ABSTRACT E-BOOK

OC1

EARLY T-CELL RECEPTOR REPERTOIRE FEATURES PREDICT LONG-TERM OUTCOME IN PAEDIATRIC IMMUNE THROMBOCYTOPAENIA

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Immune thrombocytopaenia (ITP) is an acquired autoimmune bleeding disorder characterised by platelet destruction. Most children experience a self-limiting course, but approximately one-third develop persistent or treatment-refractory disease. Identifying early immune features that distinguish transient from chronic ITP remains an important clinical need, as clinical presentation alone does not reliably predict long-term outcome. Although dysregulated T-cell responses have been implicated in ITP pathogenesis, how early T-cell receptor (TCR) repertoire features relate to long-term clinical outcome remains unclear.

We studied 52 paediatric patients with primary ITP and 18 age-matched healthy controls. High-throughput bulk TCRβ repertoire sequencing was performed using the Illumina MiSeq platform. To characterise clonal dynamics and cellular phenotype, we integrated bulk repertoire data with longitudinal sampling and performed single-cell RNA and paired TCR sequencing using 10x Genomics in a subset of patients.

Clonal T-cell expansions were detectable at diagnosis, indicating early repertoire disruption. Absence of expanded clonotypes at diagnosis identified children who subsequently achieved sustained remission, whereas their presence was associated with delayed or absent remission ($p = 0.019$). In patients with expanded clonotypes who achieved remission, GLIPH2 motif-based analysis identified greater TCR similarity groups per patient compared with non-remission patients, suggesting a shared antigen.

Longitudinal tracking demonstrated persistence of expanded clonotypes over multiple years in non-remission patients, while remission patients exhibited clonal contraction. Single-cell analysis revealed expanded clonotypes localised predominantly to CD8 effector memory and TEMRA compartments with terminal differentiation features. CD8 clonotypes in non-remission patients exhibited more advanced differentiation states with increased inflammatory pathway activity. Cell–cell communication analysis identified strengthened inflammatory signalling in refractory disease, with increased interactions between CD4 central memory T cells, CD8 effector populations, B cells, and monocytes

These findings demonstrate that early TCR repertoire features, including clonal expansion, persistence, transcriptional state, and intercellular communication, are associated with long-term clinical outcome in paediatric ITP, supporting the potential utility of TCR repertoire profiling as a prognostic tool at diagnosis.

OC2

CIRCULATING CD8 T CELLS AS A POTENTIAL BIOMARKER OF NON-RESPONSE TO RITUXIMAB IN ITP

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Background: Immune thrombocytopenia (ITP) is a rare autoimmune disease characterized by isolated thrombocytopenia and potential life-threatening bleeding. Approximately 70% of adults develop chronic ITP and require second-line therapies. Maintenance strategies commonly include thrombopoietin receptor agonists and rituximab. The latter achieving response rates of 60% at one year and 30% at five years. However, reliable clinical or biological predictors of rituximab response are lacking.

Objectives: To identify immune signatures associated with long-term response to rituximab, we analyzed baseline immune profiles in adult patients with ITP.

Methods: Single-cell RNA sequencing (scRNA-seq) and multiparameter flow cytometry were performed on cryopreserved PBMC collected before rituximab administration from 38 adults enrolled in clinical trials between 2010 and 2020 (Table 1). Rituximab response (R) was defined at 5-year follow-up as a platelet count >30×10^9/L with at least a twofold increase from baseline and without additional ITP therapy. Others were classified as non-responders (NR). For scRNA-seq, 4 R and 4 NR patients matched for age, sex, disease duration, and prior treatments were compared.

Results: scRNA-seq revealed 246 genes significantly upregulated in CD8 T-cell subsets from NR patients. These genes enrich activation pathways, with prominent involvement of TCR-related signaling (NFAT, JUND, NFKB) and cytokine pathways, particularly interferon-γ (IFN-γ).

Flow cytometry showed no significant differences in the distribution of CD8 T cell subsets (naive, central memory, effector memory, TEMRA) between groups. However, NR patients displayed a markedly higher proportion of IFN-γ–producing CD8 T cells at baseline (2.6% [2-3.8] vs. 1.4% [0.9-1.9], p=0.0002), predominantly within memory subsets. Furthermore, preliminary results based on a subset of our cohort (14 R and 14 NR) also showed an increased frequency of $CD57^+$ effector memory CD8 T cells in NR patients, consistent with a more terminally differentiated phenotype (23% [12.6-31.6] vs. 13% [9-16], p=0.02).

Conclusion: These findings highlight a baseline state of heightened CD8 T-cell activation in patients who subsequently fail rituximab, suggesting that CD8 T cell-mediated immunity may
play a more important role than B cell-driven mechanisms in these individuals. Validation in independent cohorts could support the development of stratified therapeutic strategies and refine clinical decision-making in ITP.

Table 1. Patients' characteristics

	Responders n=20		Non-responders n=18		*p-value*
Age (years)	58	[45-69]	64	[45-75]	0.61*
Gender					
Men	11	55%	9	50%	0.99**
Women	9	45%	9	50%	
Platelets at sampling (x10^9/L)	21	[10-35]	14	[5-27]	0.28*
Duration if ITP evolution (months)	12.5	[4-111]	42	[4-60]	0.89*
ITP course					
Newly diagnosed (<3 months)	4	20%	4	22.2%	0.99**
Persistent (3-12 months)	5	25%	3	16.7%	0.7**
Chronic (>12 months)	11	55%	11	61.1%	0.75**
Type of ITP					
Primary	13	65%	15	83.3%	0.28**
Secondary	7	35%	3	16.7%	
Previous treatments received					
Steroids	19	95%	16	88.9%	0.59**
IVIg	8	40%	8	44.4%	0.99**
TPO receptor agonists	5	25%	3	16.7%	0.7**
Dapsone	10	50%	7	38.9%	0.53**
Rituximab	3	15%	0	0%	0.23**
Splenectomy	5	25%	0	0%	0.05**
Others	4	20%	1	5.6%	0.2**
Treatments received <4 weeks prior to sampling					
Steroids	6	30%	7	38.9%	0.73**
IVIg	0	0%	1	5.6%	0.5**
TPO receptor agonists	2	10%	3	16.7%	0.65**
Dapsone	5	25%	3	16.7%	0.7**
Others	1	5%	2	11.1%	0.59**
Number of rituximab cycles (1g D1-D15) received during the follow-up					
1 cycle	15	75%	18	100%	-
2 cycles	2	10%	0	0%	-
3 cycles	3	15%	0	0%	-

*Data reported as median [1st quartile-3rd quartile] or number with %. *Mann-Whitney test, **Fisher's exact test.*
ITP = Immune thrombocytopenia; IVIg = Intravenous immunoglobulin; TPO = Thrombopoietin.

OC3

DARATUMUMAB CAN LEAD TO LONG-LASTING REMISSIONS IN PATIENTS WITH REFRACTORY IMMUNE THROMBOCYTOPENIA BUT WITH A HIGH INCIDENCE OF SEVERE INFECTIONS

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Introduction

Daratumumab, an anti-CD38 antibody, have been shown to be a promising treatment in immune thrombocytopenia (ITP). The aim of this study was to assess safety and efficacy of daratumumab given for refractory ITP.

Patients and methods

We conducted an observational, retrospective, multicenter study throughout the network of the French reference center for adult immune cytopenias. We included adult patients receiving compassionate off-label treatment by daratumumab for ITP between 01/01/2020 and 01/01/2026. Complete response (CR) was defined by platelet count >100x109/L and response (R) by platelet count 30 to 100x109/L with at least a 2-fold increase from baseline.

Results

Twenty-six patients (43% females) with a median age of 68 years [range 21-88] were included. ITP was secondary in 42%, with a median duration of 76 months [range 1-594], and a median of 6 [range 2-11] previous treatment lines.

After a median of 5 [range 2-20] daratumumab infusions, patients achieved overall response (CR+PR) in 52%, including 40% CR and 12% PR, with a median time to response of 29 days [range 6-84]. Relapse-free survival probability at 24 months was 54%. Among patients, 76% were receiving stable ITP treatments and 56% also

had ITP treatments initiated or dose-escalated within six weeks before or after the first daratumumab infusion. Only 2 patients received daratumumab as monotherapy, and both achieved complete response.
Adverse events occurred in 11 (42%) patients, including 7 (27%) with infectious events requiring hospitalization (bacterial pneumonia n=4, bacteriemia n=3, urinary tract infections n=2, acute tonsillitis n=1), 3 with transient neutropenia (but without infection), and 3 with immediate infusion reaction. During follow-up, 6 patients (23%) died (3 from refractory disease, 2 from sepsis, and 1 from heart failure). In the 6 months following daratumumab, among the 19 patients with available gamma globulin assessment without intravenous immunoglobulin administration, 8 (42%) had concentrations below 6g/L.
Discussion
Overall, these results suggest that daratumumab has the potential to induce durable remissions even in multirefractory ITP patients. However, this came at the cost of a high rate of severe infections in this particular group of heavily treated, frequently splenectomized, immunocompromised and fragile patients. Careful assessment of benefit/risk balance is therefore warranted before daratumumab administration.

OC4

GENERATION OF SYNTHETIC PATIENTS IN IMMUNE THROMBOCYTOPENIA: EXPERIENCE FROM THE ITALIAN GIMEMA ITP0918 REGISTRY

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Background
Immune thrombocytopenia (ITP) is a rare and clinically heterogeneous disorder, characterized by variable bleeding risk, treatment strategies, and outcomes. Large observational registries such as the GIMEMA ITP0918 study provide essential real-world evidence, but their use is often constrained by limited sample size in specific subgroups and by data sharing and privacy concerns. Synthetic data generation represents an emerging strategy to augment real-world datasets while preserving patient confidentiality and the underlying clinical structure.
Methods
Individual-level data from 1087 patients enrolled in the GIMEMA ITP0918 registry were used to generate a synthetic cohort of 2000 patients reproducing 43 demographic, clinical, laboratory, bleeding, treatment, and outcome variables. Missing values were not imputed prior to synthesis; rather, the synthesis process aimed to preserve the observed patterns of missing data. Synthetic patients were generated using Classification and Regression Trees (CART) implemented in the synthpop R package, incorporating clinical constraints to ensure logical and medical coherence. The fidelity of the synthetic cohort was assessed through statistical comparisons of marginal distributions and inter-variable relationships between real and synthetic patients. Data fidelity was further evaluated using one-way and two-way propensity mean squared error (pMSE) measures and standardized pMSE ratios.
Results
The synthetic cohort closely mirrored the real ITP0918 population across key characteristics (Table 1). No statistically significant differences were detected between real and synthetic patients for the variables assessed, with statistical tests evaluated at the conventional 0.05 significance level. All one-way and two-way pMSE ratios fell within the recommended threshold of 10, confirming the acceptable fidelity of the replicates.
Conclusions
This study shows that synthetic patient generation based on the GIMEMA ITP0918 registry is both feasible and robust, producing virtual cohorts that faithfully preserve the clinical and statistical structure of the real ITP population. By ensuring data privacy while maintaining high data fidelity, synthetic datasets represent a valuable resource for methodological research and exploratory analyses. This approach may facilitate the development of virtual trials and contribute to more efficient and inclusive clinical research in immune thrombocytopenia and other rare hematologic diseases.

Table 1. Summary of Main Baseline Characteristics: Real vs Synthetic ITP0918 Cohorts
Categorical variables are summarized as absolute frequencies and percentages, whereas continuous variables are reported as medians with ranges. Comparisons between groups were conducted using the chi-square test or Fisher's exact test for categorical variables, as appropriate, and the Wilcoxon rank-sum test for continuous variables. Percentages were calculated after exclusion of missing data in both cohorts.

Characteristic	Real (N = 1,087)	Synthetic (N = 2,000)	p-value
Demographics			
Age at diagnosis, median (range), years	52 (2–92)	53 (2–92)	0.70
Unknown	6	12	
Female sex, n (%)	632 (58.1%)	1,172 (58.6%)	0.80
Sedentary lifestyle, n (%)	633 (60.9%)	1,144 (59.4%)	0.40
Unknown	47	75	
Disease characteristics			
Disease phase at enrolment, n (%)			0.80
– Newly diagnosed	220 (20.4%)	415 (20.9%)	
– Persistent	116 (10.7%)	196 (9.9%)	

– Chronic	745 (68.9%)	1,377 (69.3%)	
Unknown	6	12	
Splenectomized patients at enrolment, n (%)	109 (10.0%)	209 (10.5%)	0.70
Unknown	2	6	
≥1 thrombosis risk factor at enrolment, n (%)	622 (57.4%)	1,164 (58.6%)	0.50
Unknown	4	14	
Laboratory values at enrolment			
Platelet count, median (range) $\times 10^9$/L	89 (1–832)	89 (1–832)	>0.90
Unknown	5	14	
Hemoglobin, median (range), g/dL	13.4 (0.1–17.8)	13.4 (0.1–17.8)	0.30
Unknown	24	37	
White blood cells, median (range) $\times 10^9$/L	7.3 (1.3–30.6)	7.4 (1.3–30.6)	0.70
Unknown	28	42	
ITP treatments (enrolment), n (%)			
Corticosteroids	370 (34.0%)	639 (32.0%)	0.20
Eltrombopag	414 (38.1%)	762 (38.1%)	>0.90
Romiplostim	171 (15.7%)	334 (16.7%)	0.50
High Dose Dexamethasone	115 (10.6%)	209 (10.5%)	>0.90
Immunoglobin (intravenous)	69 (6.3%)	125 (6.3%)	>0.90

OC5

THE PROLONG TRIAL: A TWO PHASE RANDOMIZED PLACEBO-CONTROLLED TRIAL TO OPTIMIZE RITUXIMAB RESPONSE WITH DEXAMETHASONE AND MAINTENANCE THERAPY WITH LOW DOSE RITUXIMAB IN IMMUNE THROMBOCYTOPENIA

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Rituximab (R), a chimeric anti-CD20 monoclonal antibody that targets B cells is a widely used 2nd-line treatment in ITP. It induces durable responses in about 40% of patients; however, half of these will relapse over time.

The primary objective was to determine if R maintenance therapy is superior to placebo in prolonging responses among ITP patients who respond initially to R. Secondary objectives investigated if the initial response to R could be improved by adding dexamethasone (DXM), as well safety, bleeding and patient reported outcomes

PROLONG was a prospective, multi-center, international, double-randomized study evaluating in the first randomization whether adding dexamethasone to R improves response and in the second randomization whether maintenance therapy with R prolongs responses in patients who initially respond to R.

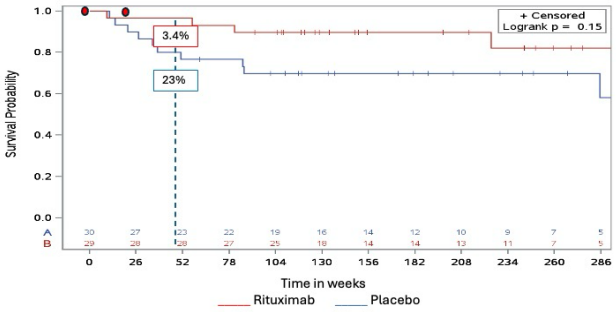
Adults with primary ITP <1 year, platelet count <30x10^9/L, and corticosteroid failure were enrolled. In the open-label induction phase, patients were randomized to R alone or R plus DXM. Responders at week 24 entered a double-blind maintenance phase and were randomized to R or placebo. The primary endpoint was sustained response during maintenance while the main secondary endpoint was response to induction with R +/- DXM.

