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OP0290

EMAPALUMAB (ANTI-INTERFERON-GAMMA MONOCLONAL ANTIBODY) IN PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME (MAS) COMPLICATING SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA)

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Background: MAS is a severe complication of rheumatic diseases and occurs most frequently in patients with sJIA. Data from animal models and from observational studies in patients suggest that interferon gamma (IFN γ) is a driver of the hyperinflammation and hypercytokinemia observed in MAS.

Objectives: To assess the pharmacokinetics, efficacy, and safety of intravenous (IV) infusions of emapalumab, a fully human anti-IFN γ monoclonal antibody, in patients with MAS in the context of sJIA.

Methods: This ongoing, pilot, open-label, single-arm study (NCT03311854) includes patients with MAS (2016 ACR/EULAR criteria) on a background of confirmed, or high presumption of, sJIA, and with inadequate response to high-dose IV glucocorticoids. Emapalumab is initiated at 6mg/kg (1 dose) and continued at 3mg/kg twice weekly for a total of 4 weeks, or less upon achievement of complete response (CR). CR is defined as an absence of MAS clinical signs plus white blood cell and platelet counts above the lower limit of normal, LDH, AST and ALT <1.5 x upper limit of normal, fibrinogen >100mg/dL, and ferritin decreased by $\geq 80\%$ or to <2,000 ng/mL.

Results: We report preliminary data from the first 9 patients (median age [range] 11.6 [2.1-25.3] years) enrolled (7 in Europe and 2 in the USA). All patients had failed high-dose methylprednisolone, of which there were prior treatment failures from cyclosporin A (n=4) and from anakinra (n=4). Treatment with emapalumab resulted in rapid IFN γ neutralization, as demonstrated by the decrease in CXCL9 levels (Figure 1), and subsequent deactivation of T cells, as indicated by the decrease in sIL-2R levels. CR was achieved in all patients after a median of 23 (12-56) days. A progressive improvement in all clinical and laboratory parameters of MAS was observed (Table 1 and Figure 2). Glucocorticoids were tapered in all patients (median % tapering -92%; range -45% to -98% at Week 8). Emapalumab infusions were well tolerated by all patients, with no discontinuation. CMV reactivation was reported in 1 patient as a serious event possibly related to emapalumab and resolved with antiviral treatment.

Table 1. Time to response for key clinical and laboratory parameters.

Parameters	Median baseline value (range)	Median days of treatment (range)
D-dimers to <1000 mg/L	12,480 (550-89,552)	15 (1-49)
sIL-2R to <2000 ng/L	4596 (1664-20,954)	21 (6-37)
Ferritin <500 mg/L	29,240 (716-192,584)	21 (9-42)
Physician visual analog scale of MAS activity ≤ 1	9.0 (2-10)	19 (9-56)
All MAS laboratory parameters within range of CR	NA	21 (15-55)
All MAS parameters within range of CR	NA	23 (12-56)
Glucocorticoid tapering at ≤ 1 mg/kg prednisolone equivalent*	NA	42 (16-50)

*Data incomplete for 1 patient

Figure 1. Rapid neutralization of IFN γ . Each line represents an individual patient (n=9).

Figure 2. Ferritin levels and platelet counts over time.

Conclusion: Emapalumab administration led to rapid neutralization of IFN γ and was efficacious in controlling MAS with a favorable safety profile. These results support the pathogenic role of IFN γ in MAS/sJIA and the therapeutic value of IFN γ neutralization in MAS patients who have failed standard of care.

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OP0291

TOFACITINIB FOR THE TREATMENT OF POLYARTICULAR COURSE JUVENILE IDIOPATHIC ARTHRITIS: RESULTS OF A PHASE 3, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED WITHDRAWAL STUDY

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