Dr Mathias Rummel | Mathias.Rummel@innere.med.uni-giessen.de

Poster# **MDS-882**

A Phase 2 Study of Ianalumab in Patients With Primary Immune Thrombocytopenia Previously Treated With ≥2 Lines of Therapy (VAYHIT3)

Charlotte Bradbury,[1] Tugrul Elverdi,[2] Karolin Trautman,[3] Mathias Rummel,[4] Alessandra Borchiellini,[5] Huyen Tran,[6] Jae-Ho Yoon,[7] Nichola Cooper,[8] Guillaume Moulis,[9] Thomas Stauch,[10] Sebastian Grosicki,[11] Fabienne Le Gac,[12] Alex Allepuz,[12] Patrick Urban,[12] Renxin Lin,[13] Tomás José González-López,[14] David J. Kuter[15]

[1]Faculty of Health Sciences, University of Bristol, Bristol, UK; [2]Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Internal Medicine, Division of Hematology, Istanbul, Türkiye; [3]Medical Clinic I, University Hospital Carl Gustav Carus at the TU Dresden, Dresden, Germany; [4]Department of Hematology & Oncology, University Hospital Gießen, Gießen, Germany; [5]Division of Hematology, University of Turin, and AOU Città Della Salute e Della Scienza, Turin, Italy; [6]Department of Clinical Haematology, Alfred Hospital, and Australian Centre for Blood Diseases, Monash University, Melbourne, Victoria, Australia; [7]Department of Hematology, Catholic Hematology Hospital, Seoul St. Mary's Hospital, and Leukemia Research Institute, College of Medicine, The Catholic University of Korea, Seoul, South Korea; [8]Imperial College Healthcare NHS Trust, London, UK; [9]Department of Internal Medicine, Toulouse University Hospital-Purpan Hospital, Toulouse, France; [10]Department of Internal Medicine II, Hematology and Oncology, University Hospital Jena, Jena, and Labor Volkmann, Karlsruhe, Germany; [11]Department of Cancer Prevention, Faculty of Public Health, Medical University of Silesia, Katowice, Poland; [12]Novartis Pharma AG, Basel, Switzerland; [13]China Novartis Institutes for BioMedical Research Co., Ltd., Shanghai, China; [14]Hospital Universitario de Burgos, Burgos, Spain; [15]Hematology Division, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

KEY FINDINGS & CONCLUSIONS

- The primary analysis of VAYHIT3 based on 41 patients provides preliminary results on the efficacy (as assessed during the first 25 weeks after treatment start) and tolerability of a short course of ianalumab administered intravenously (IV) in heavily pretreated patients with primary immune thrombocytopenia (ITP), with no new safety signals detected up to the data cutoff
  - Nearly half of the patients (44%) achieved a confirmed response (ConfR), with most experiencing it during the first 2 months, and more than half of the responders (56%) maintained a stable response at 6 months
  - There were no discontinuations due to adverse events (AEs). Infusion-related reactions (IRRs) and infections were grade 1 or 2, except 1 grade 3 infection
- Ianalumab is currently being investigated in the ongoing phase 3 studies VAYHIT1 (NCT05653349) and VAYHIT2 (NCT05653219) as first- and second-line treatments for primary ITP, respectively

This study is sponsored by Novartis Pharma AG
Originally presented at: EHA2025 Congress; June 12-15, 2025; Milan, Italy
Poster presented at: SOHO 2025; September 3-6, 2025; Houston, TX

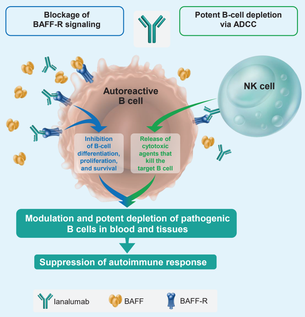
INTRODUCTION

- The B-cell–activating factor (BAFF) signaling pathway is crucial for B-cell proliferation, differentiation, and survival, and it has the potential to become a compelling therapeutic target for autoimmune conditions such as immune thrombocytopenia (ITP) (**Figure 1**)[1,2]
- Ianalumab is a fully human anti–BAFF receptor monoclonal antibody with a dual mechanism of action[3-5] and is under investigation for primary ITP

