Abstract: PB2636

Title: VAYHIT1: A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PHASE III TRIAL OF IANALUMAB VERSUS PLACEBO IN ADDITION TO FIRST-LINE CORTICOSTEROIDS IN PATIENTS WITH PRIMARY IMMUNE THROMBOCYTOPENIA (ITP)

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Background:

ITP is characterized by low platelet count due to immune-mediated destruction of platelets. Clinical manifestations of ITP include bleeding events, which can be severe or life threatening. Current ITP medical therapies rarely lead to durable responses after discontinuation, either in the first line (eg corticosteroids) or later lines (eg thrombopoietin receptor agonists, rituximab). B cells play an important role in the pathophysiology of ITP, with autoreactive B-cell activation leading to the production of antiplatelet autoantibodies. B-cell activating factor (BAFF) is a regulator of B-cell differentiation, proliferation and survival, mediated by interaction with the BAFF receptor (BAFF-R). BAFF levels are elevated in patients with ITP and correlate with increased disease activity. Ianalumab is an investigational, fully human immunoglobulin G1 monoclonal antibody that targets BAFF-R. It has a novel dual mechanism of action: depletion of B cells by direct antibody-dependent cellular cytotoxicity (enhanced by afucosylation of its Fc portion) and inhibition of B-cell functions through BAFF-R blockade.

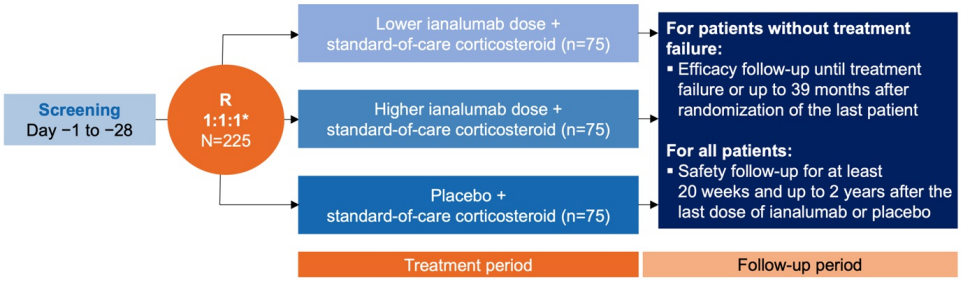
Aims:

VAYHIT1 (NCT05653349, EudraCT no. 2022-001672-34) is a multicenter, randomized, double-blinded, Phase III study that will assess the efficacy and safety of ianalumab versus placebo in addition to first-line corticosteroids in adults with primary ITP.

Methods:

VAYHIT1 will enroll approximately 225 participants. Eligible participants will have primary ITP diagnosed within 3 months of initiating corticosteroid (predniso[lo]ne or dexamethasone) therapy, a platelet count <30 G/L before starting first-line therapy and have responded (platelet count ≥50 G/L) to corticosteroids (+/− intravenous Ig [IVIg]) at any time prior to randomization. Exclusion criteria include receiving previous ITP treatment (except for corticosteroids and/or IVIg up to 28 days before randomization). Participants will be randomized in a 1:1:1 ratio to a lower ianalumab dose, a higher ianalumab dose or placebo (75 participants in each arm) (**Figure**). Ianalumab or placebo will be administered intravenously every 4 weeks. Corticosteroids will be administered as per the standard of care regimen selected prior to randomization. After the treatment period, all participants will enter a follow-up period to be monitored for efficacy until treatment failure and safety for up to 2 years. The primary endpoint is the time from randomization to treatment failure, defined as platelet count <30 G/L later than 8 weeks from randomization, need for a rescue treatment (any treatment for ITP given to rapidly increase platelet count, eg corticosteroids, IVIg or platelet transfusion) later than 8 weeks from randomization, start of second-line ITP therapy, or death. Secondary endpoints include response rate and complete response rate (proportion of participants with any platelet count of ≥50 G/L and ≥100 G/L, respectively, in the absence of rescue or new ITP treatment), time from randomization to complete response, proportion of participants with bleeding events, proportion of participants with severe infection, frequency of adverse events and change from baseline in Immune Thrombocytopenic Purpura Patient Assessment Questionnaire domain scores of symptoms, fatigue, bother and activity.

Figure. VAYHIT1 study design



*Randomization will be stratified by the type of first-line corticosteroid treatment (predniso[lo]ne or dexamethasone)
R, randomization

Results:

At the time of writing, no patients have been randomized into the VAYHIT1 study.

Summary/Conclusion:

The Phase III VAYHIT1 study will assess the ability of ianalumab in addition to corticosteroids to prolong time to treatment failure in patients with primary ITP.