The intent-to-treat population included 127 patients (mean age 44 years, 57% females) randomized to receive DXM (n=63) or no DXM (n=64) in addition to R. At week 24, 24 (37.5%) patients achieved response to R

monotherapy vs 38 (60.3%) to R+DXM (p=0.01). The addition of DXM resulted in faster response and prolonged time to first bleeding episode (p=0.03) without compromising safety.
59 out of 127 (46%) responded and were randomized to maintenance with R (n=30) or placebo (n=29). During the follow-up five of 29 (20.8%) patients lost response in the R group compared to 10 of 30 (33.3%) in the placebo group (p=0.15). The probability of relapse at 1 year was 6.9% (95%CI:1.7-24.8) in the R vs 23.3% (95%CI:11.8-42.8) in the placebo group indicating that most of the relapses in the placebo group occurred during the 1st year (Figure). There was no difference in the time to first infection (p=0.11).

The PROLONG study demonstrates that the response to rituximab can be enhanced by the addition of moderate-dose DXM and that early relapses may be prevented through low-dose R maintenance therapy. However, this latter strategy requires confirmation in future trials before being adopted into routine clinical practice.

Figure: time to loss of response during the during maintenance phase



Loss of Response: 2 consecutive platelet counts <50 x10^9/L at 1-8-week interval, and/or, use of any ITP-directed therapies for bleeding or thrombocytopenia

OC6

BCMA-TARGETING T-CELL-ENGAGER THERAPY INDUCES SUSTAINED REMISSION IN IMMUNE THROMBOCYTOPENIA

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Immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by isolated thrombocytopenia due to immune-mediated platelet destruction. The condition is characterized by a breakdown of immune tolerance; wherein autoreactive B- and plasma cells generate auto-reactive antibodies predominantly targeting platelet membrane glycoproteins. These autoantibodies mediate accelerated platelet clearance through Fc receptor-dependent phagocytosis and complement activation, culminating in thrombocytopenia and increased bleeding risk.1,2 Current therapies like glucocorticoids, immunoglobulins (IVIG), anti-CD20 antibodies, spleen tyrosine kinase (SYK) inhibitors, bruton's tyrosine kinase (BTK) inhibitors as well as platelet-stimulating agents can improve thrombocytopenia but, in many patients, do not result in sustained therapy free remissions.3–5 T-cell engaging therapies such as chimeric antigen receptor (CAR) T-cells and bispecific antibodies targeting the B- and plasma cell surface antigens like CD19 or BCMA have been successfully applied in the treatment of several autoimmune diseases. Teclistamab is a bispecific antibody co-targeting CD3 on T-cells and BCMA on plasma cells approved for multiple myeloma.6–10 Here, we report on the use of teclistamab in two patients with multi-drug refractory severe ITP.

Case 1:

A 33-year-old woman with Evans syndrome initially presented with prednisolone-dependent episodes of mixed type autoimmune hemolytic anemia (AIHA). Four years after the initial diagnosis, she developed recurrent severe immune thrombocytopenia (ITP), with platelet counts <10/nL, accompanied by mucosal bleeding. Comprehensive evaluation excluded underlying malignancy or viral infection. She had previously received multiple lines of ITP therapy, including immunosuppressive agents (prednisolone, dexamethasone, azathioprine), thrombopoietin-receptor agonists (TPO-RAs; sequentially eltrombopag, romiplostim, and avatrombopag), rituximab, and the Syk kinase inhibitor fostamatinib, all administered at the highest recommended doses without achieving a durable response. Last treatment consisted of avatrombopag, fostamatinib, and prednisolone (20–30 mg/day) and recurrent cycles of dexamethasone/IVIGs for bleeding episodes (Figure 1A; Supplementary Table 1). In this therapy-refractory situation we initiated an off-label therapy with teclistamab. After obtaining written informed consent, teclistamab was started using step-up

dosing (s.c., 0.06mg/kg d1, 0.3mg/kg d3, 1.5mg/kg d7) with standard premedication consisting of antipyretics, H1-antihistamines and dexamethasone. After second teclistamab administration the patient developed self-limiting cytokine release syndrome (CRS) grade 1. In total, four doses of teclistamab 1.5mg/kg were administered on day 7, 22, 29 and 39 without further acute toxicities. Platelet counts began to rise on day 2, exceeding 50/nL by day 3 and 200/nL by day 6 post teclistamab. Treatment with avatrombopag and fostamatinib was discontinued on day 6 and 8, respectively. Prednisolone was discontinued by week 3. Platelet counts remained stable within the normal range from day 6 through last follow-up on day 141. The patient's hemoglobin recovered by day 19 and returned to the normal range by day 28. Bone marrow evaluation revealed normalized megakaryopoiesis and absence of plasma cells while immunoglobulin IgG levels steadily decreased and were substituted once. Immunoglobulin light chains kappa and lambda became undetectable on day 38 indicating effective clearance of plasma cells. By week 5, the direct antiglobulin test (DAT) was negative for the first time since the diagnosis of AIHA, indicating clearance of autoantibodies against erythrocytes. Toxicities included transient neutropenia and a self-limiting gastrointestinal infection. The patient remains in good general condition without infections and is in treatment-free remission of both ITP and AIHA (Figure 1 B&C).

Case 2:

A 74-year-old man presented with a 5-month history of ITP. After initially achieving a complete remission with glucocorticoids/IVIGs the patient relapsed with prolonged refractory severe thrombocytopenia and associated bleeding events (WHO grade III). Bone marrow evaluation demonstrated increased megakaryoposis and no evidence of an underlying hematologic malignancy (Figure 2A; Supplementary Table 1). The patient was treated with immunosuppressant agents (prednisolone, dexamethasone, cyclophosphamide), TPO-RAs (romiplostim and avatrombopag), rituximab and fostamatinib/avatrombopag combination without response. Even addition of dexamethasone/immunoglobulins did not lead to platelet counts above 5/nl. Splenectomy was not feasible due to the inability to increase platelet counts. Given thrombocytopenia-associated nasal hemorrhage requiring erythrocyte transfusions, an off-label therapy with teclistamab was started. Teclistamab was initiated with step-up dosing (0.06mg/kg d1, 0.3mg/kg d3, 1.5mg/kg d8) with the standard premedication. The patient received tocilizumab after developing fever that was inadequately controlled by antipyretic treatment. However, blood cultures revealed bacteremia and fever resolved with antibiotic therapy. Platelet counts began to rise on day 8, exceeding 50/nL by day 9 and 100/nL by day 11, enabling discontinuation of fostamatinib on day 10 and avatrombopag on day 11. Platelet counts peaked transiently at 122/nL on day 14 before decreasing again by day 20. Analysis of patient platelets identified residual IgG autoantibodies against glycoproteins IIb/IIIa and Ib/IX. (All detailed laboratory results in the supplementary). Avatrombopag was reinitiated on day 19, prompting renewed platelet elevation. By day 30 platelet counts again normalized (189/nL), prompting discontinuation of avatrombopag. At the most recent follow-up on day 106 the patient exhibited stable platelet counts at 186/nL, undetectable anti-platelet antibodies and showed good general condition without bleeding or infection signs. Transient neutropenia was successfully treated with G-CSF. The patient developed hypogammaglobulinemia with kappa/lambda light chains and B cells being undetectable at day 21 and day 10 respectively. Bone marrow investigation demonstrated that the initial therapies (including glucocorticoids, rituximab) reduced B cells but not plasma cells while after teclistamab both, B cells and plasma cells, were completely depleted.

Discussion:

We demonstrate that teclistamab, an approved and readily available off-the-shelf treatment, can induce a rapid and sustained hematologic response in patients with multi-drug refractory ITP with acceptable tolerability. These two cases thus highlight the efficacy of BCMA-directed T-cell engager therapy in the management of multi-drug refractory, antibody-mediated hematologic autoimmune diseases. The unexpected rapid response observed within days of teclistamab therapy despite the immunoglobulin half-life of >3 weeks can be explained by the swift and complete plasma-cell eradication by teclistamab and fast consumption of anti-platelet antibodies, which rapidly shifts the balance between autoantibodies and available platelets towards platelets. Bone marrow investigations imply that sole B cell depletion by fostamatinib or rituximab while sparing plasma cells was not sufficient for inducing response in our patients. Instead, depletion of plasma cells by teclistamab was associated with rapid platelet response implying that auto reactive plasma cells are primarily driving ITP. In a case report of a patient with relapsed multiple myeloma and concomitant chronic ITP treatment with teclistamab resulted in sustained normalization of

platelet counts, however simultaneously a deep hematologic response of the myeloma was achieved. It thus can't be conclusively determined whether adequate anti-myeloma therapy was responsible for the observed recovery of platelet counts.11 From a clinical perspective, this underscores the high potential of teclistamab therapy for refractory ITP. Compared with anti-CD38 therapy such as daratumumab, which has previously been used for refractory ITP, fixed-duration teclistamab may offer a more targeted and rapid plasma-cell directed approach with the potential for long-term benefit.12,13 This may be due to less effective or incomplete clearance of plasma cells. Splenectomy, although effective in 60% of ITP cases, is not considered an appropriate therapy anymore because of the high perioperative bleeding risk and the lifelong risk of overwhelming post-splenectomy infection.14 The two patients are now in remission for 13 and 20 weeks, respectively. Longer follow-up will be essential to assess the durability of response and potential cure of ITP by teclistamab. This would require, besides sustained hematologic response, the absence of auto-immune antibodies and recovery of normal B- and plasma cells as has been observed after CAR T-cell therapies for multiple myeloma and lupus erythematosus.15,16 The advantage of bispecific antibodies over CAR T-cells in autoimmune disease is the immediate availability, better tolerability and flexible therapy management in case of side effects, no requirement of conditioning chemotherapy and likely lower costs if therapy duration is limited. The successful and well-tolerated treatment of these two cases provides a basis for prospective clinical trials to confirm the safety, efficacy and determination of the optional dosage of BCMA-directed T-cell engaging therapies in the treatment of ITP and AIHA.

P01

LUNA3 PHASE 3 STUDY OF RILZABRUTINIB VS PLACEBO: MODIFIED DURABLE PLATELET RESPONSE BY INTERNATIONAL WORKING GROUP (IWG) CRITERIA IN EUROPEAN ADULTS WITH PERSISTENT/CHRONIC PRIMARY IMMUNE THROMBOCYTOPENIA (ITP)

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IWG-defined platelet response in ITP comprises a clinically meaningful, safe platelet threshold rarely used in studies. The covalent, reversible BTK inhibitor rilzabrutinib acts through multi-immune modulation, showing durable responses, favorable safety, and improved HRQOL in ITP. Analyses here report modified durable response per IWG criteria from LUNA3 European ITP patients receiving rilzabrutinib vs placebo (NCT04562766; 2023-509401-71).

Patients were randomized 2:1 to oral rilzabrutinib 400 mg bid or placebo for 24 weeks in the double-blind (DB) period. After the initial 12 weeks, non-responders either discontinued or received rilzabrutinib for 28 weeks in the open-label (OL) period. Modified durable IWG response was defined as platelet count ≥30×109/L and ≥doubled from baseline, absent bleeding for ≥50% of assessments during either the last 12 weeks of the DB (≥6 non-missing assessments) or the last 16 weeks of the OL period (≥8 non-missing assessments).

Of 81 European patients randomized in the DB, 52 received rilzabrutinib and 29 placebo; 73 patients entered the OL on rilzabrutinib. At DB baseline, patients were a median age of 48 y, 64% female, and had median of 5 prior unique ITP therapies (range, 1-15). During the DB, modified durable IWG response was observed in 42% rilzabrutinib vs 7% placebo patients (Table 1). In the OL with rilzabrutinib, 37% patients achieved modified durable IWG response (by initial DB assignment: 46% rilzabrutinib vs 22% placebo). Among patients receiving rilzabrutinib in either DB or OL periods, 57% achieved modified durable IWG response. Platelet counts were higher and more durable during the DB and OL periods for responders assigned to rilzabrutinib during DB, with some non-responding patients showing increased platelet counts in the OL.

Modified durable IWG response in rilzabrutinib-treated DB patients was higher for those receiving 1-2 (67%) relative to ≥3 prior unique ITP therapies (32%; Table 1). Prior therapy in rilzabrutinib DB patients receiving 1-2 prior unique ITP therapies included 12 (80%) patients receiving prior corticosteroids, 5 (33%) TPO-RA, 2

(13%) IVIg, 2 (13%) splenectomy, and 1 (7%) other. The 2 placebo DB durable IWG responders had ≥5 prior ITP therapies.

Overall, rilzabrutinib-treated patients showed higher modified durable response by IWG than placebo during the DB and maintained/improved responses during the OL. Higher responses were also seen in patients receiving fewer prior ITP therapies.

Table 1. LUNA3 European Patients: Modified Durable Response (≥50%) by IWG Criteria With Rilzabrutinib vs Placebo in the Double-Blind Period, Rilzabrutinib in the Open-Label Period, and Rilzabrutinib in Either Double-Blind or Open-Label Periods

	Double-Blind		Open-Label	Double-Blind or Open-Label
n/n (%)	**Rilzabrutinib**	**Placebo**	**Rilzabrutinib**	**Rilzabrutinib**
All patients	22/52 (42%)	2/29 (7%)	27/73 (37%)	26/46 (57%)
By initial double-blind treatment				
Rilzabrutinib	22/52 (42%)	N/A	21/46 (46%)	N/A
Placebo	N/A	2/29 (7%)	6/27 (22%)	N/A
By number of prior unique ITP therapies				
1-2	10/15 (67%)	0/6 (0%)	7/19 (37%)	11/13 (85%)
≥3	12/37 (32%)	2/23 (9%)*	20/54 (37%)	15/33 (45%)

*Two placebo DB responder patients had received ≥5 prior ITP therapies. N/A, not applicable.