OBJECTIVES

- VAYHIT3 (NCT05885555) assesses the safety and efficacy of ianalumab in patients with primary ITP who did not respond to ≥2 prior treatment lines
- Here, we present the results of the primary analysis, which was conducted when all patients completed the week 25 visit or discontinued earlier

Figure 1. Ianalumab's Proposed Dual Mechanism of Action

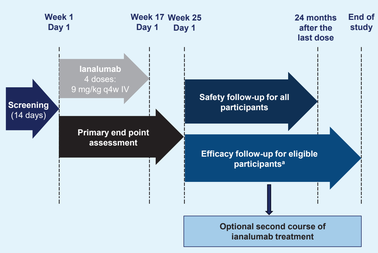


ADCC, antibody-dependent cellular cytotoxicity; BAFF, B-cell–activating factor; BAFF-R, B-cell–activating factor receptor; NK, natural killer.

METHODS

- This phase 2, open-label, single-arm study enrolled adults with primary ITP previously treated with at least a corticosteroid and a thrombopoietin receptor agonist (TPO-RA) and with no previous splenectomy
  - Eligible patients had loss of response, no or insufficient response, or intolerance to the last ITP therapy; had a platelet count of <30 G/L; and were assessed by the investigator as needing treatment
- Patients received ianalumab 9 mg/kg IV every 4 weeks for a total of 4 doses; concomitant therapy with corticosteroids and/or TPO-RAs could be continued if clinically indicated and the dose was stable ≥14 days before ianalumab initiation (**Figure 2**)
- The primary end point is ConfR, defined as platelet count of ≥50 G/L at ≥2 consecutive assessments ≥7 days apart between weeks 1 and 25, without rescue for ≥4 weeks or start of new ITP treatment before reaching ConfR
- Secondary objectives were quality of response and safety

Figure 2. VAYHIT 3 Study Design

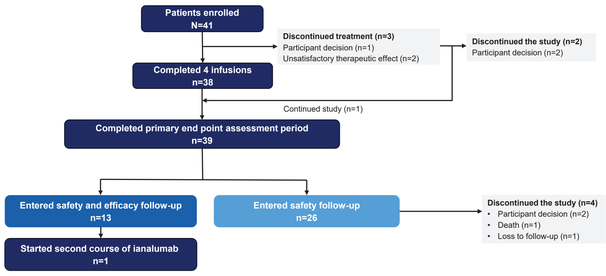


Data cutoff: February 5, 2025.
Participants were allowed to continue background corticosteroids and/or TPO-RA on which they had not responded at time of study entry. The dosage of the background treatment must have remained stable for ≥14 days prior to initiating ianalumab and could not be increased once the study drug commenced. Patients received premedication prior to the first 2 ianalumab infusions (paracetamol 1000 mg, antihistamine per institutional guidelines, and corticosteroid [prednisolone 50 mg or equivalent]).
ITP, immune thrombocytopenia; IV, intravenous; q4w, every 4 weeks; TPO-RA, thrombopoietin receptor agonist.
[a] At week 25 day 1: platelet count of ≥30 G/L and ≥4 weeks since last rescue and no new ITP treatment.

