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A phase 2 open-label study to assess the tolerability of ianalumab (VAY736) with investigator's choice thrombopoietin receptor agonist in patients with primary immune thrombocytopenia: VAY2EXPLORE study design

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INTRODUCTION

- ITP is an immune-mediated disease characterized by transient or persistent decrease of platelets and, depending on the degree of thrombocytopenia, increased risk of bleeding[1]
- Ianalumab is a monoclonal antibody targeting B cells through a novel dual mechanism of action of inhibition of B-cell activation and survival via B-cell activating factor receptor (BAFF-R) blockade and enhanced depletion of B cells via antibody-dependent cellular cytotoxicity (ADCC)[2-4]
- In the phase 3 VAYHIT2 study (NCT05653219), ianalumab plus the TPO-RA eltrombopag demonstrated significantly prolonged time to treatment failure versus eltrombopag alone[5]
- VAY2EXPLORE builds on prior ianalumab data in ITP by extending evaluation to investigator's choice (IC) TPO-RAs in a pretreated population. The study is designed to evaluate the tolerability of ianalumab 9 mg/kg with ongoing TPO-RA, and whether the TPO-RA can be tapered off while maintaining durable response off treatment

OBJECTIVE

- To investigate the tolerability of ianalumab with ongoing IC TPO-RA background treatment in patients with ITP

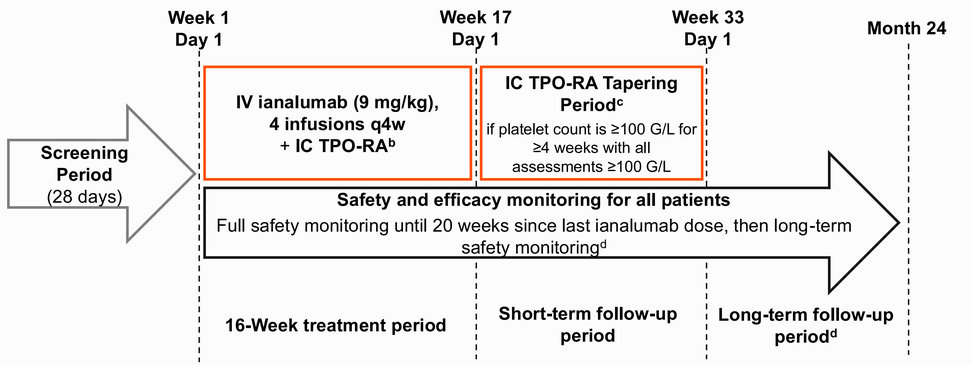
METHODS

Study Design

- VAY2EXPLORE (NCT07421167) is a phase 2, multicenter, open-label trial to investigate the tolerability of ianalumab with ongoing IC TPO-RA background treatment in adults with ITP previously treated with 1-4 treatments
- Approximately 149 patients with ITP will be enrolled, with 25-60 patients on each IC TPO-RA (eltrombopag, avatrombopag, and romiplostim). The study will also enroll up to 15 patients with Evans Syndrome (ES) in an exploratory cohort
- The study will consist of a screening period of up to 28 days prior to first ianalumab dose, a treatment period of 16 weeks in which patients will receive 4 monthly ianalumab infusions (9 mg/kg every 4 weeks) with ongoing IC TPO-RA background treatment, an IC TPO-RA tapering period up to 16 weeks, and a long-term safety and efficacy follow-up period of 15 months (**Figure 1**)
- Patients may taper IC TPO-RA during the 16-week tapering period if platelet counts have been ≥100 × 10^9/L for ≥4 weeks
- A summary of key inclusion and exclusion criteria can be found in **Table 1**
- The primary objective is tolerability of ianalumab during the 16-week treatment period, defined as patients who do not experience discontinuation due to adverse events (AEs), AEs leading to dose reduction/dose rate reduction, or AEs leading to ianalumab interruption (**Table 2**)
- Secondary objectives include safety of ianalumab, effect of ianalumab plus IC TPO-RA treatment on platelet count, and tapering rates of IC TPO-RA

Figure 1. VAY2EXPLORE Study Design

The study schema is the same for the main cohort (~149 patients with primary ITP[a]) and the exploratory cohort (~15 patients with primary ES)



AE, adverse event; ITP, immune thrombocytopenia; D, day; ES, Evans Syndrome; IC, investigator's choice; ITP, immune thrombocytopenia; IV, intravenous; q4w, every 4 weeks; SAE, serious adverse event; TPO-RA, thrombopoietin receptor agonist; W, week.
[a] Enrollment target of 149 patients with ITP, with ≥25 patients on each IC TPO-RA treatment; the IC TPO-RA treatment type will be capped at up to 40% (ie, up to 60 patients) of the total ITP population.
[b] Eltrombopag, avatrombopag, or romiplostim, administered according to the respective US prescribing information and with no change in dose for ≥14 days prior to the start of ianalumab.
[c] TPO-RA tapering should start after W17D1 if platelet count has been ≥100 G/L for ≥4 weeks with all platelet count assessments during these 4 weeks ≥100 G/L. Dose reduction of the TPO-RA is allowed prior to the tapering period if clinically indicated. Tapering should be completed by W33D1. However, if the TPO-RA cannot be tapered off by the W33D1 visit, the patient will continue to be monitored in the study.
[d] Long-term safety monitoring: only collection of AEs/SAEs potentially related to B-cell depletion and SAEs assessed by the Investigator as related to ianalumab. If B-cell depleting therapy starts, only SAEs assessed by Investigator as related to ianalumab will be collected.

