2ND meeting of the European Research Consortium on ITP

NEW INSIGHTS INTO IMMUNE THROMBOCYTOPENIA

Paris Crowne Plaza Paris République

April 23-24, 2026

ERC

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Anti-CD38 monoclonal antibodies in ITP: current status

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Disclosures of

Waleed Ghanima

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
SOBI	+		+			+	
Grifols	+		+			+	
Sanofi	+		+			+	
Novartis			+			+	
Amgen						+	
Takeda			+			+	

Where do we stand with available agents?

- We have 3 agents
  - Daratumumab
  - CM313
  - Mezagitimab

- Scientific evidence
  - Conducted 6 phase 1/2 clinical trials
  - Ongoing clinical trials: one phase 3 (mezagitimab)
  - Other ongoing trials: 6

CD-38 - ubiquitous transmembrane glycoprotein

Functional roles:

- **Enzymatic activity**→ synthesizes and hydrolyses cyclic adenosine 5'-diphosphate-ribose (cADPR)
- **Inflammation and infection**→participates in cell adhesion and signaling
- **Immunoregulation**→ influences activation, proliferation , cytokine secretion, and metabolic regulation of immune cells

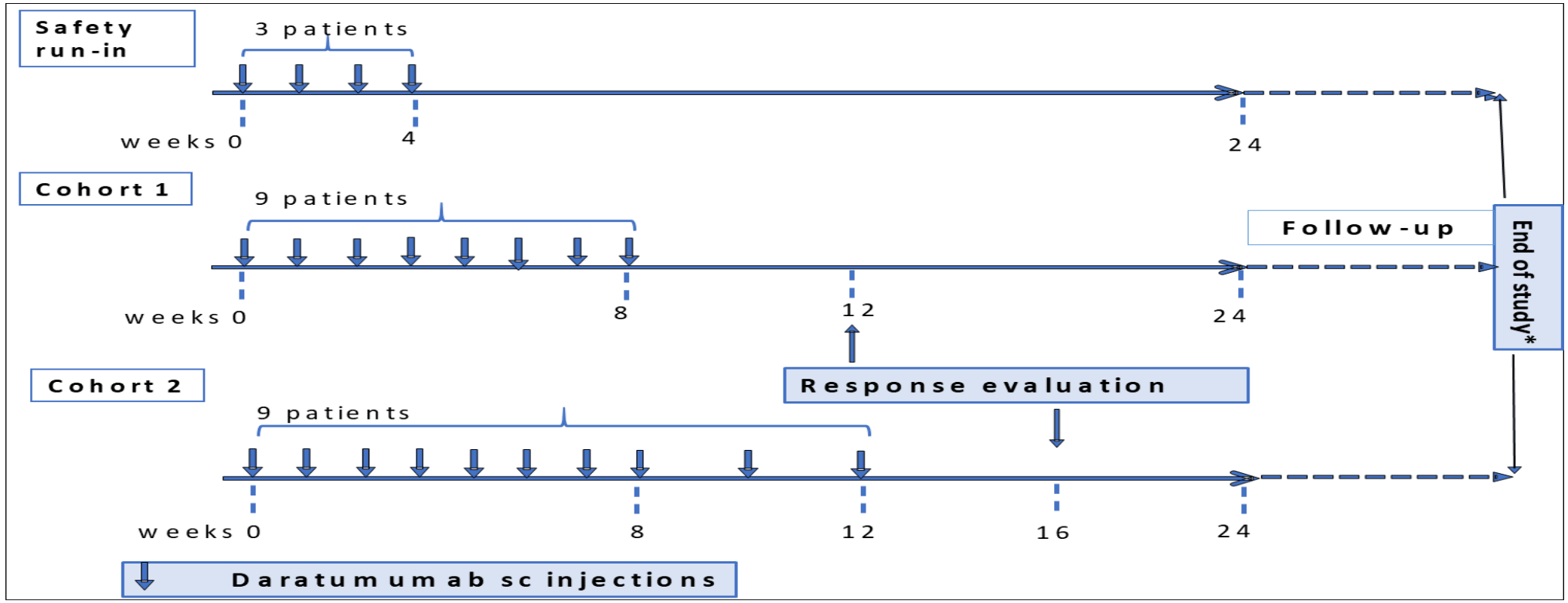
Normal expression

