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POSTER ABSTRACTS

201.GRANULOCYTES, MONOCYTES, AND MACROPHAGES

A Phase 1b Study of ELA026, a Monoclonal Antibody Targeting Signal Regulatory Protein-$\alpha/\beta 1/\gamma$, in Patients with Newly Diagnosed and Previously Treated Secondary Hemophagocytic Lymphohistiocytosis

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Introduction: ELA026 is under investigation in secondary hemophagocytic lymphohistiocytosis (sHLH), a life-threatening, hyperinflammatory condition that is most often triggered by malignancies, autoimmune disorders, and infectious diseases. There are no approved therapies for sHLH, and current treatment approaches, particularly for malignancy-associated HLH (mHLH), are suboptimal. For example, in adult patients with mHLH, median overall survival (mOS) is approximately 2 months (Lee et al. 2023). ELA026 is a monoclonal antibody directed against signal regulatory protein-$\alpha/\beta 1/\gamma$ and is intended to target the activated myeloid and T cells that drive sHLH.
Methods: This is an open-label, single-arm, Phase 1b global multicenter study (NCT05416307) to evaluate the safety, efficacy, pharmacokinetics, and pharmacodynamics of ELA026 in newly diagnosed and previously treated sHLH patients, aged 12 years or older (6 years or older in select countries including the US). In Cohort 1, an intra-patient dose escalation of ELA026 occurs in the absence of a dose limiting toxicity (DLT) and optimal biomarker response. Response is evaluated as described in Locatelli et al. 2020.
Results: Six mHLH patients enrolled in Cohort 1 with median age of 50 years (range 21-67). Three patients were refractory to etoposide-based therapies and/or anti-cytokine therapies. No DLTs or study drug-related serious adverse events occurred. Five patients were deemed evaluable for efficacy based on >1 week of ELA026 exposure (efficacy assessment is pending). All 5 patients received concurrent chemotherapy for their malignancies. As of July 31, 2023, 3 patients are alive and 2 patients have died from complications of malignancy (mOS has not been reached but has exceeded 3 months). Three patients who had periods of ELA026 monotherapy displayed early, progressive monocyte and lymphocyte reductions with associated improvements in C-reactive protein and other sHLH-associated biomarkers. Updated study results and progress will be provided at the meeting.
Conclusion: Preliminary data suggest ELA026 is well tolerated in sHLH patients and induces early biomarker changes that warrant further clinical investigation.

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