P02

THE USE OF NEXT GENERATION SEQUENCING TO AID DIAGNOSIS AND TREATMENT IN IMMUNE THROMBOCYTOPENIA PATIENTS

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Background: Immune thrombocytopenia (ITP) is a rare autoimmune bleeding disorder characterised by low platelet counts, unpredictable bleeding and impaired quality of life. Although traditionally considered an acquired condition, increasing evidence suggests a genetic contribution. Clinical next-generation sequencing (NGS) has identified inborn errors of immunity (IEI) in ITP patients and can also detect inherited thrombocytopenia (IT) misdiagnosed as ITP. Genetic testing is available via the NHS Genomic Medicine Service R15 and R90 panels; however, evidence to guide patient selection is limited. Family history (FH) is the only consistently reported clinical predictor, while other associations remain inconsistent and underpowered. Methods: We analysed 171 patients with autoimmune cytopenia who underwent NGS using the R15 panel (n=98), R90 panel (n=37), or both (n=36). R90 testing was performed in 73 patients with chronic ITP (43 childhood-onset, 30 adult-onset). R15 testing included 134 patients (81 adult-onset, 53 childhood-onset), of whom 96% had chronic ITP. The remaining had autoimmune haemolytic anaemia or neutropenia. Associations between clinical variables (including FH, platelet nadir, mean platelet volume, Evan's syndrome and response to steroids/IVIg) and a genetic diagnosis of IT or IEI were assessed using chi-squared testing. Results: A diagnosis of IT was identified in 13.7% (n=10) genes ANKRD26, ETV6, MYH9, ITGA2B, ITGB3, VWF, and GFI1B, variants of uncertain significance (VUS) associated with IT were detected in a further 17.8%. Earlier genetic diagnosis could have prevented immunosuppressive therapy in 34.8% of patients with IT. Family history (16.7%) was the only clinical variable significantly associated with a diagnosis of IT. 4.5% (n=6) had an underlying IEI in genes RAG1, NFKB1, NLRP12, CFI, UNC13D and STXBP2, while 3.0% had a 'hot' VUS in an IEI gene, where further investigation could enable reclassification. Incidental cancer predisposition syndromes were identified in 2.2% through whole-genome sequencing, which is higher than expected in the general population. Genetic diagnosis of IEI in three adults and one child resulted in curative bone marrow transplantation. Evan's syndrome (11.9% participants) or presence of another autoimmune disease (24.6%) were not significantly associated with an IEI. Conclusion: NGS improves diagnostic accuracy in autoimmune cytopenias and can enable curative treatment in selected patients. Our findings emphasise the importance of integrated clinical genetics services, including genetic counsellors, to manage incidental findings especially cancer predisposition syndromes. Despite being the largest study to date, clinical predictors of genetic diagnoses remain limited, underscoring the need for continued sequencing to better define the genetic basis of autoimmune cytopenia.

P03

EFFECTIVENESS AND SAFETY OF AVATROMBOPAG FOR THE TREATMENT OF ADULTS WITH NEWLY DIAGNOSED, PERSISTENT, OR CHRONIC IMMUNE THROMBOCYTOPENIA: INTERIM RESULTS FROM THE PHASE 4 ADOPT STUDY

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Background

Avatrombopag (AVA), a thrombopoietin receptor agonist (TPO-RA), is approved for adults with chronic immune thrombocytopenia (ITP) who have insufficient response to prior therapy. While its efficacy and safety are established in clinical trials, real-world data remain limited. ADOPT is aphase 4, multicenter, observational study assessing AVA outcomes in clinical practice.

Aims

To report interim efficacy and safety results stratified by ITP disease phase.

Methods

ADOPT is being conducted across 9 European countries and includes adults (≥18 years) with primary ITP initiating or already receiving AVA; secondary ITP was excluded. Retrospective data were collected for up to 12 months pre-AVA treatment; prospective data were collected for up to 12 months post-enrollment. Outcomes: cumulative weeks with PC ≥30×109/L (primary endpoint) or 50×109/L (secondary endpoint) during treatment. Safety endpoints: serious adverse events (SAEs), adverse events of special interest (AESIs; eg, thromboembolic events, clinically significant bleeding), and adverse events (AEs) leading to discontinuation. Results were descriptivve and stratified by disease phase: newly diagnosed(<3 months), persistent(3 to <12 months), chronic(>12 months).

Results

As of 12 November 2024, 200 patients were enrolled (newly diagnosed, n=19; persistent, n=19; chronic, n=162); 51 (25.5%) had completed the study. Mean age at baseline 51.0-60.6 years; 55.5% female. Prior TPO-RA use: >⅔ in persistent/chronic, <⅓ in newly diagnosed. Mean weekly AVA dose ranged from 119.9 mg (chronic) to 195.6 mg (newly diagnosed) and the median cumulative dosing duration was 52.3 weeks for all

groups. Median cumulative number of weeks with PC ≥30×10⁹/L was high across groups, ranging from 49.7 (persistent) to 52.1 (newly diagnosed). A similar pattern was observed for the PC ≥50×10⁹/L cutoff. Use of concomitant ITP treatments and rescue therapy was 26.3% and 5.3%, respectively, in the newly diagnosed group; 42.1% and 21.1% in the persistent group; and 35.8% and 9.9% in the chronic group. AEs were comparably prevalent across groups and included 6 AEs resulting in AVA discontinuation and 10 AESIs, including atheroembolism, cerebral venous thrombosis, deep vein thrombosis, and pulmonary embolism. Three deaths were reported, none of which were determined to be AVA-related.

Conclusion

Interim ADOPT data suggest AVA is effective and well tolerated across ITP phases in real-world practice.

Table. Baseline patient characteristics, interim treatment characteristics, and interim effectiveness/safety outcomes.

	Newly diagnosed[a] (n=19)	Persistent[b] (n=19)	Chronic[c] (n=162)
Baseline patient characteristics			
Age, y, mean (SD)	60.6 (16.8)	51.0 (23.1)	56.4 (17.6)
Female sex, n (%)	5 (26.3)	10 (52.6)	96 (59.3)
Days from ITP diagnosis to first AVA treatment, median (IQR)	41.0 (28.0, 72.0)	209.0 (127.0, 253.0)	2853.5 (1237.0, 5289.0)
Previous treatment with TPO-RA, n (%)	6 (31.6)	13 (68.4)	109 (67.3)
Interim treatment characteristics			
Weekly AVA dose, mg, mean (SD)	195.6 (174.5)	127.6 (90.7)	119.9 (67.1)
Cumulative AVA dosing duration, weeks, median (IQR)	52.3 (52.3, 52.3)	52.3 (52.1, 52.3)	52.3 (52.1, 52.3)
Use of concomitant ITP treatments, n (%)	5 (26.3)	8 (42.1)	58 (35.8)
Use of rescue therapy, n (%)	1 (5.3)	4 (21.1)	16 (9.9)
Interim effectiveness outcomes			
Cumulative number of weeks with PC ≥30×10⁹/L, median (IQR)	52.1 (52.1, 52.1)	49.7 (22.1, 52.1)	51.1 (46.4, 52.1)
Cumulative number of weeks with PC ≥50×10⁹/L, median (IQR)	52.1 (49.0, 52.1)	44.1 (22.1, 47.1)	48.4 (42.9, 52.1)
Interim safety outcomes			
Patients with AEs, n (%)	3 (15.8)	3 (15.8)	28 (17.3)
Treatment-related AEs	0	0	11 (6.8)
AEs resulting in discontinuation	0	0	3 (1.9)
Patients with SAEs, n (%)	3 (15.8)	3 (15.8)	16 (9.9)
Deaths	2 (10.5)	0	1 (0.6)
Patients with AESIs, n (%)	0	2 (10.5)[d]	8 (4.9)[e]

AVA, avatrombopag; IQR, interquartile range; ITP, immune thrombocytopenia; IVIG, intravenous immunoglobulin; SD, standard deviation; TPO-RA, thrombopoietin receptor agonist.

[a]Less than 3 months from ITP diagnosis to first AVA treatment.

[b]Three to <12 months from ITP diagnosis to first AVA treatment.

[c]Twelve months or more from ITP diagnosis to first AVA treatment.

[d]Includes 1 report of embolism and 1 uncoded.

[e]Includes 1 report each of atheroembolism, deep vein thrombosis, thrombosis, pulmonary embolism, cerebral venous thrombosis, and uncoded.

P04

EFFECTIVENESS AND SAFETY OF AVATROMBOPAG FOR TREATMENT OF IMMUNE THROMBOCYTOPENIA IN OLDER PATIENTS AND THOSE WITH COMORBIDITIES OR PRIOR TPO-RA EXPOSURE: INTERIM RESULTS FROM THE PHASE 4 ADOPT STUDY

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Background: Avatrombopag (AVA) is a thrombopoietin receptor agonist (TPO-RA) approved for treating immune thrombocytopenia (ITP) in adults. While clinical trials have demonstrated AVA's efficacy and safety, real-world data remain limited, particularly in certain subpopulations. Patients aged ≥65 y and those with comorbidities or prior TPO-RA exposure may have increased thromboembolic events (TEEs) risk. ADOPT is an ongoing phase 4 multicenter, observational study evaluating AVA outcomes in routine clinical practice.

Aims: To report interim effectiveness and safety results from ADOPT in patients aged ≥65 y and those with comorbidities or prior TPO-RA exposure.

Methods: Adults (≥18 years) with established ITP initiating or receiving AVA were included; secondary ITP was excluded. Retrospective data covered 12 months pre-AVA; prospective data up to 12 months post-enrollment across 60 centers in 9 European countries. Primary endpoint: cumulative weeks with platelet count (PC) ≥30×109/L during AVA treatment. Secondary endpoints: weeks with PC ≥50×109/L and prevalence of serious adverse events (SAEs) and AEs of special interest (AESI; TEE or clinically significant bleeding). Analyses were descriptive by subgroups: ≥65 y, comorbidities (TEE risk factors), and prior TPO-RA exposure.

Results: As of 12 Nov 2024, 200 patients enrolled; 51 (25.5%) completed the study. Subgroup distribution: ≥65 y (n=73), comorbidities (n=89), prior TPO-RA exposure (n=128: eltrombopag [ELT], n=58; romiplostim [ROM], n=45; ELT+ROM, n=25). Mean ages 50.3 y (ELT+ROM) to 75.2 y (≥65 y); 55.5% female. Mean cumulative AVA doses 5783.3 (≥65 y) to 8126.2 mg (ELT+ROM). Median cumulative dosing duration: 52.3 weeks for all groups. Concomitant ITP therapy: ~39% (≥65-y/comorbidities) and 26.7%–56.0% (prior TPO-RA). Rescue therapies use: ≤20%. Median weeks with PC ≥30×109/L: 46.3 (ELT+ROM) to 52.1 (ELT); similar for PC ≥50×109/L. All patients with ≥8 weeks of follow-up maintained PC ≥50×109/L for ≥8 consecutive weeks. AEs: 16.0%–23.3%; SAEs 10.3%–16.9%. AESI: 6.7%–8.0% (included atheroembolism, deep vein thrombosis, pulmonary embolism, and cerebral venous thrombosis). To date, 3 non–AVA-related deaths have been reported.

Conclusion: In this interim real-world analysis AVA was effective across subgroups (≥65 y, comorbidities, prior TPO-RA) with no new safety concerns. These findings provide valuable insights for optimizing treatment strategies in diverse real-world populations.

P05

FOSTAMATINIB FOR ITP SECONDARY TO ANTIPHOSPHOLIPID SYNDROME OR CONNECTIVE TISSUE DISEASES: A RETROSPECTIVE COHORT STUDY OF 32 PATIENTS

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Background – Fostamatinib has been approved for patients with immune thrombocytopenia (ITP), but few data are available for patients with ITP secondary to connective tissue disease (CTD) such as systemic lupus erythematosus (SLE) or antiphospholipid syndrome (APS). Based on available studies, thrombotic and infectious complications seem limited in patients receiving fostamatinib, making its use attractive in secondary ITP. The aim of this study was to assess the safety and efficacy of fostamatinib in patients with ITP secondary to CTD and/or APS.

Methods – We conducted an observational, retrospective, multicenter study throughout the network of the French reference center for adult immune cytopenia including adult patients receiving treatment by fostamatinib (2022-2025) for ITP secondary to SLE, Sjogren disease (SD), systemic sclerosis (SSc), mixed CTD, and/or APS according to international criteria. Clinical and biological data were collected retrospectively through a standardized form. Complete response (CR) was defined by platelet count >100 $x10^9$/L and response (R) by platelet count 30 to 100 $x10^9$/L with at least a 2-fold increase from baseline.

Results – We included 32 patients (84% female) with ITP secondary to APS (69%) and/or SLE (47%), SD (19%), and SSc (3%). At fostamatinib introduction, median age was 57 years (range 21-86), 77% had chronic ITP (median duration of 7,8 years [range 0-41]) with a median platelet count of 27 $x10^9$/L (range 0-385).

Patients had received a median of 3.5 (range 1-7) previous therapeutic lines. Associated treatments included corticosteroids in 56% and TPO receptor agonists (TPO-RAs) in 31%. Fostamatinib was given for a median duration of 13 months (range 0,5-31) and eventually stopped in 7 patients (22%: treatment failure, n=4; adverse event, n=3). During follow-up, 1 patient had an ischemic stroke, 8 had infectious events including 1 severe colitis, 8 had mild digestive symptoms, 4 had elevated liver enzymes and 2 had moderate hypertension. At 3 months, 37,5% achieved CR and 9% R. Only 1 patient with TPO-RA at fostamatinib introduction was able to discontinue it during follow-up (10%).

Discussion – Overall, fostamatinib was safe in patients with APS and/or CTD. These retrospective data suggested that it provided clinical benefit in patients with mild disease, but did not reduce the need for TPO-RA therapy in refractory, anticoagulated APS patients, for whom alternative therapeutic options may be required.

P06

REAL-WORLD OUTCOMES OF AVATROMBOPAG AFTER PRIOR TPO-RA THERAPY IN IMMUNE THROMBOCYTOPENIA: A STUDY FROM THE SPANISH ITP GROUP (GEPTI)

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Introduction: Avatrombopag (AVA) is an oral thrombopoietin receptor agonist (TPO-RA) without food interactions and is increasingly used in immune thrombocytopenia (ITP). Evidence suggests that AVA may be effective after inadequate response or intolerance to eltrombopag (ELT) or romiplostim (ROMI). Real-world results from large cohorts remain limited.

Objective: To evaluate efficacy and safety outcomes in ITP patients who switched from ELT or ROMI to AVA in routine clinical practice.

Methods: A nationwide, multicentre, retrospective study of adult ITP patients switching from ELT/ROMI to AVA with a treatment gap ≤30 days. Effectiveness was defined as achieving platelet counts ≥50×10^9/L (PR) or ≥100×10^9/L (CR) without bleeding. Concomitant treatments, persistence on AVA and treatment-emergent adverse events (TEAEs) were recorded.

Results: Two hundred and eight patients were included. Median age at switch was 56 years (42–71) and median follow-up 62 weeks. Chronic ITP was present in 187/208 (89.9%). Switching was due to lack of efficacy in 115/208 (55.3%), convenience in 66/208 (31.7%) and TEAEs in 27/208 (13.0%). Previous treatments were ELT in 126/208 (60.6%) and ROMI in 82/208 (39.4%). Median interval between stopping ELT/ROMI and starting AVA was 1 day (0–2). Median dose to achieve response was 140 mg/week.