- **Immune cells**
  - Plasma cells → highly and uniformly expressed in plasmablasts, short- and long-lived plasma cells
  - B cells
  - T cells → activated T cell, Tregs, and some memory subsets
  - NK cells
  - Monocytes and neutrophils
  - Innate lymphoid cells
- **Other tissues:**
  - Erythrocytes and platelets
  - Non-hematopoietic tissues: epithelial cells, smooth muscle, pancreatic islets, brain (astocytes), prostate, kidney, gut

Piedra-Quintero et al. Front immunol.2020

Daratumumab

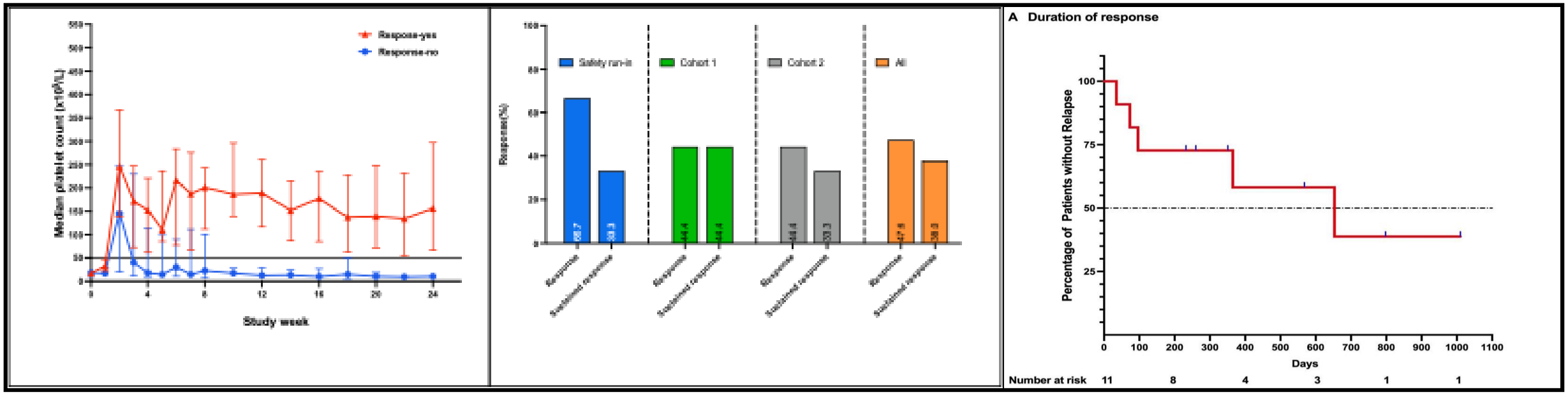
DART STUDY – a phase trial to study the safety and efficacy of subcutaneous Daratumumab in adults with ITP



Primary endpoints: for safety was assessed as the number and severity of adverse events grade ≥2 during the study. for efficacy was defined as 2 consecutive platelet counts ≥50x10^9/L at week 12 for the safety run-in/Cohort 1, and at week 16 for Cohort 2

Tsykunova G , Ghanima W, Blood Adv 2025-
DOI: 10.1182/bloodadvances.2025017279

Efficacy



Response rates:

- **48%** at weeks 12/16
- **38%** at week 24
- **28%** at the end of the study

Tsykunova - Ghanima . Et al BloodAdv 2025

Safety

Treatment- related adverse events (number of patients; %)