RESULTS

- At data cutoff (February 5, 2025), 41 patients were enrolled, of whom 39 completed the primary end point assessment period (**Figure 3**)
  - Two patients discontinued treatment early due to patient decision

Figure 3. Patient Disposition



- Baseline demographics and disease characteristics are shown in **Table 1**
  - Median (range) patient age was 55 (18-80) years; 51% of patients were female
  - All patients received prior corticosteroids and TPO-RAs; 46% received prior rituximab, and 51% received other immunosuppressants

Table 1. Patient Demographics and Baseline Disease Characteristics

Characteristic	Ianalumab (N=41)
Age, median (range), years	55 (18-80)
Male, n (%)	20 (49)
Race, n (%)[a]	
Asian[b]	8 (20)
White	32 (78)
Hispanic or Latino, n (%)[a]	6 (15)
Platelet count, median (range), G/L	8 (0-29)
ITP duration, median (range), years[c]	4.2 (0-41)
No. of prior lines of treatment, median (range)	6 (2-13)
≥4 Prior lines, n (%)	36 (88)
Type of prior medications, n (%)	
Corticosteroids	41 (100)
TPO-RA	41 (100)
IVIG or anti-D immune globulin	33 (81)
Rituximab	19 (46)
Other immunosuppressant[d]	21 (51)
Other treatment	23 (56)
Fostamatinib	10 (24)

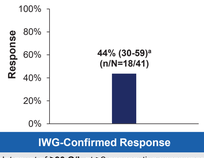
ITP, immune thrombocytopenia; IVIG, intravenous immunoglobulin; TPO-RA, thrombopoietin receptor agonist.
[a] 1 patient had a missing race and ethnicity assessment. [b] Includes Chinese (n=4), Korean (n=2), Indian (n=1), and other (n=1). [c] Time from initial diagnosis of ITP was calculated from the date of initial diagnosis to the screening date. [d] Azathioprine (n=10), cyclosporine (n=7), mycophenolic acid (n=12), sirolimus (n=2), tacrolimus (n=1), and vincristine (n=2).

- Of the 41 patients included in the efficacy analysis, 18 (44%) achieved ConfR (**Figure 4**)
  - Of the 18 participants with ConfR, 8 responded in the first month, 5 in the second month, and 5 between the third and fifth months
  - Median time to ConfR in responders was 6 weeks
- 9 of 10 patients with a stable response had a complete response at week 25, defined as a platelet count of ≥100 G/L in the absence of rescue treatment or new ITP treatment

Figure 4. Key Efficacy End Points: ConfR (Primary End Point), SR, IWG-ConfR,[6] and IWG-SR[6]

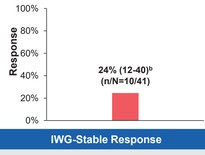
Primary End Point: Confirmed Response

- Platelet count of ≥50 G/L at ≥2 consecutive assessments ≥7 days apart between weeks 1 and 25
- No rescue therapy within ≥4 weeks of platelet count assessment or start of new therapy before ConfR



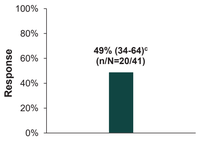
Stable Response

- Platelet count of ≥50 G/L on a ≥75% of assessments between weeks 19 and 25
- No rescue therapy within ≥4 weeks of platelet count assessment or start of new therapy before SR



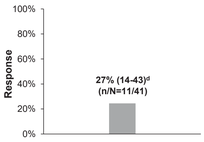
IWG-Confirmed Response

- Platelet count of **≥30 G/L** at ≥2 consecutive assessments ≥7 days apart between weeks 1 and 25 **with ≥a 2-fold increase from baseline**
- No rescue therapy within ≥4 weeks of platelet count assessment or start of a new therapy before ConfR



IWG-Stable Response

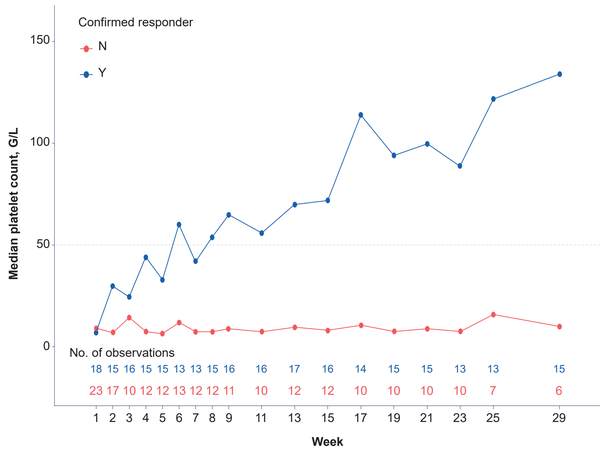
- Platelet count of **≥30 G/L** on ≥75% of assessments between weeks 19 and 25 **with ≥a 2-fold increase from baseline**
- No rescue therapy within ≥4 weeks of platelet count assessment or start of a new therapy before SR