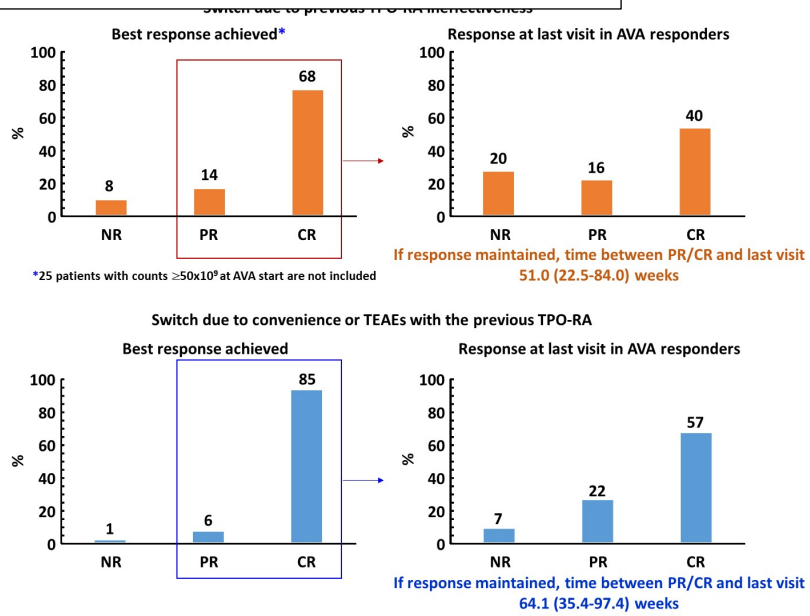
Among patients switching due to lack of efficacy, 91% achieved R and 76% achieved CR. In those switching for convenience or TEAEs, 92/93 (98.9%) achieved response, and CR was reached in 92% (Figure 1). Response was observed in 44/46 (96%) who had previously failed both ELT and ROMI. Platelet counts remained >100×10^9/L at 3, 6 and 12 months across all subgroups.

Around half of ELT/ROMI non-responders initiated AVA with concomitant treatments, and up to 55% discontinued these while on AVA. Concomitant treatment use was less common in convenience/TEAE switchers, but discontinuation rates were similar.

No TEAEs were reported in 79% of patients. AVA was discontinued due to TEAEs in 11/208 (5%), including myelofibrosis (1), gastrointestinal discomfort (1), thrombocytosis (1), progression of mesenteric venous thrombosis (1), ischaemic stroke (2), myxoma (1), follicular lymphoma (1) and headache (3).

Conclusions: AVA was effective and well tolerated in ITP patients switching from ELT or ROMI, including those previously refractory to both drugs. Responses were rapid and sustained, with many patients discontinuing concomitant therapies. Safety was favourable, supporting AVA as a suitable alternative TPO-RA in real-world ITP management.

Figure 1. Efectiveness of AVA after switching from ELT or ROMI



P07

EFFICACY AND SAFETY OF AVATROMBOPAG IN 240 PATIENTS WITH CHRONIC IMMUNE THROMBOCYTOPENIC PURPURA: RESULTS OF THE ITALIAN MULTICENTER STUDY AVA-01-CE

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Introduction: Chronic immune thrombocytopenia (ITP) is an acquired autoimmune bleeding disorder characterized by immune-mediated platelet destruction and impaired platelet production. While first-line therapy with corticosteroids and/or intravenous immunoglobulin (IVIG) is effective in most patients, a substantial proportion relapse or become refractory, requiring second-line treatments. Thrombopoietin

receptor agonists (TPO-RAs), including Avatrombopag (Ava), represent a key therapeutic option.
Aim of the Study: To evaluate the efficacy and safety of Ava in a real-world cohort of chronic ITP patients, with particular focus on outcomes according to prior exposure to other TPO-RAs.
Methods: This multicenter retrospective study included adult patients with primary ITP treated with Ava in routine clinical practice across 20 Italian centers between June 2022 and October 2024. Primary endpoints were overall response rate (ORR; platelets ≥50 × 10^9/L without rescue therapy), time to response (TTR), and duration of response (DoR). Secondary endpoints included baseline characteristics, dose modifications, need for rescue therapy, and adverse events of special interest (AESIs).
Results: A total of 240 patients were included (median age 60.5 years; 64.2% female). Patients had received a median of two prior therapies, and 55.8% had been previously exposed to another TPO-RA. Median baseline platelet count was 15 × 10^9/L. Median TTR was 14 days, and median DoR was 13.2 months. At a median follow-up of 11.5 months, 70.9% of patients remained on treatment with a median platelet count of 132 × 10^9/L. Durable response on treatment was observed in 66.7% of patients, while 9.2% were refractory, 6.2% relapsed, and 2.9% achieved sustained response off treatment (SROT). Response was significantly associated with younger age, fewer prior therapies, prior TPO-RA exposure, and baseline platelet count, whereas sex and concomitant steroid use were not. Thrombotic and bleeding events occurred in 4.6% and 7.9% of patients, respectively, leading to discontinuation in nine cases. Four malignancies (1.7%) and four deaths were recorded.
Conclusions: In this large Italian real-world cohort, Avatrombopag demonstrated high efficacy and an acceptable safety profile, including in heavily pretreated patients and those previously exposed to other TPO-RAs. Longer follow-up is warranted to further assess durability of response.

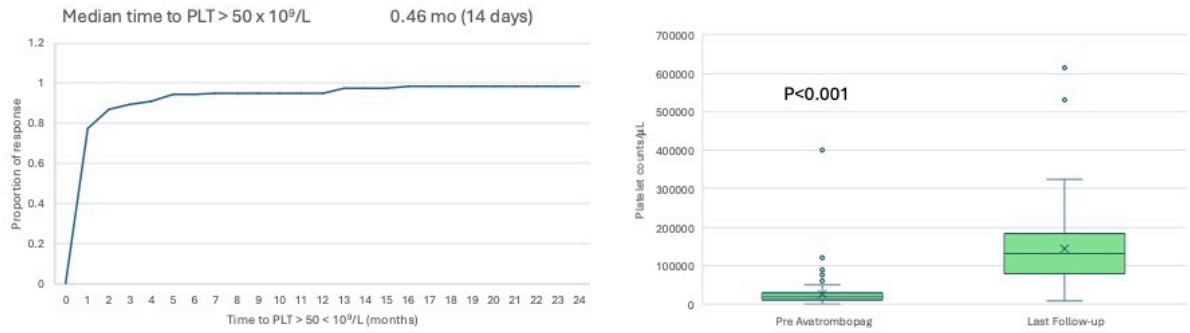

Figure 1 A and B. (A) Kaplan–Meier curve showing time to achieve platelet counts >50 × 10^9/L after starting treatment. (B) Platelet count response and treatment persistence in patients with chronic immune thrombocytopenia treated with Avatrombopag, significance was evaluated with a P-value <0.001.

P08

PLATELET TRANSCRIPTOMIC PROFILING IN IMMUNE THROMBOCYTOPENIA INDICATES COORDINATED PLATELET ACTIVATION AND REDUCED MITOCHONDRIAL GENE EXPRESSION

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In immune thrombocytopenia (ITP), platelet-intrinsic alterations and their potential contribution to ITP pathogenesis remain poorly understood. Although anucleate, platelets preserve a functional transcriptome that may reflect disease-specific alterations. However, transcriptome-wide analyses of circulating platelets in ITP are lacking. We therefore performed RNA sequencing of purified platelets to assess feasibility and characterize platelet RNA profiles in ITP.

Peripheral blood samples from 6 ITP patients (platelets 24-45/µl, without ITP-specific treatment at sampling), 6 patients with chemotherapy-induced thrombocytopenia matched for platelet count, 6 patients with ITP in treatment-free remission, and 8 healthy controls were analyzed. RNA sequencing was performed on rRNA-depleted libraries after platelet purification by dual leukocyte depletion, followed by differential expression and functional enrichment analyses.

RNA yield per platelet was increased in ITP, consistent with predominance of young, RNA-rich platelets. Active ITP samples showed marked transcriptomic differences compared with healthy controls, whereas remission samples were more similar to controls.

Functional enrichment analyses in ITP versus healthy controls showed coordinated upregulation of platelet activation-related pathways, such as vesicular trafficking, cytoskeletal remodeling, adhesion, and calcium signaling, alongside marked downregulation of mitochondrial transcripts, including respiratory chain components and mitochondrial tRNAs. At the transcriptional level, this pattern is consistent with an activation-primed state with altered mitochondrial integrity, and resembles features described in procoagulant platelets.

To assess disease specificity, platelets from patients with post-chemotherapy thrombocytopenia during marrow recovery were analyzed as a comparator. While both conditions shared transcriptional features, platelet activation pathways showed more prominent and coordinated enrichment in ITP, with additional immune-related signatures, suggesting disease-specific changes.

Our study demonstrates that platelet transcriptome profiling is feasible in ITP despite low platelet counts, enabling detailed molecular characterization in this challenging context. While limited by cohort size and lack of functional validation, the observed transcriptional changes may affect platelet function in vivo and contribute to disease-specific characteristics of ITP.

P09

A MULTICENTER, RANDOMIZED, OPEN-LABEL STUDY OF DEXAMETHASONE VERSUS ROMIPLOSTIM PLUS DEXAMETHASONE AS FIRST LINE TREATMENT IN PATIENTS WITH NEWLY DIAGNOSED IMMUNE THROMBOCYTOPENIA: INTERIM RESULTS OF RODEX STUDY

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Background:
Corticosteroids remain the standard first-line treatment for immune thrombocytopenia (ITP), yet less than 40% of patients achieve a sustained response off treatment for 6 months (SROT). Prior reports in difficult-to-treat ITP have suggested that combining immunosuppressive agents with thrombopoietin receptor agonists may yield response rates. However, no data are available on SROT outcomes using this approach as first line treatment. We present first interim analysis from RODEX study.
Methods:
RODEX (ClinicalTrials.gov NCT05723326) is a randomized (1:1), open-label, phase 3 trial comparing dexamethasone (DEX) to dexamethasone plus romiplostim (ROM+DEX) as first line treatment in adults (≥18

years) with newly diagnosed primary ITP and platelet count <30×10^9/L. Patients received dexamethasone as monotherapy 40mg/day for 4 days up to 3 cycles either a single cycle dexamethasone followed by weekly subcutaneous romiplostim. Primary endpoint is SROT and secondary endpoints include early response, relapse rate, safety (CTCAE v4.03), and quality of life (SF-36 v2, FACIT-F, ITP-PAC). Cost-effectiveness and healthcare resource utilization are also being assessed.

Results:

Between December 2022 and April 2025, a total of 124 were randomized: 63 to DEX and 61 to ROM+DEX. Patient characteristics are described in table 1. Early platelet response (≥50×10^9/L at 4 weeks) was 69.9% DEX and 70% ROM+DEX (p>0.05). Among evaluable responders, SROT at 6 months and platelet>50x109/L was 30.2% DEX vs 59.9% ROM+DEX (p=0.018) and SROT at 12 months platelet>50x109/L 29.3% DEX vs 40.5% ROM+DEX, still no able to be compared. In DEX arm, patients received a mean of 3 dexamethasone cycles. In ROM+DEX arm median Rom treatment duration was 14.5 weeks (range 2-37) and maximal dose used 3.5mcg/kg (3-5). Treatment failure was higher in DEX arm 23.8% vs 6.3% in ROM+DEX (p=0.038).

Although detailed SAE rates are pending, Interim data suggest better tolerance in the ROM+DEX group with less dexamethasone AE related (DEX 39.7% vs ROM+DEX, 16.7%, p=0.018). There was no difference in thrombosis, bleedings or death rates.

Conclusion:

These interim results suggest that ROM+DEX SROT and reduces treatment failure and SROT compared to DEX as monotherapy as first line treatment in newly diagnosed ITP. The combination regimen appears safe and better tolerated, potentially due to reduced corticosteroid exposure.

Table 1. Patient characteristics

Patient characteristics	ROM+DEX N=61	DEX alone N=63	p
Age (years), mean (SD)	52.1 (18.2)	52.1 (17.8)	1.000
Females, n (%)	33 (55.0%)	35 (55.6%)	0.951
Caucasian, n (%)	56 (93.3%)	52 (82.5%)	0.244
Clinical data			
Time from ITP diagnosis to inclusion (days), median (IQR)	0.0 (-0.1,0.0)	0.0 (-0.1,0.0)	0.787
WHO bleeding assessment at diagnosis, n (%)			0.525
Grade 0	22 (37.3%)	30 (47.6%)	
Grade 1	27 (45.8%)	25 (39.7%)	
Grade 2	9 (15.3%)	8 (12.7%)	
Grade 3	1 (1.7%)	0 (0.0%)	
Platelet at diagnosis, mean (SD)	10.6 (9.8)	12.1 (10.0)	0.226
Underlying diseases, n (%)			
Cardiovascular disease	10 (16.9%)	9 (14.3%)	0.685
Diabetes	9 (15.3%)	6 (9.5%)	0.335
Psychiatric disorder	2 (3.4%)	2 (3.2%)	1.000
Active hepatic disease	0 (0.0%)	1 (1.6%)	
Renal insufficiency	0 (0.0%)	0 (0.0%)	-
Chronic obstructive pulmonary disease	0 (0.0%)	0 (0.0%)	-

SD: Standard Deviation; IQR: Interquartile Range

P10

COULD THE GUT MICORBIOME BE THE KEY TO BETTER TREATMENT IN ITP?

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Immune thrombocytopenia (ITP) is a rare autoimmune disorder characterised by immune-mediated platelet destruction and impaired platelet production, leading to thrombocytopenia and an increased risk of bleeding, fatigue, and cognitive impairment. Bleeding manifestations range from minor mucocutaneous bleeding to life-threatening haemorrhage. Although the pathogenesis of ITP is incompletely understood, immune dysregulation plays a central role. The gut microbiome has been implicated in the development and modulation of several autoimmune diseases; however, its role in ITP has not been systematically explored. Anecdotal reports from patients suggest that interventions such as antibiotics, probiotics, or fasting may influence platelet counts, supporting a potential microbiome-immune interaction in this condition.

We conducted a case-control study to compare gut microbiome profiles between patients with ITP and healthy controls and to explore associations between microbiome composition and disease characteristics. Eighteen patients with ITP (nadir platelet count ≤30 × 10^9/L) were recruited from Hammersmith Hospital, along with four related healthy controls. An additional forty unrelated healthy controls were included from an independent cohort. Stool samples were analysed using 16S rRNA gene sequencing and quantitative PCR to assess microbiome composition and diversity.

The demographics and clinical characteristics of the population studied are presented in Table 1. ITP patients had significantly reduced gut microbiome diversity compared to healthy controls ($p = 1.16 \times 10^{-12}$). Patients with lower platelet counts or longer disease duration exhibited the lowest microbiome diversity ($p = 0.04$ and $p = 0.04$, respectively). In a patient engagement event involving 13 participants, the majority of patients reported willingness to try microbiome-targeted therapies, with 92% open to probiotics or prebiotics and 58% open to faecal microbiota transplantation (FMT).

These findings suggest that gut microbiome disturbances are associated with ITP, particularly in severe or long-standing disease. Further studies are warranted to determine causality and to evaluate microbiome-targeted therapies as potential novel treatment strategies. High levels of patient engagement support the feasibility of future interventional studies.

Table 1: Demographics and clinical characteristics of the population studied

	Patients (N=18) Median (range)	Related controls (N=4) Median (range)	All controls (N= 40) Median (range)
Age, years	43 (19,65)	33.5 (24.5, 44)	34 (21, 56)
Female, n (%)	13 (72)	2 (50)	22 (55)
Ethnicity, n (%)			
Asian or Asian British	4 (22)	2 (50)	19 (47.5)
Black, Black British, Caribbean or African	1 (5.5)	0	0
Mixed or multiple ethnic groups	3 (17)	0	0
Other ethnic group	0	0	2 (5)
White	10 (55.5)	2 (50)	19 (47.5)

	Patients (N=18) Median (range)
Age at the time of ITP diagnosis, years	25 (7,61)
Duration of disease, months	126 (4,572)
Nadir platelet count, x 10^9/L	2 (0,13)
Number of ITP treatment types received	3 (1,18)
Platelet count at the time of study visit, x 10^9/L	115 (2,366)
Patients receiving ITP treatment at the time of study visit, n (%)	13 (72)

5.