- Infusion-related reactions:
  - grade 2: 2 (9.5%)
  - grade 3: 1 (4.7%)
- Injection site reactions: grade 1: 2 (9.5%)
- Infections: grade 1: 1(4.5%); grade 2 -1 (4.7%)
- Diarrhoea: grade 2: 2 (9.5%)

Treatment - emergent adverse events: infections, mostly viral (38%)

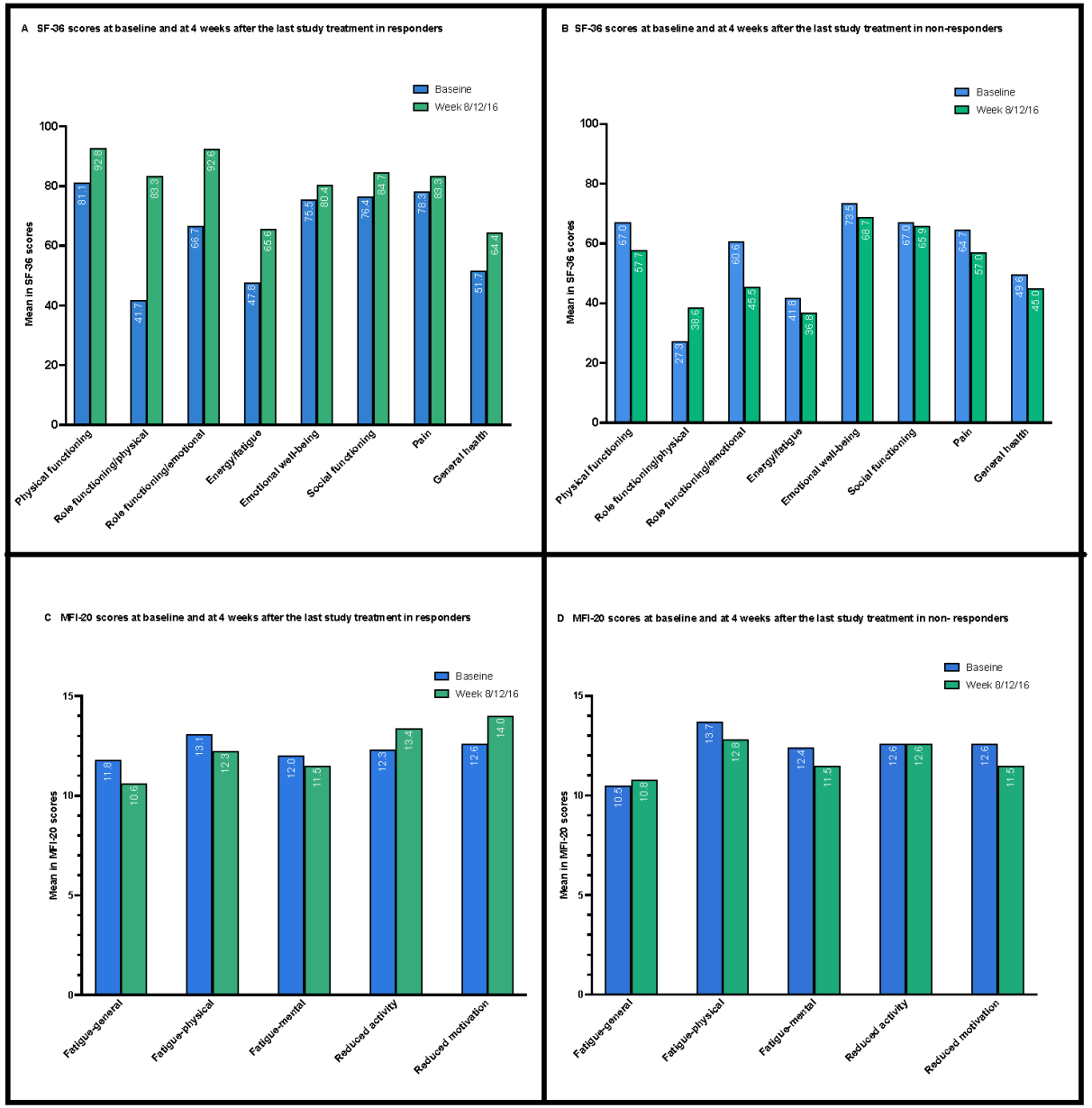
Serious adverse events:

IRR grade 3

SARS-CoV-2 infection with acute renal failure, grade 3.