Table 1. Summary of Key Inclusion and Exclusion Criteria

Key Inclusion Criteria	Key Exclusion Criteria
• Patients aged ≥18 years with signed informed consent	• Patients being treated with a TPO-RA for >6 months
• ITP cohort	• Current life-threatening bleeding (related to thrombocytopenia)
– Diagnosis of primary ITP that has responded to corticosteroid or IVIG treatment (response defined as platelet count ≥50 G/L)	• Prior splenectomy within 6 months of first administration of ianalumab
– Received ≥1 prior treatment for ITP	• Patients with laboratory abnormalities as listed in protocol[b]
– Platelet count <100 G/L while receiving a TPO-RA[a]	• Patients with significantly compromised liver disease (Child-Pugh 7 to 9) and decompensated liver disease (Child-Pugh 10 to 15)
• ES cohort	• Treatment with a B-cell depleting therapy (eg, rituximab, belimumab) within 12 weeks prior to the first administration of ianalumab. Patients who are refractory to rituximab will be excluded:
– Diagnosis of primary ES with active thrombocytopenia (platelet count <100 G/L) with wAIHA for whom a TPO-RA is appropriate	– Patients who have not achieved a response (defined as platelet count ≥30 G/L and at least doubling from baseline within 12 weeks in the absence of rescue therapy) following completion of a standard course of rituximab
– Inadequate response or relapse after corticosteroid treatment	• Known history of primary or secondary immunodeficiency, or a positive HIV (ELISA and Western blot) test result
– Diagnosis confirmed by current or past positive DAT (IgG+ with or without C3+) and evidence of hemolysis	• ITP cohort: Patients exposed to >4 prior treatments for ITP, secondary thrombocytopenia, use of immunosuppressant drugs other than corticosteroids or rituximab
– Any supportive care treatment administered for wAIHA must be stable for ≥4 weeks prior to enrollment	• ES cohort: life-threatening hemolysis, secondary ES, patients with autoimmune hemolytic anemia other than wAIHA

ALT, alanine aminotransferase; AST, aspartate aminotransferase; DAT, direct antiglobulin test; ELISA, enzyme-linked immunosorbent assay; ES, Evans Syndrome; IgG, immunoglobulin G; ITP, immune thrombocytopenia; IVIG, intravenous immunoglobulin; TPO-RA, thrombopoietin receptor agonist; ULN, upper limit of normal; wAIHA, warm autoimmune hemolytic anemia.
[a] Patients may already be receiving a TPO-RA or may start a TPO-RA at screening. All patients should be on a stable dose of TPO-RA for ≥14 days prior to first dose of ianalumab. During the screening period, a documented assessment of platelets <100 G/L is mandatory for enrollment. For patients who received rescue medication before screening, platelet count results obtained prior to the start of the rescue therapy should be used to assess eligibility if collected within 14 days prior to screening.
[b] Laboratory abnormalities include neutrophils <1000/mm^3, serum creatinine >1.5 × ULN, IgG <5 g/L, AST >3.0 × ULN, ALT >3.0 × ULN, and for the ITP cohort only: hemoglobin <10 g/L and total bilirubin >1.5 × ULN.

Table 2. Summary of Endpoints

Primary Objective	Related Endpoints
• To evaluate the tolerability of ianalumab during the treatment period (16 weeks)	• Proportion of participants who are able to tolerate ianalumab (9 mg/kg), defined as those who do not experience any of the following during the treatment period (up to Week 16): – Discontinuation due to AE (not efficacy) – AEs leading to dose reduction/dose rate reduction – AEs leading to ianalumab interruption
Secondary Objectives	**Related Endpoints**
• To evaluate the safety of ianalumab during the entire study period	• Type, frequency, and severity of AEs during the entire study period • Other safety parameters
• To evaluate the effect of ianalumab plus IC TPO-RA on platelet count	• Proportion of patients with platelet count ≥30 G/L, ≥50 G/L, ≥100 G/L at defined timepoints in the absence of rescue and new ITP treatments • Change from baseline in platelet count for prespecified subgroups (<30, 30 to <50, 50 to <100 G/L) at defined timepoints in the absence of rescue and new ITP treatments
• To evaluate tapering rates of IC TPO-RA	• Proportion of patients with successful IC TPO-RA tapering in absence of rescue and new ITP treatments by the end of the tapering period

AE, adverse event; IC, investigator's choice; ITP, immune thrombocytopenia; TPO-RA, thrombopoietin receptor agonist.

KEY FINDINGS & CONCLUSIONS

- The VAY2EXPLORE study will build on previous research and evaluate the tolerability and potential benefit of combining ianalumab with thrombopoietin receptor agonist (TPO-RA) therapy in patients with immune thrombocytopenia (ITP)

STUDY STATUS

- The VAY2EXPLORE trial has been recruiting since May 2026
- An interim analysis will be conducted when the first half of the ITP population (~75 patients) have completed the 16-week treatment period or discontinued earlier to allow for the assessment of safety
- A primary analysis will be conducted when all patients with ITP have been followed up for ≥16 weeks or have discontinued the study early

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References

1. Rodeghiero F, et al. *Blood.* 2009;113(11):2386-2393.
2. McWilliams EM, et al. *Blood.* 2013;122(21):4185:642.
3. Dörner T, et al. *Ann Rheum Dis.* 2019;78(5):641-647.
4. McWilliams EM, et al. *Blood Adv.* 2019;3(3):447-460.
5. Cuker A, et al. *N Engl J Med.* 2026;394(15):1503-1513.

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