P11

ANALYSIS OF THE CLINICAL PROFILE AND THERAPEUTIC STRATEGIES OF THE UK SECONARY AND ALTERNATIVE PAEDIATRIC ITP REGISTRY

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Introduction: The UK Childhood ITP Registry (UKCITP) opened to recruitment in January 2007 and closed in January 2024 with final data entry in March 2024. This analysis describes the patient (pt), and disease characteristics of UK children diagnosed with secondary ITP or having had an alternative cause identified.

Methods: Pt were included if they were classified as having secondary ITP, if they had platelet count >100 x 109/L (plt) at diagnosis or an alternative cause of thrombocytopenia was identified.

Results: 2242 pts were classified as primary ITP or plt >100 at diagnosis. 29 cases were classified as secondary ITP or an alternative cause of ITP.

Age at presentation peaked at 2-5y. The male-to-female ratio (M:F) at diagnosis showed a bi-modal pattern, with female predominance in the <2y (0.25:1) and 6-11y (0.75:1) group

Pt were discharged from follow up once counts remained >150. Mean follow up (FU) for documented plt counts was 22.7 months (mo). At presentation, 21 pt (72%) had plt <20 x 109/L. 72% had plt<150 at 6mo and 31% at 12mo.

11 pt (38%) received first-line therapy at diagnosis, all with intravenous immunoglobulin (IVIg). Nine pt (31%) received a single course of first-line therapy and 2 (7%) required multiple courses. Rescue therapy was given to 9 pt (31%), mostly corticosteroids; 5 pt received a single course while 4 required ≥3. Second-line therapy was required in 3 pt (10%)No patients underwent splenectomy.

Bone marrow aspiration was performed in 59%, at a median of 115 days from diagnosis. Cytogenetic patients were performed in 5 pt: 4 (80%) had normal findings and 1 tested positive for Falconi anaemia. 12 pt were tested for ANA, 14% were positive.

Conclusion: When compared with our previous analysis of the UKCITP primary cohort, age of presentation was highest in the <2y cohort, suggesting that immune immaturity may contribute to disease manifestation. Both cohorts demonstrated comparable disease severity at presentation. Whereas a clearly defined switch

from male to female predominance, occurred in the primary cohort at age 6-11y, no such pattern existed for the secondary cohort.
Our data suggests that standardisation of investigations for ITP patients is critical to identify secondary ITP which may need a different treatment approach.

Secondary Causes of ITP	**Alternative Causes of ITP**
Evans Syndrome	Acute Myeloid Leukaemia
Inflammatory Bowel Disease	Myelodysplastia
Immunodeficiency	Bone Marrow Failure

Table 1: Secondary and Alternative Causes of ITP

P12

EFFICACY AND SAFETY OF PIRTOBRUTINIB IN ADULTS WITH ITP - A PHASE 1/2 DOSE-FINDING STUDY IN PROGRESS

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Introduction: Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by reduced platelet counts and increased risk of bleeding. Pirtobrutinib, a highly selective, non-covalent, reversible Bruton tyrosine kinase (BTK) inhibitor, may offer advantages for patients with ITP due to its optimized pharmacokinetic properties, once-daily dosing, and specificity for BTK. Preclinical ITP models show pirtobrutinib effectively reduces B-cell activity and autoantibody production. This phase 1/2 study aims to optimize the dosing of pirtobrutinib in adults pre-treated for primary ITP.

Methods: This study consists of 2 parts: phase 1 dose escalation and phase 2 dose optimization. Phase 1 is an open-label portion where dose escalation will be driven by the BOIN method.~ 9-18 participants will be enrolled into sequential dose levels, starting at the lowest dose of oral pirtobrutinib, once daily for 12 weeks. The primary objective is to assess the safety and tolerability of pirtobrutinib and select doses for phase 2. Secondary objectives will assess the efficacy by platelet response rate, the extent of disease control, and describe the PK of pirtobrutinib. Phase 2 is a randomized double-blind dose optimization design where ~ 10 participants will be randomized to evaluate ≥2 dose levels of pirtobrutinib versus placebo. Patients will be treated for 12 weeks to assess the stability of response. The primary objective is to assess the efficacy of pirtobrutinib versus placebo, by stable platelet response rate (platelet count ≥50 k/µL on ≥ 4 of 6 consecutive biweekly visits between weeks 14-24, without rescue therapy and prohibited concomitant medications affecting efficacy). Secondary objectives will evaluate the safety, PK, and additional efficacy endpoints of pirtobrutinib. Patients aged ≥18 with confirmed diagnosis of primary ITP for ≥3 months prior to enrollment, and history of response to ≥1 prior line of therapy are eligible. Exclusion criteria include treatment other than corticosteroids or TPO-RA for ITP within 2 weeks of visit 1, use of anticoagulants or antiplatelet therapy, history of any thrombotic or embolic event within 12 months before screening, hematologic malignancy, and significant cardiovascular disease.

Results: This study is a Trial in Progress, and enrollment is ongoing.

P13

REAL-WORLD SAFETY AND EFFICACY OF AVATROMBOPAG IN ADULTS WITH IMMUNE THROMBOCYTOPENIA: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

Abstract 4

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Background

Immune thrombocytopenia (ITP) is associated with bleeding risk and a clinically relevant incidence of thromboembolic events (TEEs). Concerns regarding vascular safety persist with thrombopoietin receptor agonists (TPO-RAs). Avatrombopag (AVA), a second-generation oral TPO-RA, is increasingly used in clinical practice;

however, comprehensive real-world data on its efficacy and safety remain limited. This systematic review and meta-analysis aimed to evaluate AVA exclusively in routine clinical settings.

Methods

Following PRISMA 2020 guidelines, retrospective and prospective observational studies published since 2020 reporting AVA use in adults with ITP were analyzed. Primary endpoints were TEEs and platelet response—complete response (CR:

$\geq 100\times10^9$/L) and response ($\geq 50\times10^9$/L)—in the absence of rescue therapy.

Secondary endpoints included time to response, treatment discontinuation, and adverse events (AEs). Random-effects models were applied.

Results

Fifteen studies met inclusion criteria. The pooled incidence of thromboembolic events was 2.82% (95% CI: 1.61–4.27; n=763) (Fig. 1A), corresponding to 3.29 events per 100 patient-years. Overall response (platelet count > 50 x 109/L in the absence of rescue therapy) was achieved in 91.99% of patients (95% CI: 89.25–94.41; n=679) (Fig. 1B). Complete response (platelet count > 100 x 109/L in the

absence of rescue therapy) occurred in 80.03% of patients (95% CI: 72.94–86.35; n=425). Median time to platelet response was 11.1 days (n=495). Treatment

discontinuation occurred in 18.86% of patients (n=1,054), and avatrombopag-related adverse events were infrequent (4.05%; 4.56 per 100 patient-years; n=557).

Conclusions

Real-world evidence confirms the high efficacy and favorable safety profile of avatrombopag in adult ITP, with rapid platelet recovery and a low incidence of thrombotic events. These findings support its use as an effective and well-

tolerated option in routine clinical practice.

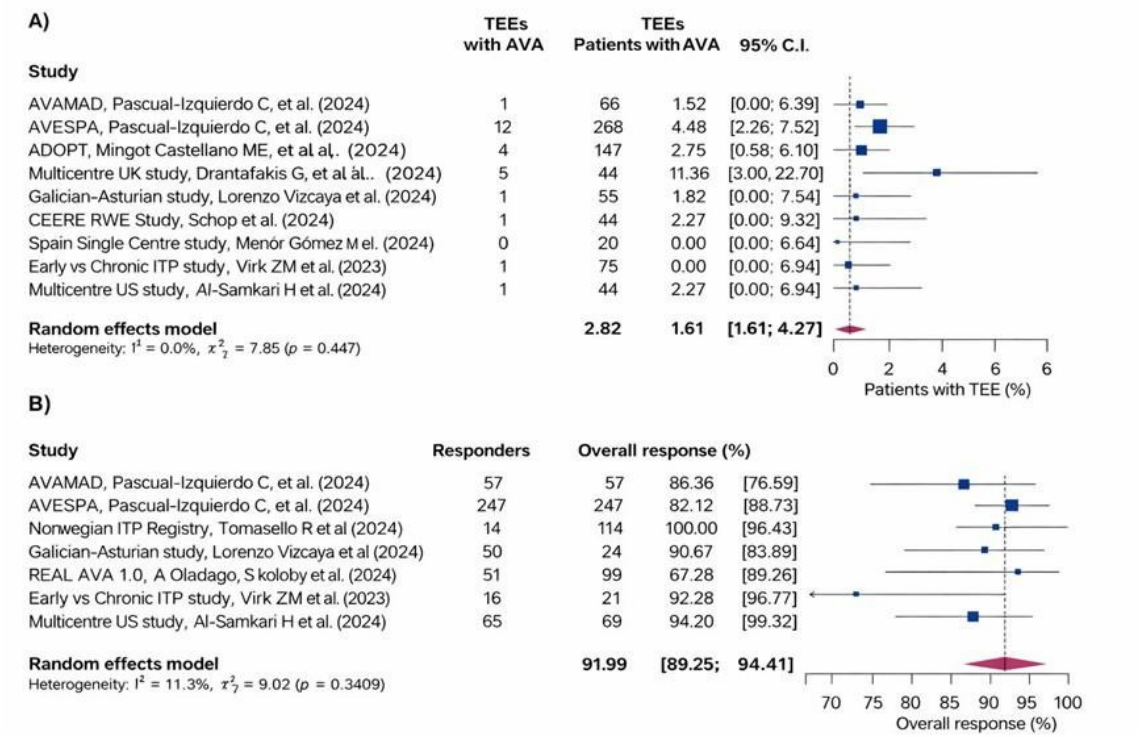

Figure 1. Safety and efficacy outcomes of avatrombopag in adult immune thrombocytopenia
(A) Pooled proportion of patients experiencing thromboembolic events during avatrombopag treatment.
(B) Pooled proportion of patients achieving an overall response (platelet count ≥50 × 10^9/L) in the absence of rescue therapy.
Abbreviations: AVA, avatrombopag; CI, confidence interval; ITP, immune thrombocytopenia; TEE, thromboembolic event.

P14

AVATROMBOPAG IN TPO-RA–NAIVE ADULTS IN ACUTE, PERSISTENT, AND CHRONIC PHASES OF ITP: RESULTS FROM THE REAL-AVA 3.0 RETROSPECTIVE STUDY

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Introduction: Avatrombopag (AVA) is a thrombopoietin receptor agonist (TPO-RA) approved for the treatment (tx) of immune thrombocytopenia (ITP). Real-world (RW) evidence on AVA is limited in patients (pts) with TPO-RA–naive ITP. We describe RW tx patterns and clinical outcomes in TPO-RA–naive pts receiving AVA in the US.

Methods: This is a retrospective chart review of TPO-RA–naive adults with primary ITP who initiated AVA on/after 1 Jul 2019, with ≥6 mo of follow-up after AVA initiation. Pts were followed from AVA initiation until the earliest of last contact, death, or study end (20 Jan 2025). Response was defined as achieving a meaningful platelet count (PC) (response thresholds: ≥30×109/L, ≥50×109/L, and ≥100×109/L) at least once in the absence of rescue tx. Among responders, response durability was defined as the percent of time on AVA with a PC above the response threshold.

Results: Of 200 pts treated with AVA, 33.5% (n=67) had chronic ITP and 66.5% had acute (n=61) or persistent (n=72) ITP. The majority of pts were female (59.5%). The mean (SD) age was 57.5 (15.0) years. Demographics were similar between pts with chronic ITP and pts with acute/persistent ITP. The median AVA tx duration was 9.1 mo for pts with chronic ITP and 7.7 mo for acute/persistent ITP. Few pts required concomitant or rescue tx while on AVA; among pts who received concomitant steroids/immunosuppressants, all reduced or discontinued use of ≥1 of these concomitant medications (Table 1). Response rates and durability of response were high across groups (Table 1). PCs ≥50×109/L were achieved in 93.8% of pts with baseline PC <50×109/L with chronic ITP and 95.5% with acute/persistent ITP, with median response durability of 88.3% and 88.4%, respectively. PCs ≥30×109/L were achieved in ≥98% of pts with baseline PC <30×109/L in each group with median response durability ≥93%. At last follow-up, >70% of pts remained on tx with AVA. The AVA discontinuation rate was 25.5% (chronic ITP: 20.9%; acute/persistent ITP: 27.8%). The most common reasons for discontinuing AVA were achieving target PC, lack of efficacy, and pt preference (Table 1). Among pts who discontinued AVA, 19.6% (57.1% with chronic ITP and 5.4% with acute/persistent ITP) had subsequent ITP tx. Of these pts, 12.5% with chronic ITP and none with acute/persistent ITP discontinued tx.

Conclusions: In the RW setting, AVA yielded a high rate of sustained platelet response in TPO-RA–naive pts with chronic or acute/persistent ITP.

Table 1. Clinical characteristics, treatment patterns, and clinical outcomes with AVA by phase of ITP

	Patients with chronic ITP (n=67)	Patients with acute or persistent ITP (n=133)
Clinical characteristics		
PC closest to but prior to index initiation, %		
<30×10^9/L	83.6	84.2
≥30×10^9/L to <50×10^9/L	13.4	15.0
≥50×10^9/L to <100×10^9/L	3.0	0
≥100×10^9/L	0	0.8
Treatment patterns		
ITP treatments prior to AVA,[a] %		
Corticosteroids	95.5	92.5
Immunoglobulins	47.8	45.9
Rituximab	38.8	21.1
Splenectomy	11.9	0.8
Concomitant ITP medication while on AVA,[b] %		
Corticosteroids	3.0	8.3
Immunoglobulins	1.5	1.5
Reduced/discontinued ≥1 concomitant steroid/immunosuppressant while on AVA,[c] %	100	100
Rescue therapy use while on AVA,[d] %	7.5	9.0
Median duration of AVA treatment, months (IQR)	9.1 (6.8–11.8)	7.7 (6.2–10.3)
Discontinued AVA treatment, %	20.9	27.8
Reason for discontinuing AVA,[e] %		
Achieved target PC	6.0	16.5
Lack of efficacy	9.0	1.5
Patient preference	3.0	4.5
Splenectomy	0	3.8
Death	0	3.0
Financial factors	4.5	0.8
Received other ITP therapy after AVA discontinuation,[f] n/n (%)	8/14 (57.1)	2/37 (5.4)
Clinical outcomes		
Platelet response, among patients below that threshold at baseline, n/N (%)		
PC ≥30×10^9/L	56/56 (100.0)	110/112 (98.2)
PC ≥50×10^9/L	61/65 (93.8)	126/132 (95.5)
PC ≥100×10^9/L	50/67 (74.6)	100/132 (75.8)
Median response durability,[g] %		
PC ≥30×10^9/L	93.5	93.1
PC ≥50×10^9/L	88.3	88.4
PC ≥100×10^9/L	68.5	71.1

[a]Treatments in ≥10% of patients in either group. [b]Concomitant medications administered in >1 patient in either group. [c]Among patients who received ≥1 concomitant steroid/immunosuppressant during AVA therapy; 2 patients with chronic ITP and 11 patients with acute/persistent ITP received ≥1 concomitant steroid/immunosuppressant during AVA therapy. [d]Concomitant ITP-related medication given during AVA treatment to manage acute worsening of thrombocytopenia or bleeding. [e]Reasons reported by >2 patients in either group; patients may have had ≥1 reasons for discontinuation. [f]Among patients who discontinued AVA treatment; 14 patients with chronic ITP and 37 patients with acute/persistent ITP discontinued AVA treatment. [g]Response durability is the percent of time on AVA with a PC above the prespecified thresholds in the absence of rescue therapy.