Tsykunova - Ghanima . Et al BloodAdv 2025

PROs



Tsykunova - Ghanima . Et al BloodAdv 2025

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Daratumumab in Relapsed or Refractory Pediatric Immune Thrombocytopenia

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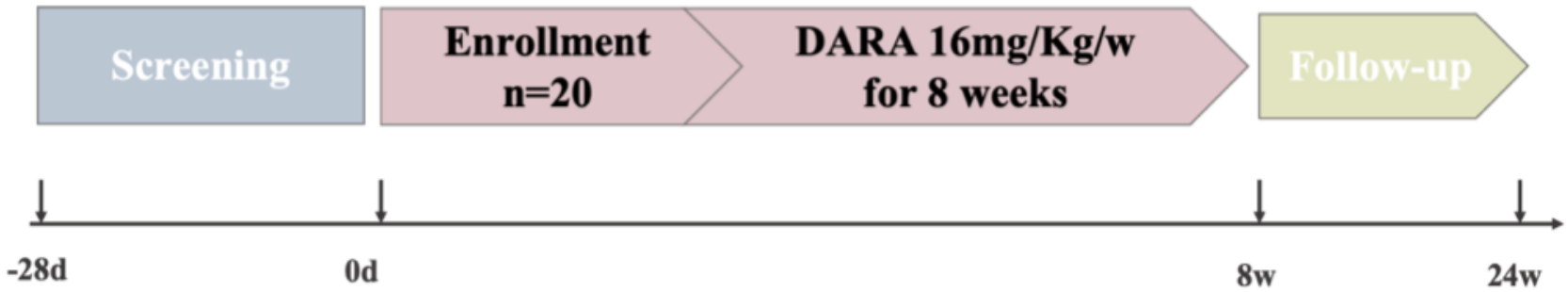
CORRESPONDENCE

