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Title: Treating pemphigus vulgaris (PV) and foliaceus (PF) by inhibiting the neonatal Fc receptor: phase 2 open-label trial with efgartigimod

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Efgartigimod, an engineered Fc fragment that inhibits the activity of the neonatal Fc receptor (FcRn), was evaluated in an open-label phase 2 adaptive trial (NCT03334058). 34 mild to moderate PV and PF patients were enrolled to evaluate the safety, pharmacodynamics, pharmacokinetics, and efficacy of efgartigimod. In four sequential cohorts, efgartigimod was dosed at 10 or 25 mg/kg intravenously with various dosing frequencies, as monotherapy or add-on therapy to low-dose oral prednisone. Patients treated with efgartigimod had mostly mild to moderate adverse events balanced between doses. A strong correlation between serum IgG level reduction, anti-desmoglein (Dsg) autoantibody level reduction and improvement of pemphigus disease area index scores and clinical outcomes was observed throughout the trial. The median pharmacodynamic effects at day 29 following 4 weekly infusions were 62% and 66% reductions in total IgG at 10 and 25 mg/kg, respectively. A rapid clearance of anti-Dsg antibodies was observed, which reached a median 61% reduction from baseline for anti-Dsg-1 and 49% reduction for anti-Dsg-3 antibodies at the end of the induction phase. Disease control (DC) was achieved in 28 of 31 patients (90%) after a median time of 17 days. Six of eight patients who started efgartigimod monotherapy at baseline achieved DC. Complete clinical remission was achieved with prolonged maintenance therapy in 64% of patients (14/22 total; 5/7, 10 mg/kg; 9/15, 25 mg/kg) after a median time of 92 days in combination with corticosteroids (median daily dose 0.26 mg/kg, range 0.06-0.48). 14 relapses were reported in 11 patients who achieved DC (39%), with a median time to first relapse of 211 days. A phase 3 trial of efgartigimod in PV and PF (NCT04598451) is ongoing.