AVA, avatrombopag; IQR, interquartile range; ITP, immune thrombocytopenia; PC, platelet count.

P15

DEVELOPMENT OF THE ITP CONTROL TOOL (ITP-CT): A PATIENT-REPORTED OUTCOME MEASURE INTEGRATING CLINICAL AND PATIENT PERSPECTIVES ON DISEASE CONTROL.

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Background: Immune thrombocytopenia (ITP) is a rare autoimmune disorder driven by complex immune dysregulation leading to low platelet counts, increased bleeding risk, and substantial physical, psychosocial, and quality-of-life burdens. The lack of a framework to holistically assess patient-perceived disease control remains a barrier to patient-centered care in ITP. We report stage I of the ITP control tool (ITP-CT) development, which aims to define ITP control through panel discussions incorporating clinical and patient perspectives.

Methods: Four expert ITP clinicians and four ITP patient representatives from patient advocacy groups convened as an expert panel to define the dimensions of “ITP control”. Experts completed a pre-meeting survey to identify relevant variables. Each expert attended one of three virtual meetings consisting of presentations, structured discussions, and feedback rounds. Following panel meetings, an ITP-CT draft was developed and refined according to post-panel surveys.

Results: Over 50% of survey respondents rated multiple bleeding events and psychosocial impacts as highly important to defining ITP control. Clinicians considered treatment side effects extremely important, while patient representatives rated them moderately important. All respondents considered emergency room visits extremely important. Panel discussions highlighted the importance of low/fluctuating platelet counts, frequent/prolonged bleeding events (nosebleeds, menstrual bleeding, blisters, bruising), physical fatigue

and emotional impacts such as anxiety or sadness. Broader impacts on work, social activities and the need for emergency interventions were also emphasized. Patient representatives emphasized the significance of physical fatigue and cognitive impacts, while clinicians prioritized bleeding and side effects. These insights informed 8 variables for the ITP-CT: 1) bleeding/bruising, 2) physical fatigue, 3) brain fog/difficulty concentrating, 4) platelet count experience, 5) emotional well-being, 6) daily activities, 7) social interactions and 8) emergency care. Items were drafted with variations in frequency, severity, and bother, using a 4-week recall period. The ITP-CT draft was refined via post-panel survey feedback and validated through Stage II patient interviews.

Conclusions: Stage I of ITP-CT development established a framework grounded in clinical priorities and patient-lived experience, strengthening the foundation for patient-centered ITP care.

P16

ANTIBODY-MEDIATED PLATELET APOPTOSIS IN ITP INVOLVES FCγRIIA-DEPENDENT AND FCγRIIA-INDEPENDENT SIGNALING PATHWAYS

Abstract 29

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Platelet apoptosis contributes to platelet destruction in immune thrombocytopenia (ITP). However, the precise signaling pathways involved remain incompletely characterized. This study aims to elucidate the signaling pathways involved in antibody-mediated platelet destruction by employing monoclonal antibodies (mAbs) and autoantibodies (AAbs) targeting glycoprotein (GP) Ib/IX or GPIIb/IIIa complexes. Washed human platelets were used to evaluate antibody-induced apoptosis. Apoptosis was assessed via flow cytometry by identifying P-selectin negativity (CD62P−), phosphatidylserine exposure (Annexin V+), and alterations in mitochondrial membrane potential (TMRE−). Initially, 13 distinct mAbs targeting GPIb/IX or GPIIb/IIIa were screened to identify mAbs capable of inducing platelet apoptosis. Concurrently, sera from ITP patients harboring GP-specific AAbs were evaluated for their capacity to induce platelet apoptosis. To investigate the signaling pathways involved, platelets were pretreated with FcγRIIA blocking mAb (IV.3) followed by assessment of apoptosis. In the screening study, 4 of 13 mAbs were identified to induce platelet apoptosis. Among ITP patient sera, 3 of 8 (37.5%) with anti-GPIb/IX antibodie, 18 of 28 (64.3%) with anti-GPIIb/IIIa antibodies and 22 of 34 (64.7%) with both antibodies induced apoptosis in washed platelets. Blockade of platelet FcγRIIA effectively inhibited apoptosis induced by antibodies against GPIIb/IIIa but had no inhibitory effect on apoptosis induced by antibodies against GPIb/IX. Platelet destruction triggered by anti-GPIb/IX and anti-GPIIb/IIIa antibodies involves distinct signaling pathways. Elucidating these divergent pathways may facilitate the development of targeted therapeutic strategies for ITP.

P17

CLINICAL CHARACTERISTICS, TREATMENT STRATEGIES, AND RESPONSE PATTERNS IN EVANS SYNDROME

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Introduction:

Evans syndrome (ES) is a rare autoimmune disorder characterized by the simultaneous or sequential occurrence of immune thrombocytopenia (ITP), autoimmune hemolytic anemia (AIHA) and/or autoimmune neutropenia (AIN). Evidence-based guidelines remain limited, particularly in adult populations.

Objective:

To describe the clinical features and treatment outcomes in a Spanish cohort of patients with ES enrolled in RESTI (Spanish Registry of ITP).

Methods:

Retrospective multicenter study based on RESTI. We included patients with ES, defined by the coexistence (simultaneous or sequential within 10 years) of ITP and AIHA and/or AIN based on established international criteria. Data on demographics, clinical presentation, treatments, and responses were collected using a standardized form.

Results:

A total of 76 patients were included, with a median age of 27 years (IQR: 10–54.5), 45.3% female. Thirty-three patients were younger than 18 years old (median age 10 years, IQR: 4.5–12.5). AIHA was present in 71%, and AIN in 36%. Median follow-up was 306 weeks (IQR: 128–575). All patients received steroids as first-line therapy. Median time to response in ITP was 9 days, 14 days in AIHA and AIN in a median of 3 days. For ITP, response rates were 60.3% (CR 75%), AIHA 80% (84% CR) and neutropenia 76%.

Second-line treatments included rituximab in 14 patients (375 mg/m²/week; four cycles). Among them, ITP responses included 40% CR, 20% R. In WAIHA, 50% achieved CR. Among two patients with neutropenia,

one responded. Mycophenolate was used in a total of 22 patients, all of them pediatric, with response rates of 54% in ITP and 43% in AIHA. The median time to response was 28 days (IQR: 18.5–70) in ITP and 65 days (IQR: 26.2–189) in AIHA.

Fostamatinib was used in 9 adult patients with concurrent ITP and AIHA. Median baseline platelets were 13 $\times 10^9$/L and hemoglobin 9.5 g/dL. All patients were on concomitant therapy. Median time to ITP response was 14 days (IQR:6-25.5) with a response rate of 78%. Median time to response for AIHA was 54 days (IQR: 22-292) with a response rate of 44%.

Thrombopoietin receptor agonists (TPO-RAs) showed no efficacy in AIHA (5 patients).

Conclusion:

Corticosteroids remain a cornerstone of therapy. Rituximab and Mycophenolate demonstrated moderate efficacy across lineages, while fostamatinib showed rapid, durable responses in both ITP and AIHA. The lack of response to TPO-RAs in AIHA underscores the need for lineage-specific therapeutic strategies.

P18

ONE-YEAR EFFICACY AND SAFETY OF AVATROMBOPAG FOR CHRONIC IMMUNE THROMBOCYTOPENIA IN JAPANESE ADULTS

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Avatrombopag (AVA) is a thrombopoietin receptor agonist approved in the US and EU for treating adults with chronic immune thrombocytopenia (ITP). We report results from the open-label extension (OLE) of a phase 3 trial evaluating the efficacy and safety of AVA in Japanese patients. Adults with chronic ITP and prior insufficient treatment response were enrolled in the 26-week core phase at a starting dose of AVA 20 mg daily; dosing was adjusted during the trial to maintain a platelet count (PC) of ≥50x109–<200x109/L. Patients completing the core phase continued to the OLE. Efficacy and safety data were collected through 1 year, including PCs, treatment-emergent adverse events (TEAEs), and adverse events of special interest (AESIs; thromboembolic or bleeding events). Of 19 enrolled patients, 15 completed the core phase and entered the OLE; as of 31 July 2024, 3 (20%) had discontinued and 12 were ongoing, with a mean AVA exposure duration of 61.9 weeks. Median PCs remained in the target range throughout the trial; 60% of patients did not require rescue therapy in the extension phase by the data cutoff. TEAEs were reported for 19 (100%) patients during the trial, including 4 AVA-related AEs and 3 AEs leading to AVA withdrawal. One serious AESI (heavy menstrual bleeding) and 2 nonserious AESIs (peripheral arterial occlusive disease and AVA-related cerebrovascular accident in the same patient) occurred. No deaths have been reported. Results of this ongoing OLE trial show that AVA is efficacious and well tolerated up to 1 year, confirming previously reported core-phase results.

P19

DETECTION OF PLATELET-SPECIFIC PATIENT ANTIBODIES USING HUMAN IPSC-DERIVED MEGAKARYOCYTES

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Platelet-specific antibodies play a central role in the pathophysiology of immune thrombocytopenia (ITP) and fetal-neonatal alloimmune thrombocytopenia (FNAIT), yet their reliable detection remains a diagnostic challenge. Current gold-standard assays rely on fresh donor cells, posing difficulties in availability and standardization across laboratories. This study evaluates the feasibility of using induced pluripotent stem cell (iPSC)-derived megakaryocytes as a scalable and standardized alternative for detecting platelet antibodies in a modified monoclonal antibody-specific immobilization of platelet antigens (MAIPA) assay. Human iPSCs were differentiated into megakaryocytes in vitro using stirred bioreactors, with confirmed expression of key glycoproteins (GPIIb/IIIa, GPIb/IX, GPIa) by flow cytometry. Performance was tested using the WHO reference reagent for human platelet antigen (HPA)-1a and 12 clinical samples containing well-characterized alloantibodies targeting HPA-1a, HPA-1b, HPA-3a, HPA-3b, and HPA-5b. Additional experiments assessed binding of autoantibodies from ITP patients. The WHO anti-HPA-1a reference showed comparable binding between donor platelets and iPSC-derived megakaryocytes with strong correlation (r equals 0.94) in optical density (OD) values. Alloantibodies against HPA-1a, HPA-1b, and HPA-3b were reliably detected, while anti-HPA-3a and anti-HPA-5b showed lower OD values compared to standard MAIPA. Both alloantibodies from FNAIT patients and autoantibodies from ITP patients demonstrated specific binding to iPSC-derived megakaryocytes in flow cytometry. iPSC-derived megakaryocytes represent a promising standardized source for platelet antibody detection in both FNAIT and ITP diagnostics, though sensitivity for certain HPA systems may require optimization through genetic modification to enhance glycoprotein expression or antigen presentation.

P20

CAN MACHINE LEARNING PREDICT INHERITED CAUSES OF THROMBOCYTOPENIA? A FEASIBILITY STUDY

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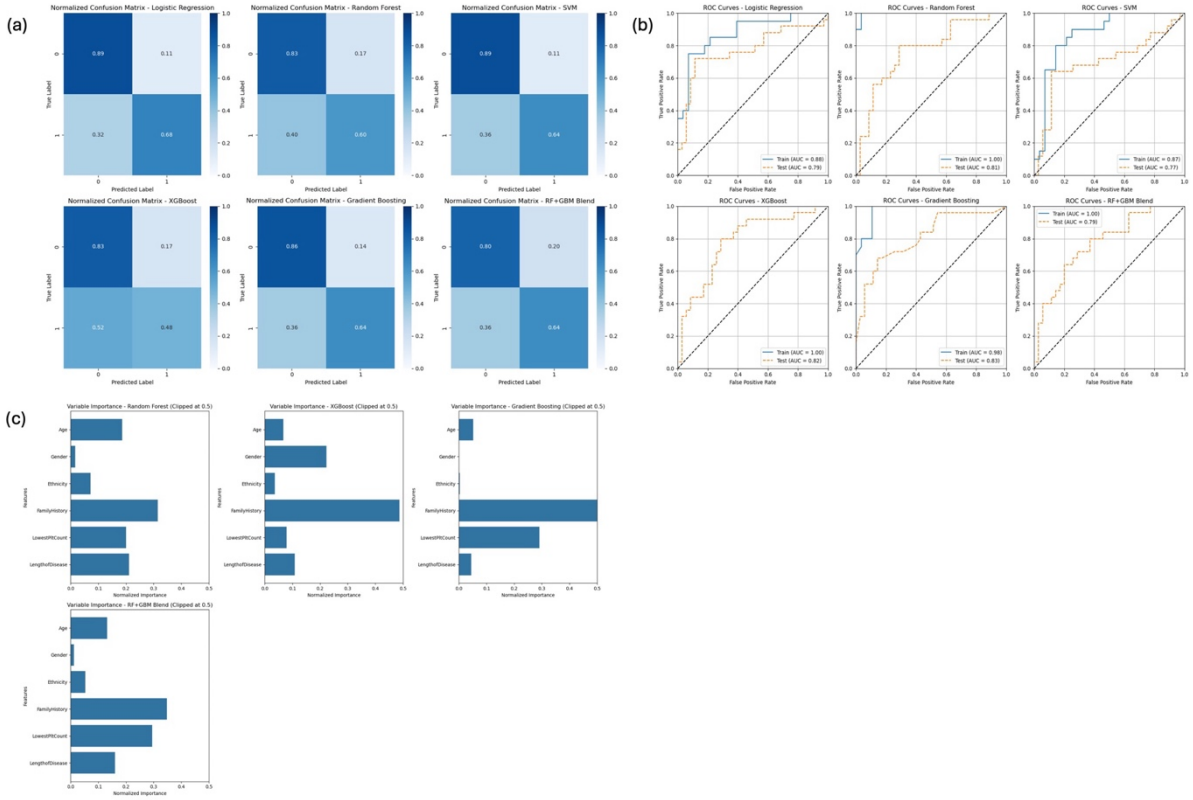
Background: Inherited thrombocytopenias are Mendelian platelet disorders that can be misclassified as immune thrombocytopenia which potentially exposes patients to ineffective immunosuppression. The NHS England R90 Bleeding & Platelet Disorders gene panel provides a diagnosis tool for inherited thrombocytopenias. The R90.1 consists of whole exome sequencing or medium panel and R90.2 consists of F5, F11, MYH9, ENG, ACVRL1, F7, F8, F9, F10, VWF, MLPA or equivalent. In our prior R90 evaluation, longer disease duration, family history and higher platelet nadir were associated with a genetic yield. We hypothesised that machine learning (ML) could improve upon traditional clinical criteria to optimise selection for genetic testing.