Daratumumab in Relapsed or Refractory Pediatric Immune Thrombocytopenia



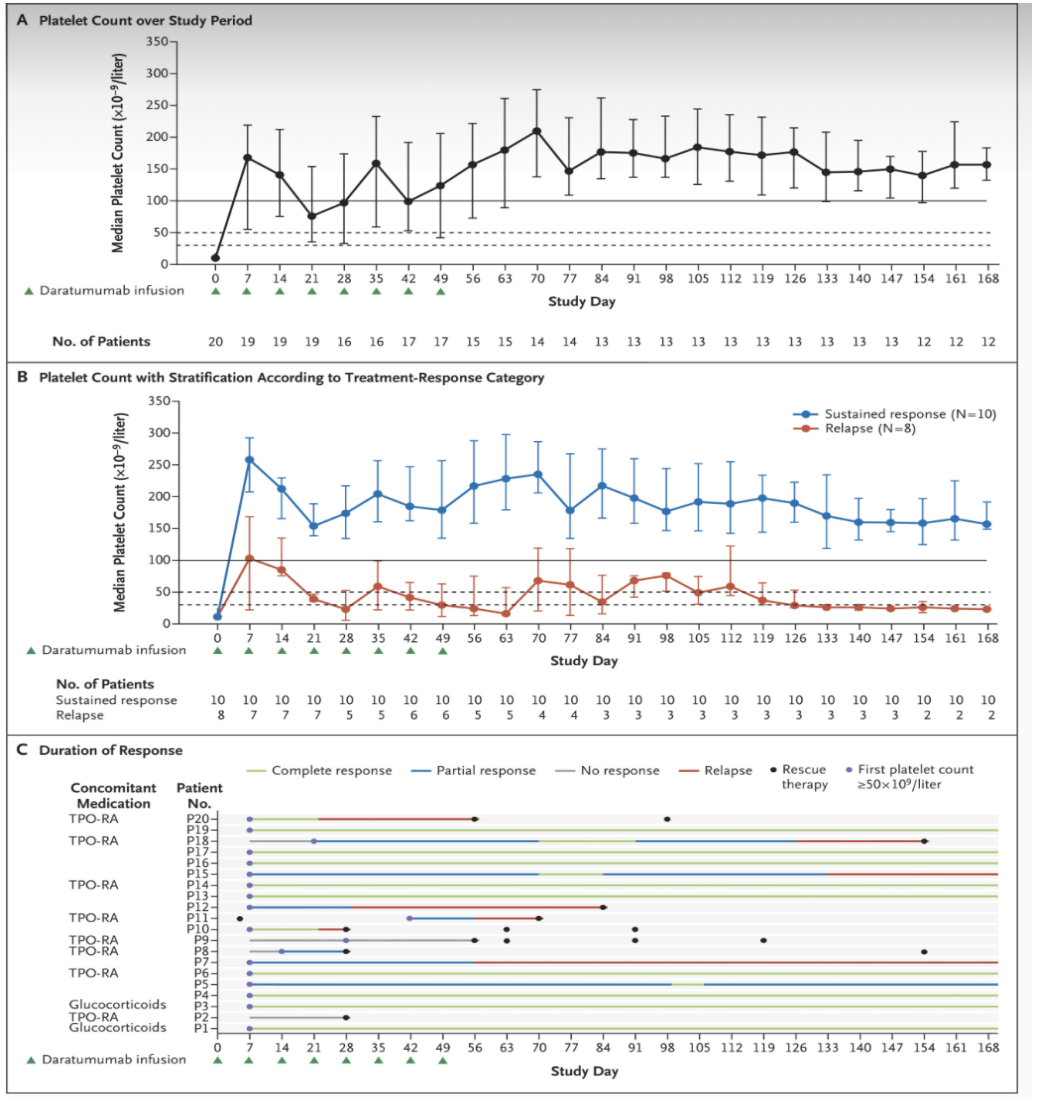
- Inclusion criteria:
- Age 12-17 years
- Persistent or chronic ITP
- Platelet count <30 × 10^9/L within 48 hours before the first study dose
- Previously failed 1st-line CS and had received and failed ≥ guideline-specified 2nd-line treatment

Efficacy endpoint:
The proportion of subjects who achieved ≥2 consecutive platelets counts >50 × 10^9/L without rescue therapy or dose escalation of concomitant treatments within 8 weeks after the first dose.

Safety

Sun et al. NEJM, 2025

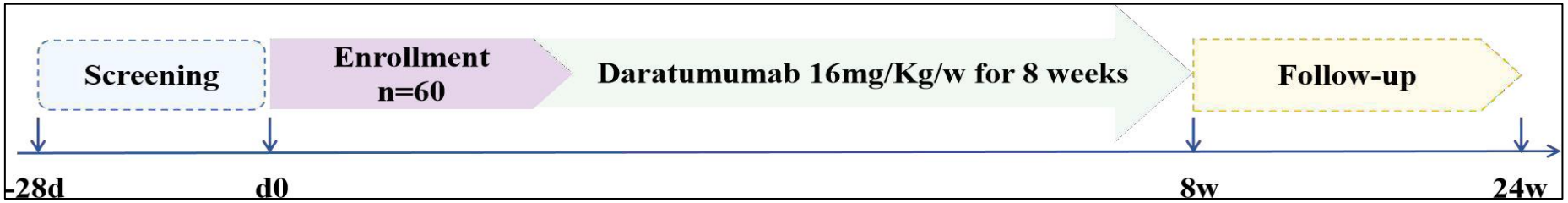
- **Efficacy:**
  - Response during first 8 weeks was achived in 18/20 **(90%)**
  - Overall response
    - **60%** at week 8
    - **60%** at week 12
    - **50%** at week 24
- **Safety:**
  - Infusion-related reactions in 35%
  - Upper respiratory tract infections in 30%



