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Efficacy and safety of the neonatal Fc receptor inhibitor efgartigimod in adults with primary immune thrombocytopenia (ADVANCE IV): a multicentre, randomised, placebo-controlled, phase 3 trial

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Abstract

Background: Primary immune thrombocytopenia is an autoimmune disorder mediated partly by platelet autoantibodies, resulting in thrombocytopenia, bleeding, and constitutional symptoms. Efgartigimod, a first-in-class novel human IgG1 Fc fragment, binds the neonatal Fc receptor with high affinity and thus reduces serum IgG concentrations, including autoantibodies. The objective of this study was to evaluate the efficacy and safety of efgartigimod in adults with persistent and chronic primary immune thrombocytopenia.

Methods: This phase 3, multicentre, randomised, double-blinded, placebo-controlled, 24-week study evaluated the efficacy and safety of intravenous efgartigimod in adults aged 18 years or older with chronic or persistent primary immune thrombocytopenia who had an average platelet count of less than 30 000, had responded to at least one previous immune thrombocytopenia therapy, and were on a concurrent therapy at baseline or had received at least a second previous immune thrombocytopenia therapy. The study took place in 71 participating sites from Asia, Europe, and North America. Patients were randomly assigned 2:1 to receive either efgartigimod (10 mg/kg) or placebo intravenously for the first 4 weeks, after which the dosing schedule could be altered to once per week or every other week depending on the patients' platelet count. The primary endpoint, evaluated in the chronic population, was sustained platelet count response (≥50 × 109 for at least 4 of the last 6 weeks). This study is registered with ClinicalTrials.gov (NCT04188379) and is completed.

Findings: A total of 205 patients were screened from Dec 9, 2019, to Feb 3, 2022, and 131 (86 in the efgartigimod group; 45 in the placebo group) were randomly assigned. These patients represented a population with long-term disease who had a mean time since diagnosis of 10·6 years and 67% (88/131) of whom had received at least three previous immune thrombocytopenia

treatments. 22% (17/78) of patients with chronic immune thrombocytopenia receiving efgartigimod reached the primary endpoint compared with 5% (2/40) of those receiving placebo (p=0·032; adjusted difference in response, 16% [95% CI 2·6-26·4]). The median number of weeks of disease control in patients with chronic immune thrombocytopenia was 2·0 (IQR 0·0-11·0) for efgartigimod versus 0·0 (0·0-1·0) for placebo (p=0·0009). Efgartigimod was well tolerated; most adverse events were mild to moderate in severity. The most common adverse events of interest in both groups were headache (16% in efgartigimod and 13% in placebo), haematuria (16% in efgartigimod and 16% in placebo), and petechiae (15% in efgartigimod and 27% in placebo). **Interpretation:** Efgartigimod significantly increased sustained platelet count responses compared with placebo in patients with chronic immune thrombocytopenia, including those who had received multiple previous immune thrombocytopenia therapies. Upon completion of the ADVANCE IV study, patients could enroll in the ongoing open-label extension. Subcutaneous efgartigimod is currently being evaluated in patients with immune thrombocytopenia in the ADVANCE SC+ trial.

Link all'articolo: https://pubmed.ncbi.nlm.nih.gov/37778358/