Methods: We used the dataset from of our previously reported R90 service evaluation. Sixty adults and children tested from Jan 2023 - Dec 2024 were analysed. Predictors were age, sex, ethnicity, family history of thrombocytopenia, platelet count nadir and duration of thrombocytopenia. The outcome was positive genetic yield. Six ML models (logistic regression [LR], random forest [RF], support vector machine [SVM], gradient boosting [GBM], XGBoost, and a RF+GBM blend) were trained using repeated stratified five-fold cross-validation with grid-search hyperparameter tuning to maximise mean AUC. Out-of-fold predictions were used to estimate accuracy, sensitivity and specificity. Calibration was assessed with decile plots.

Results: Twenty-five of 60 patients had a positive genetic yield (41.7%). All models discriminated inherited from non-inherited cases (Figure 1a). GBM achieved the highest AUC (0.83), followed by XGBoost (0.82) and RF (0.81). LR and the blended model achieved AUC of 0.79, and SVM achieved

0.77. XGBoost showed lower sensitivity (0.48) and accuracy (0.68) despite a high AUC. Calibration was best for tree-based methods, with modest under-prediction in the highest-risk decile for LR. XGBoost and the blended model produced the fewest misclassifications (Figure 1b). Tree-based variable importance consistently ranked family history, disease duration and platelet nadir as the strongest predictors (Figure 1c).

Conclusion: In this feasibility study, ML distinguished inherited from non-inherited thrombocytopenia using routinely available variables. Performance should be interpreted cautiously given the sample size. The findings support larger multi-centre datasets and external validation to optimise referrals for genetic testing in thrombocytopenia.



P21

CHARACTERIZATION OF PATIENTS WITH IMMUNE THROMBOCYTOPENIA IN SPAIN. PRELIMINARY RESULTS FROM RESTI: SPANISH REGISTRY OF PRIMARY IMMUNE THROMBOCYTOPENIA

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1: Zaragoza, 2: Sevilla, 3 :Salamanca, 4: Toledo, 5,21: Barcelona, 6, 20, 11, 15: Madrid, 7: Palma de Mallorca, 8: Cádiz, 9,10,17: Málaga, 12 :Castellón, 13: Lugo, 14: Granada, 16: Coruña, 18: Oviedo, 19: Bilbao,

Background: Primary immune thrombocytopenia (ITP) is a heterogeneous autoimmune disorder characterized by increased platelet destruction and impaired platelet production. Despite advances in disease understanding, real-world epidemiological and treatment data remain scarce in Spain. The Spanish

Immune Thrombocytopenia Registry (RESTI) was created to generate comprehensive national data on patient characteristics and treatment patterns.

Materials and Methods: RESTI is a nationwide, multicenter, observational, ambispective registry promoted by the GEPTI-SEHH Working Group. It includes pediatric and adult patients with a presumptive diagnosis of ITP or immune-mediated thrombocytopenia (platelet count $<100 \times 10^9$/L) after informed consent.

Results: To date, 925 patients have been included. The main demographic characteristics are shown in Table 1. Regarding treatments, most patients (85%) received at least one treatment during follow-up, while 15% remained untreated. Corticosteroids were the most frequently used first-line therapy (95%), with prednisone (67.3%) and dexamethasone (39.7%) being the most commonly prescribed agents. Methylprednisolone (13.2%) and deflazacort (0.9%) were used less frequently. Immunoglobulins were administered to 57.1% of patients, and platelet transfusions to 10.8%. Second-line and subsequent therapies were widely used, particularly thrombopoietin receptor agonists, including eltrombopag (45.4%), avatrombopag (37.9%), and romiplostim (28.8%). Fostamatinib was prescribed in 12.1% of patients, and rituximab in 10%. Overall, treatment patterns reflected substantial heterogeneity in clinical practice across centers.

Conclusion: RESTI represents the largest real-world national registry of ITP patients in Spain to date. These preliminary data provide valuable insights into current treatment strategies, highlighting extensive corticosteroid exposure and frequent use of second-line therapies. RESTI constitutes a robust platform for future epidemiological, clinical, and outcomes-based research in ITP. Ongoing patient inclusion and extended follow-up will allow evaluation of disease evolution, therapeutic responses, and long-term outcomes, contributing to improved stratification strategies and evidence-based decision-making within the Spanish healthcare system. Ultimately, RESTI aims to support harmonization of clinical practice and to serve as a reference framework for future national and international collaborative studies.

P22

INDIRECT COMPARISON OF ORAL THROMBOPOIETIN RECEPTOR AGONISTS IN PAEDIATRIC IMMUNE THROMBOCYTOPENIA: EFFICACY, SAFETY AND ADHERENCE ANALYSIS

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Cities: 1,2 Vigo 3 Santiago de Compostela 4 A Coruña

Introduction: Chronic paediatric Immune Thrombocytopenia (ITP) requires second-line therapy, with oral Thrombopoietin Receptor Agonists (TPO-RAs)—Eltrombopag (ELT) and Avatrombopag (AVA)—being key options. Direct comparative trials are lacking. This study performs an indirect comparison to assess their relative efficacy, safety, and adherence profiles in this population.

Methods: A placebo-anchored indirect comparison (Bucher method) was conducted on pivotal paediatric trials (AVA-PED-301 vs. PETIT/PETIT2). Efficacy (Durable Response, Day 8 Response, Rescue Rate) and safety data (hepatic events, thrombosis) were assessed. A complementary Bayesian Hierarchical Model was used to explicitly adjust for population heterogeneity, as 73% of AVA-PED-301 patients were TPO-RA-exposed (refractory), compared to mostly naive patients in PETIT2. Treatment burden (dietary restrictions, monitoring) was also scored for adherence assessment. AI statistical analysis supported by Claude Sonnet 4.5

Results: Durable Response rates were 28% for AVA (vs. 0% placebo) and 40% for ELT (vs. 3% placebo). The frequentist indirect comparison showed {OR} = 0.92 (95% CI 0.03–31.2), indicating non-significant difference. The Bayesian model, after adjusting for the refractory population, estimated clinical equivalence: {OR} = 0.89 (95% Credible Interval [0.38, 1.94]), with a 71% probability of clinical equivalence. AVA showed advantages in rapid response (56% response by Day 8) and less need for rescue therapy (7% vs 19% for ELT). In safety, AVA had a superior hepatic profile (0% vs. 3.2% discontinuation for {ALT} with ELT). Furthermore, AVA requires no dietary restrictions or mandatory monthly hepatic monitoring, leading to a projected 40% better potential adherence compared to ELT (Adherence Score: AVA 2 vs. ELT 7).(See Table 1)

Conclusions: Both oral TPO-RAs demonstrated equivalent durable efficacy, but Avatrombopag offers significant clinical advantages in terms of safety and convenience. The removal of dietary restrictions and monitoring requirements makes AVA the preferred TPO-RA in paediatric ITP, particularly for patients with poor adherence risk or concomitant hepatopathy, pending confirmation via a head-to-head non-inferiority study.

Outcome	Avatrombopag (AVA-PED-301)	Eltrombopag (PETIT2)	Indirect Comparison (OR, 95% CI)
Durable Response ($\ge$50x10^9/L for $\ge$6 of last 8 weeks, no rescue)	28% (15/54) vs 0% placebo	40% (25/63) vs 3% placebo	0.92 (0.03–31.2); No significant difference
Early Response (Day 8, $\ge$50x10^9/L)	56% (p<0.0001 vs placebo)	~45% (estimated from median 8–33 days)	Avatromboag faster
Rescue Therapy Need	7% vs 43% placebo (0.58%/week)	19% vs 24% placebo (1.46%/week)	Lower with Avatrombopag
Clinically Significant Bleeding (WHO Grade 1–4)	83% vs 90% placebo (no $\ge$Grade 3)	37% vs 55% placebo	Similar trend to reduction vs placebo
Hepatic Safety (ALT elevation discontinuation)	0% (0/54)	3.2% (2/63)	Risk difference: -3.2% (-7.8% to 1.4%); favors Avatrombopag
Serious Adverse Events	9%	9%	No difference
Thrombosis	0%	0%	No difference
Convenience/Adherence	No dietary restrictions/monitoring (Score: 2/10)	Dietary restrictions/Monthly monitoring (Score: 7/10)	Projected $\approx$40% better potential adherence with AVA
Bayesian Equivalence	37.2% adjusted (Posterior Mean)	40.1% (Posterior Mean)	OR: 0.89 (0.38–1.94); **71% Prob. Equivalence**

P23

MYELOFIBROSIS IN IMMUNE THROMBOCYTOPENIA

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Introduction / BackgroundA case report of autoimmune myelofibrosis in a woman with ITP on eltrombopag is described and her full remission after rituximab. This case explores bone marrow fibrosis in ITP under eltrombopag, distinguishing drug-induced from autoimmune myelofibrosis.

Objective: To highligh the diagnostic challenge between drug-induced and immune myelofibrosis

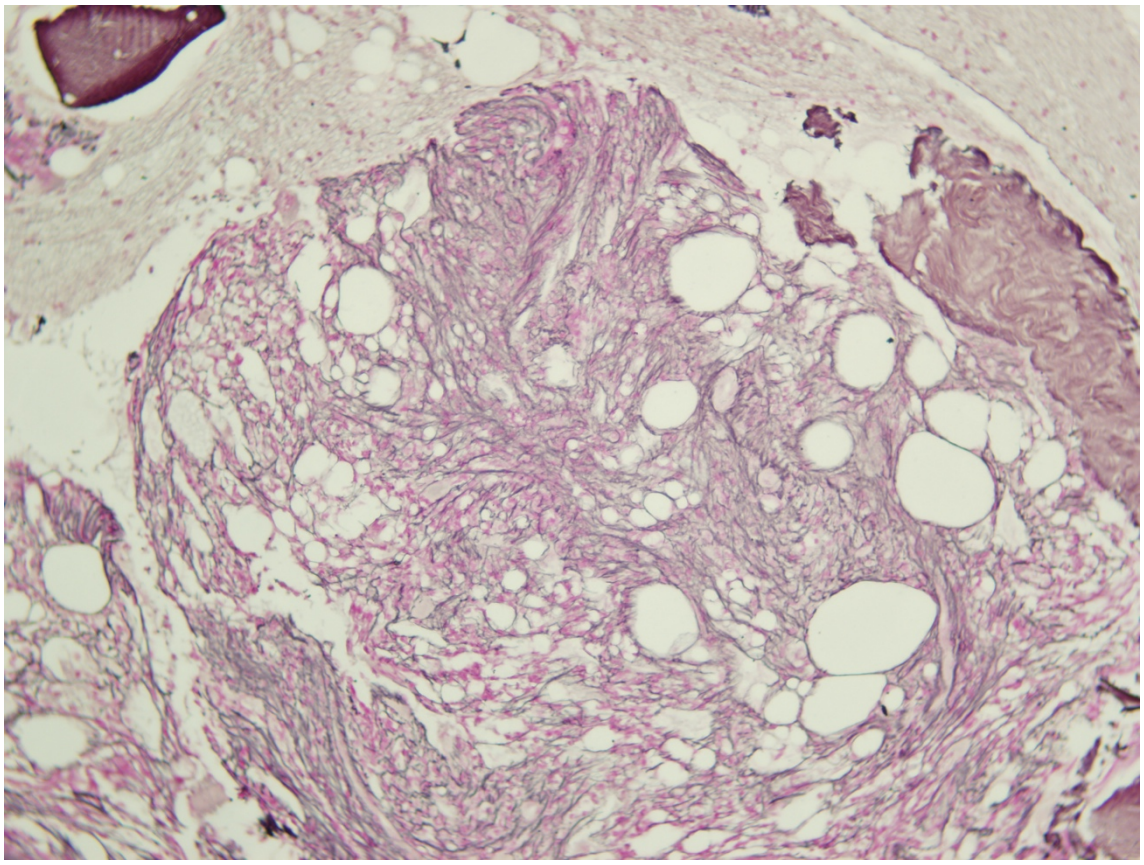
Methods / SourcesA 67-year-old woman was diagnosed with immune thrombocytopenia (ITP) in 2014, showing positive lupus anticoagulant and low-titer ANA. She achieved an initial response to corticosteroids and remained asymptomatic from autoimmune disease. In 2016, after relapse, she received intravenous corticosteroids and started eltrombopag as secondline therapy. A bone marrow aspirate performed at that time (without biopsy) showed marked megakaryocytic hyperplasia without fibrosis. She maintained good platelet response and clinical stability for several years under eltrombopag. In 2022, during routine follow-up, she presented a new relapse with platelets of 9×10^9/L and non-deficiency anemia (Hb 9.2 g/dL), with increased LDH (953 U/L) but no hemolysis. Imaging studies ruled out malignancy. Bone marrow aspirate was dry; biopsy revealed severe reticulin fibrosis (grade F3) and increased megakaryocytes. She had no constitutional symptoms. Molecular testing for JAK2, CALR, MPL, and BCR-ABL mutations was negative, excluding primary myelofibrosis. Because of steroid dependence and poor response to eltrombopag, she received rituximab (four weekly doses), achieving complete hematologic response. Both corticosteroids and eltrombopag were subsequently withdrawn, and she remains in complete remission without cytopenias.

Discussion: TPO-receptor agonists such as eltrombopag enhance megakaryocyte proliferation and may induce mild, reversible fibrosis through profibrotic cytokines (TGF-β, PDGF). However, autoimmune myelofibrosis (AIMF) arises from aberrant immune activation with T and B autoreactive cells, leading to reticulin and collagen deposition. AIMF is characterized by absence of clonal mutations, association with autoimmunity, and good response to immunosuppressive therapy. In this patient, the absence of clonal markers and full remission after rituximab, despite continuation of eltrombopag, support the diagnosis of AIMF rather than drug-induced fibrosis.

Conclusions

This case illustrates the importance of considering autoimmune mechanisms in patients with ITP who develop bone marrow fibrosis during TPO-RA therapy.

Figure 1



P24

REAL-WORLD OUTCOMES OF AVATROMBOPAG IN PERSISTENT AND CHRONIC ITP: RESULTS FROM THE REAL-AVA 3.5 STUDY

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Introduction: In patients (pts) with immune thrombocytopenia (ITP), real-world data on treatment response remains limited, particularly among those who switch between thrombopoietin receptor agonists (TPO-RAs). Here, we describe treatment patterns and clinical outcomes among adults in the US with acute/persistent or chronic ITP who switched from eltrombopag (ELT) or romiplostim (ROMI) to avatrombopag (AVA).

Methods: This was a US retrospective chart review of adults with primary ITP who initiated ELT or ROMI on or after 01 Jul 2019, switched to AVA within 30 days of discontinuing the prior TPO-RA, and had ≥6 months of follow-up from AVA initiation. Pts were followed from AVA initiation until the earliest of last contact, death, or study end (21 Mar 2025). Response was defined as achieving ≥1 meaningful platelet count (PC) (response thresholds: ≥30×109/L, ≥50×109/L, or ≥100×109/L) in the absence of rescue therapy. Among responders, durability of response was defined as the percent of time on AVA with a PC above the response threshold.