Sun et al. NEJM, 2025

Daratumumab in patients with immune thrombocytopenia: a single-center, open-label, phase 2 trial

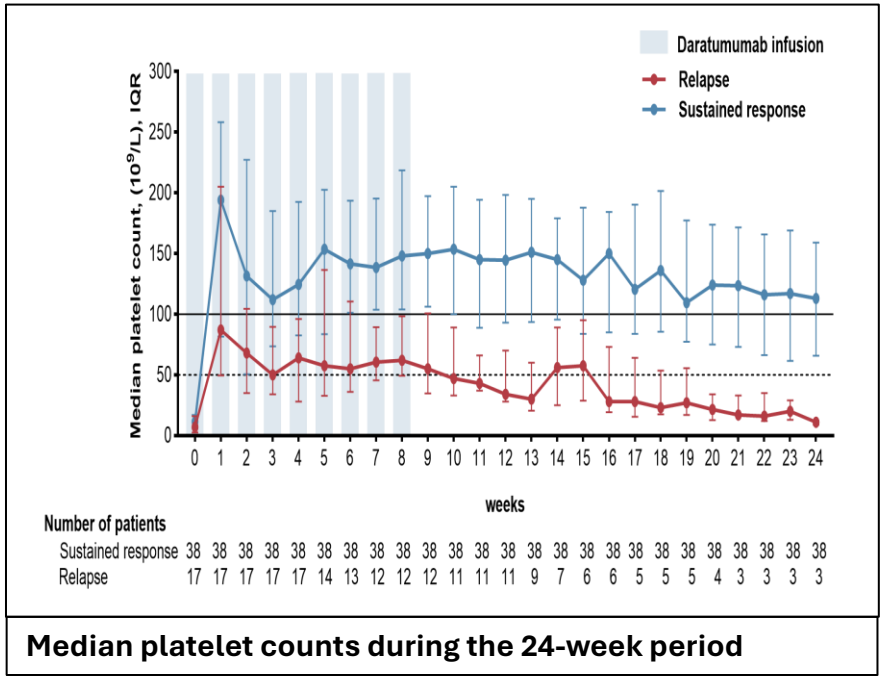
Yunfei Chen,[a,b,c] Zhengjie Hua,[a,b,c] Yanmei Xu,[a,b,c] Jia Chen,[a,b,c] Qing Wen,[a,b,c] Ting Sun,[a,b,c] Huiyuan Li,[a,b,c] Xiaofan Liu,[a,b] Rongfeng Fu,[a,b] Mankai Ju,[a,b] Feng Xue,[a,b] Wei Liu,[a,b] Huan Dong,[a,b] Wenjing Gu,[a,b] Xinyue Dai,[a,b] Wentian Wang,[a,b] Ying Chi,[a,b] Xiaolei Pei,[a,b] Renchi Yang,[a,b] and Lei Zhang[a,b,*]



