22 patients (59.5%). All patients experienced at least one AE during follow-up ( **Table**), most commonly infections or infestations (27 patients [73.0%] reported an infection AE). Most AEs were mild or moderate in intensity. Four patients (10.8%) had study drug-related AEs. Overall, 56.8% of patients experienced at least one severe AE. 28 patients (75.7%) experienced at least 1 serious AE (SAE), but only 1 patient (2.7%) had a treatment-related SAE (Coombs positive hemolytic anemia). Infusion-related reactions of rash were observed in 2 patients (5.4%), but these reactions were temporary and resolved without treatment. No patients experienced AEs leading to study drug discontinuation. Nine patients died during the study (4 prior to HSCT conditioning

and 5 during the post-conditioning period). No study drug-related deaths were reported. 28 (75.7%) patients were alive at last observation or 1 year after last emapalumab dose and 33 (89.2%) survived to undergo HSCT or until 1 year after last emapalumab dose (whichever came first). 29 patients (78.4%) underwent HSCT, including 18 during long-term follow-up. 24 of the 29 (82.8%) patients who underwent HSCT were alive at last observation or 1 year after last emapalumab dose. Sustained engraftment was achieved in 23 patients (79.3%; 95% confidence interval, 61.6-90.2%). During the follow-up period, 6 patients (20.7%; 95% confidence interval [CI], 9.8-38.4%) experienced primary or secondary graft failure after undergoing HSCT and 7 patients (24.1%; 95% CI, 1.2-42.1%) had acute or chronic graft-versus-host disease. At the 12-months post-transplant visit, 25/26 (96.2%) patients maintained a complete response, while 1 (3.8%) patient was reported to have maintained a partial response. No pHLH reactivation was reported during the study.

**Conclusions:** The long-term outcomes for patients with pHLH treated with emapalumab are consistent with observations made during a phase 2/3 study. A favorable safety profile was maintained, and a high proportion of patients received HSCT and achieved long-term survival.

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