ConfR, confirmed response; IWG, International Working Group; SR, stable response.
[a] 95% Bayesian credibility interval. [b] 95% CI. [c] 95% Bayesian credibility interval for corresponding modified end points. [d] 95% CI for corresponding modified end points.

- Median platelet count continued to increase over time (**Figure 5**)
- Rates of any-grade bleeding events (according to the World Health Organization Bleeding Scale) decreased from 59% at baseline (n/N=24/41) to 22% at week 25 (n/N=8/37), and 10% at week 33 (n/N=3/30)

Figure 5. Platelet Count Over Time



Platelet counts collected ≤4 weeks after the rescue treatment or after the start of a new ITP therapy were excluded for all postbaseline visits. Baseline is the worst value during the screening period or the value on the date the first course of ianalumab treatment was started.
ITP, immune thrombocytopenia; WHO, World Health Organization.

- Safety data are shown in **Table 2**
- IRRs were reported in 6 participants (15%); all IRRs were grade 1 or 2, and no discontinuations were due to IRRs
- Infections were reported in 15 participants (37%); 1 participant (2%) experienced a grade 3 infection (*Clostridioides difficile*)
- One patient died in the posttreatment phase due to an AE of pulmonary edema. The event was reported by the investigator as not related to ianalumab

Table 2. Overview of On-Treatment AEs in VAYHIT3[a]

Event, n (%)	Ianalumab (N=41)	
	All grades	Grade ≥3
AEs	35 (85)	9 (22)
Study drug related	15 (37)	1 (2)
SAEs	6 (15)	6 (15)
Study drug related	0	0
Fatal AEs	0	0
AEs leading to study treatment discontinuation	0	0
Most frequent AEs (>10%)[b]		
Headache	9 (22)	0
Contusion	8 (20)	0
Petechiae	8 (20)	0
Purpura	8 (20)	0
IRR	6 (15)	0
URTI	5 (12)	0
On-treatment SAEs[c]		
Thrombocytopenia	2 (5)	2 (5)
Allergy to immunoglobulin therapy	1 (2)	1 (2)
Arterial disorder	1 (2)	1 (2)
Chronic kidney disease	1 (2)	1 (2)
Liver disorder	1 (2)	1 (2)
Upper gastrointestinal hemorrhage	1 (2)	1 (2)

AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; IRR, infusion-related reaction; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; URTI, upper respiratory tract infection.
[a] On-treatment AEs started during the period from the day of the first administration of the study drug to 28 days after the last administration of the study drug. Participants with multiple severity grades for an AE are counted only under the maximum grade. MedDRA version 27.1, CTCAE version 5.0. [b] No grade ≥3 AEs were reported among the most frequently observed AEs. [c] SAEs occurring during treatment or within 28 days of the last dose of the study drug were considered in this analysis. A participant with multiple severity grades for an AE is only counted under the maximum grade. MedDRA version 27.1, CTCAE version 5.0. No grade 5 AEs were reported.

References

1. Emmerich F, et al. *Br J Haematol*. 2006;136(2):309-314.
2. Zhou Z, et al. *Autoimmunity*. 2009;42(2):112-119.
3. McWilliams EM, et al. *Blood*. 2013;122(21). Abstract 4185.
4. Dörner T, et al. *Ann Rheum Dis*. 2019;78(5):641-647.
5. McWilliams EM, et al. *Blood Adv*. 2019;3(3):447-460.
6. Rodeghiero F, et al. *Blood*. 2009;113(11):2386-2393.