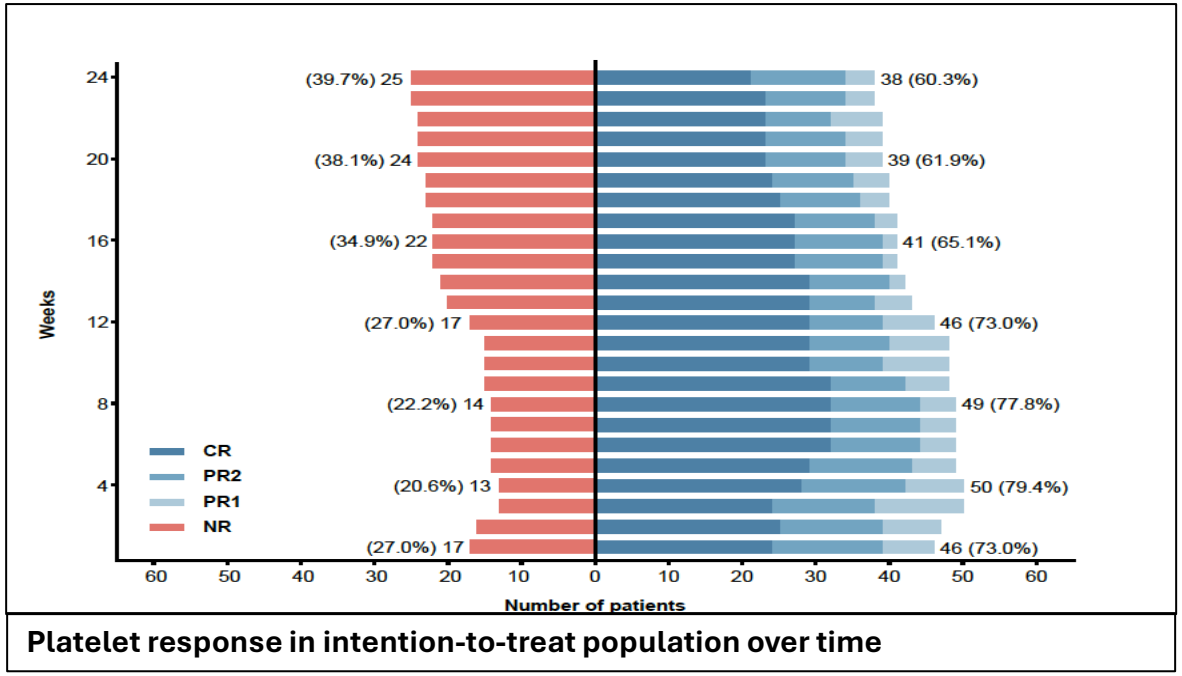
- N=63 (median age 33yr)
- Primary endpoint ≥2 consecutive platelet counts of ≥ 50 × 10^9 /L within 8 weeks
- Methylprednisolone 100 mg was given prior to the 1st and 2nd infusions, followed by 60 mg prior to each subsequent infusion + 20 mg/day on the first 2 days following first 2infusions

Chen et al. eClinicalMedicine 2026;94: 103849

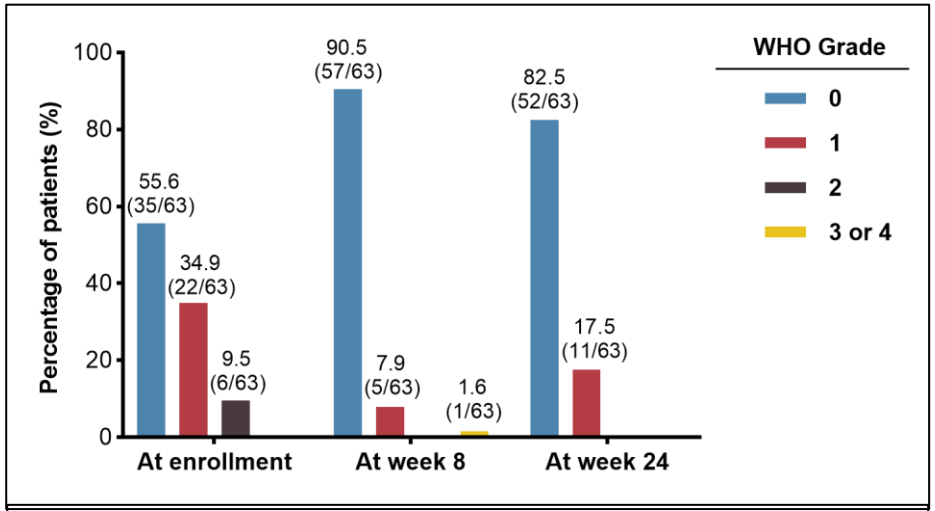
The primary efficacy endpoint was achieved in 52 (83%) patients