Results: Of 201 pts, 62.2% had chronic ITP and 37.8% had acute/persistent ITP at AVA initiation. The mean (SD) age was 56.7 (12.4) years and 60.7% were female. Pt characteristics, including baseline PCs, were generally similar between the 2 groups (Table 1). The median duration of follow-up from AVA initiation was 9.3 months and the median AVA treatment duration was 8.4 months. The most common reasons for switching to AVA were “increased efficacy” and “more convenient” (Table 1). The use of rescue therapy with AVA was low (chronic ITP: 9.6%; acute/persistent ITP: 11.8%). Among pts who received ≥1 concomitant steroid (7.5%) while on AVA, all discontinued use of concomitant steroids; no pts received concomitant immunosuppressants. At a PC threshold of 30×109/L, response was achieved with AVA in 100% of pts with chronic ITP and 96.7% with acute/persistent ITP who had a PC below that threshold at baseline; median durability was 93.2% and 94.2%, respectively (Table 1). At a PC threshold of 50×109/L, response was achieved in 94.4% and 97.6% of pts with chronic and acute/persistent ITP, respectively, who had a PC below that threshold at baseline; median durability was 89.0% and 91.7%, respectively.

Conclusions: Among pts who switched from ELT/ROMI to AVA, a clinically meaningful and durable platelet response was achieved, regardless of ITP disease duration.

PU1

OPTIMIZING ITP CARE WITH AVATROMBOPAG: INSIGHTS FROM A SINGLE-CENTER REAL-WORLD STUDY. EFFICACY & SAFETY & TREATMENT PATTERNS

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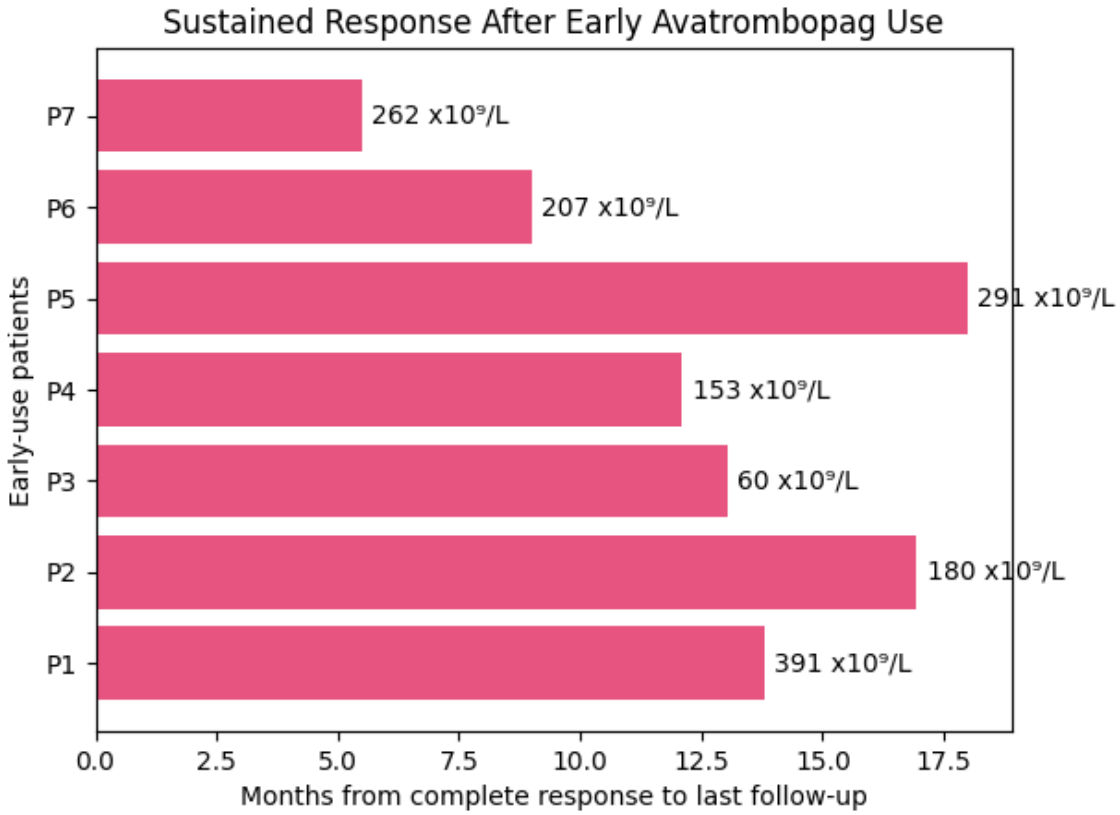
Introduction:Avatrombopag (Ava) has shown high efficacy and a favorable safety profile in clinical trials and RW studies. Our experience is in line with these findings. Methods: 28 ITP patients treated with Ava for ≥ 1month(2022–2025) are included.Endpoints: response (R) complete response (CR) rates, time to response, Platelets (PLT) thresholds ≥50 and ≥100 × 10^9/L, outcomes if prior eltrombopag (ELPG) exposure and early use. PLT counts, dosing, and safety were assessed longitudinally up to 12 months and at last follow-up.Results:Median age 48y at diagnosis and 56y at Ava initiation; male 57% and 43%. 68% chronic ITP& newly diagnosed 21%&persistent 11%. Median baseline PLT count 15×10^9/L(IQR 6-29).100% received corticosteroids (CS),40% prior therapies including:ELGP40%, romiplostim32%, rituximab 21% & splenectomy 21%; 46% had recived ≥3 treatment lines.Median time from dgs to Ava initiation was 2,6years (IQR <1–14,2y). Overall R/CR rate 89% (n=25). 75% switched to Ava for inadequate response, 15% for convenience & 10% adverse events. Median times to R and CR was 13(IRQ 7-14) and 30(14-74) days. Heavily treated patients ≥3lines required higer weekly doses. PLT remained stable between 3 and 12months(Friedman p=0.264) allowing dose reductions.Among responders,14(66%) remained on Ava, while 7(33%) maintained PLT response after discontinuation;median follow-up 15months(IQR9-25) Patients switching directly from ELPG required lower maintenance doses (80–140 mg/week) than those with remote exposure (220 mg/w; p=0.028). AE occurred in 28%, mostly mild and NO thromboembolic events observed. 32 % required temporary treatment interruptions due to high PLT counts. 7 patients received avatrombopag early seting (4p < 3monts ;3p 3-12m). The median time from corticosteroid initiation to Ava was 18 days (range 5–225 days). All those patients achieved CR;mean time to response 10 days. Treatment discontinuation was feasible in 6 of 7 patients, who maintained durable PLT responses without relapse during a follow-up ≥6 months.Figure1.Conclusion: Ava showed rapid and durable efficacy and safety profile in ITP, including heavily pretreated patients, in line with recent real-world evidence from the Spanish ITP group. Early use was associated with fast, sustained responses after withdrawal with no relapse, while switching from ELGP enabled effective PLT control at lower maintenance doses. These data support Ava as an oral option across treatment lines in routine practice.

Figure 1.


Sustained Response After Early Avatrombopag Use
Early-use patients
P7
P6
P5
P4
P3
P2
P1
262 x10⁹/L
207 x10⁹/L
291 x10⁹/L
153 x10⁹/L
60 x10⁹/L
180 x10⁹/L
391 x10⁹/L
0.0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
Months from complete response to last follow-up

PU2

CHRONIC IMMUNE THROMBOCYTOPENIA AND GENETIC TESTING IN CHALLENGING PATIENTS: A CASE SERIES

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Background

The diagnosis of primary immune thrombocytopenia (ITP) is made by exclusion. However, a relevant proportion of patients with chronic ITP may carry pathogenic variants associated with hereditary thrombocytopenia, which can influence diagnosis, management, and treatment strategy. The aim of this case series was to describe clinical indications for genetic testing in patients with ITP and to highlight the management consequences of additional genetic findings.

Methods

Retrospective case series of patients with confirmed chronic ITP who underwent extended genetic testing (panel/NGS). Platelet counts, response to therapy, and genotype–phenotype correlations were evaluated.

Results

Case 1 (male, 27 years): Chronic, multi-refractory ITP with current response to combination therapy (avatrombopag + fostamatinib). Genetic testing revealed a variant of unknown significance (ACMG class 3) in ITGB3 (NM_000212.2:c.2131C>T, exon 13), associated with platelet-type bleeding disorder-24. Family members with the same variant had stable platelet counts around 80 × 10^9/L.

Learning: Even with optimal ITP therapy, platelet counts >100 × 10^9/L are not expected.

Case 2 (male, 13 years): Platelet count 36 × 10^9/L. Initial response to prednisolone with relapse after two weeks. Family history positive for von Willebrand disease (VWD) type 2 (2A vs. 2B unclear). Genetic testing identified a likely pathogenic variant (ACMG class 4) in VWF (NM_000552.5:c.8312G>T, exon 5), consistent with VWD type 2A/IID. VWF:Ag and VWF:Act <20 U/L.

Learning: Concomitant hereditary bleeding disorders can modify treatment; patient is treated with TPO-RA and VWF concentrate.

Case 3 (female, 47 years): Long-standing platelet counts between 30–60 × 10^9/L. Suspicion of ITP, but hereditary thrombocytopenia possible. Genetic testing revealed a novel heterozygous GP1BA variant (NM_000173.7:c.284T>G), classified as VUS.

Learning: Corticosteroids are unlikely to be effective in hereditary thrombocytopenia.

Case 4 (female, 36 years): Chronic, multi-refractory ITP since 1996 with platelet counts <10 × 10^9/L. Genetic testing identified a previously unreported FLNA variant (NM_001110556.2:c.5768C>T, VUS). Segregation analysis in 16 family members showed normal platelet counts in mutation carriers, supporting the diagnosis of ITP. The patient is currently treated with an off-label anti-CD38 antibody.

Learning: Segregation analysis is crucial to interpret VUS findings.

Conclusion

Targeted genetic testing should be considered in selected patients with chronic or atypical ITP. Hereditary thrombocytopenia may coexist with ITP and has relevant implications for prognosis, bleeding risk, and therapeutic decision-making.

PU3

INFLAMMATORY HEMATOLOGICAL INDICES IN PATIENTS WITH IMMUNE THROMBOCYTOPENIA (ITP) TREATED WITH AVATROMBOPAG

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The easily measurable inflammatory hematological indices neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and hemoglobin-to-platelet ratio (HPR) have been proposed as potential biomarkers for disease assessment in immune thrombocytopenia (ITP).

The aim of this study was to evaluate the dynamics of NLR, PLR, and HPR in ITP patients before and during the treatment with avatrombopag.

A single-center retrospective observational analysis at Sisters od Mercy University Hospital Centre (Zagreb, Croatia) included 22 ITP patients after first line treatment failure when platelet values dropped below 30x109/L. Platelet counts and ratios calculated from absolute values of corresponding blood cells were assessed at baseline (T0), after 2 weeks (T1), and after 1 month of treatment (T2). The exclusion criteria were concomitant treatment with corticosteroids, rituximab or immunoglobulins and an active inflammatory process. All statistical analyses were conducted using SAS software (version 9.4, Cary, NC).

The mean ± SD age of patients was 64.09 ±15.98 years and males accounted for 50% (n=11) of the patients. Platelet counts increased markedly from baseline to follow up with median [IQR] values of 11.5[23] at T0; 138[115] at T1;129.5[94] at T2. Platelet recovery >30 ×109/L was observed in 19 (86%), and >50 ×109/L in 18 (82%) patients at T1; by T2 all patients had platelet count >50 ×109/L. Median NLR values were around 2-3 across time points (median [IQR] T0:2.54[1.62]; T1:2.73[2.72]; T2:2.09[1.78]), with interindividual variability. No statistically significant correlations were observed between platelet values and NLR values, or between their changes (ΔNLR vs. ΔPlt) at any time point (all Spearman p>0.05). Baseline NLR did not differ between patients with and without platelet recovery >50 at T1 (Wilcoxon rank-sum test,p=0.58). In exploratory linear regression analyses adjusted for baseline platelets, NLR was not independently associated with platelet count at T1 (p=0.74). HPR and PLR changed over time, primarily reflecting platelet recovery. Hemoglobin and lymphocyte counts remained stable over time (hemoglobin median [IQR] T0: 134[16]; T1:128[21]T2:134[12]; lymphocyte: T0:1.94[0.76], T1:1.78[0.78] T2:1.73[1.13]. Baseline HPR and PLR were not associated with subsequent platelet recovery.

In summary, no significant relationship was found between NLR and platelet values. HPR and PLR changed during treatment due to increase in platelet count.

PU4

MANAGEMENT OF IMMUNE THROMBOCYTOPENIA IN ELDERLY PATIENTS: CHALLENGES AND THE NEED FOR INDIVIDUALIZED THERAPEUTIC APPROACHES

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Introduction / BackgroundImmune thrombocytopenia (ITP) in elderly patients is a particularly complex clinical situation. Compared with younger people, elderly patients with ITP usually have more comorbidities, greater frailty, take more medications and have an increased risk of both bleeding and thrombotic events. These factors create a different clinical and therapeutic profile, making it necessary to optimize management strategies. The need to balance efficacy and safety in this special vulnerable group, highlights the importance of an individualized approach.

Objective: This review highlights key considerations and practical recommendations for managing ITP in elderly patients, emphasizing the need for tailored protocols for this patient group.

Methods / SourcesA narrative review was performed based on current clinical practice guidelines and consensus documents, including the GEPTI and the American Society of Hematology (ASH) guidelines and the International Consensus Report.

Discussion: Management of ITP in elderly patients requires an assessment that includes comorbidities, frailty, polypharmacy and a careful evaluation of risks and benefits. First-line treatment is usually conservative, being corticosteroids the main option; however, their use is limited by a higher risk of side effects in older adults, so lower starting doses and shorter treatment periods are recommended. For second-line, thrombopoietin receptor agonists (TPO-RAs) are a relevant option for most patients. Three agents (avatrombopag, eltrombopag and romiplostim) are available and the choice should be individualized, considering patient preferences, comorbidities, possible interactions and adherence. Avatrombopag may have some advantages in elderly, such as oral administration without food restrictions and a safety profile that does not require regular liver monitoring. Fostamatinib, an oral spleen tyrosine kinase inhibitor, can be considered in patients with higher thrombotic risk or when TPO-RAs are not suitable, although experience in the elderly is limited. Other second-line options are rituximab and splenectomy, which may be used in selected cases, but often limited by comorbidities, frailty, and the risk of infections, thrombosis or surgical complications in this age group.

Conclusions: Management of ITP in elderly patients should be individualized, considering the complexity and heterogeneity of this population. TPO-RAs are a relevant second-line option, depending the choice among them on clinical context, potential interactions, patient preferences and practical aspects such as food interactions and adherence, with avatrombopag representing a particularly suitable alternative in this setting. Fostamatinib, rituximab, and splenectomy are also alternatives for selected cases. Developing specific protocols and guidelines for elderly patients with ITP is imperative to optimize outcomes in this particularly vulnerable group.