Acknowledgements

We thank the patients who participated in this study; their time, interest, and insight are greatly appreciated. Medical writing and editorial support was provided by Ziyaad Rahman, MSc, of Nucleus Global, and was funded by Novartis Pharmaceuticals Corporation. This poster was developed in accordance with Good Publication Practice (GPP) guidelines. The authors had full control of the content and made the final decision on all aspects of this publication.

Disclosures

Charlotte Bradbury has received advisory and speaker fees from Novartis and Eli Lilly; speaker fees from Sobi, Sanofi, Bristol Myers Squibb, Pfizer, Janssen, and Bayer; and speaker fees and research funding from Amgen. Karolin Trautman has received consultancy fees from Amgen, Grifols, GSK, Novartis, Sanofi, and Sobi; honoraria from Amgen, Grifols, GSK, Novartis, Sanofi, Sobi, and Takeda; speakers bureau for Roche and Grifols. Mathias Rummel has served in an advisory role or provided expert testimony for Amgen, Novartis, Swedish Orphan Biovitrium, and CSL Behring; and received honoraria from Amgen, Novartis, Sandoz, and Swedish Orphan Biovitrium. Huyen Tran has received grants and contracts from Sanofi, Takeda, Roche and CSL Behring. Nichola Cooper has received consultancy fees from Novartis, Sanofi, Sobi, Grifols, Argenx, and Amgen; research funding from Rigel, Novartis, and Argenx; and honoraria from Sanofi, Sobi, Novartis, Grifols, Argenx, and Amgen. Guillaume Moulis reports research funding from Amgen, Grifols, Novartis, and Sanofi; advisory board for Alpine, Amgen, Argenx, Grifols, Novartis, Sanofi, and Sobi; meeting attendance grants from Amgen, Grifols, and Novartis; and speaker at educational sessions for Amgen, Grifols, and Novartis. Thomas Stauch has received consultancy fees from Novartis; membership on an entity's Board of Directors or advisory committees for Novartis, Amgen, and Grifols; research funding from Novartis, Amgen, Sobi, Argenx, and Grifols; speakers bureau for Novartis, Amgen, Sobi, Grifols, Alexion, Janssen, ACP, and AstraZeneca; and other support from Celgene/BMS. Sebastian Grosicki declares no competing interests. Fabienne Le Gac, Alex Allepuz, and Patrick Urban are employees of Novartis. Renxin Lin is an employee of China Novartis Institutes for BioMedical Research Co., Ltd. Tomás José González-López has received research funding from Amgen, Novartis, Grifols, and Sobi; and honoraria from Amgen, Novartis, Grifols, Sobi, Alpine, Argenx, and Momenta. David J. Kuter has received consultancy fees for Biocryst, Hutchmen, Novartis, Principia, Rigel, Sanofi, Alexion, Alnylam, Alpine, Amgen, Apellis, Argenx, BMS, Caremark, Cellularity, Cellphire, Chugai, Hengrui, Immunovant, Immagenebio, Ligand, Medscape, Merck Sharp Dohme, New York Blood Center, Peerview, PER, Pfizer, Platelet Disorder Support Association, Regeneron, Seismic, Sobi, Takeda, UCB, Up-To-Date, Verve, AIRx, CRICO, Daiichi Sankyo, Dianthis, Electra Therapeutics, Fuji, Hemopure, Incyte, Kezar, Kyowa-Kirn, Momenta, Nuvig, Platelet Biogenesis, Protagonist, and Zafgen; and research funding from Biocryst, Hutchmen, Novartis, Principia, Rigel, Sanofi, Alnylam, Takeda, and UCB. Tugrul Elverdi, Alessandra Borchiellini, and Jae-Ho Yoon have nothing to disclose.

Scan to obtain:

- Poster

https://tinyurl.com/Charlotte8882

Copies of this poster obtained through the Quick Response (QR) code are for personal use only and may not be reproduced without permission of the authors.