Median platelet counts during the 24-week period



Platelet response in intention-to-treat population over time



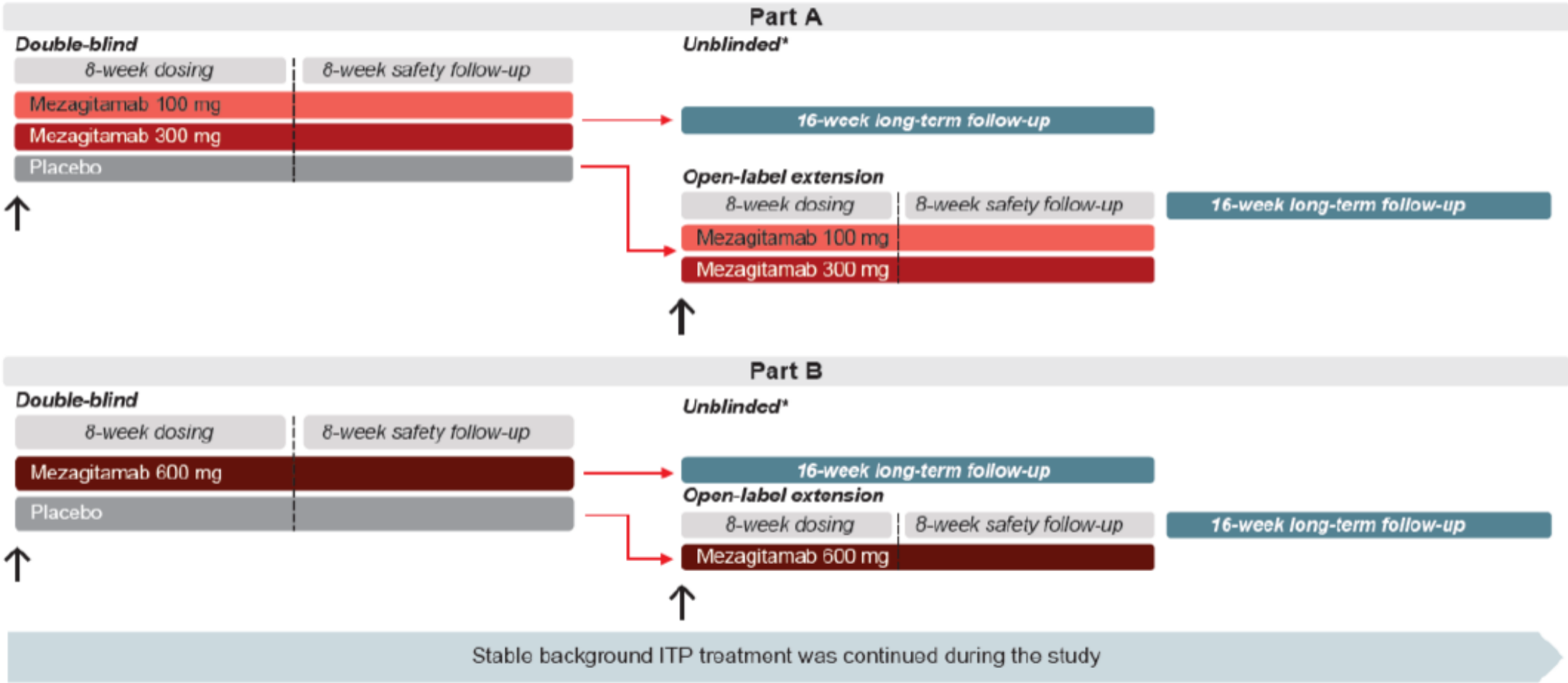
Incidence of bleeding（WHO bleeding scale）

Chen et al. eClinicalMedicine 2026;94: 103849

Mezagitimab

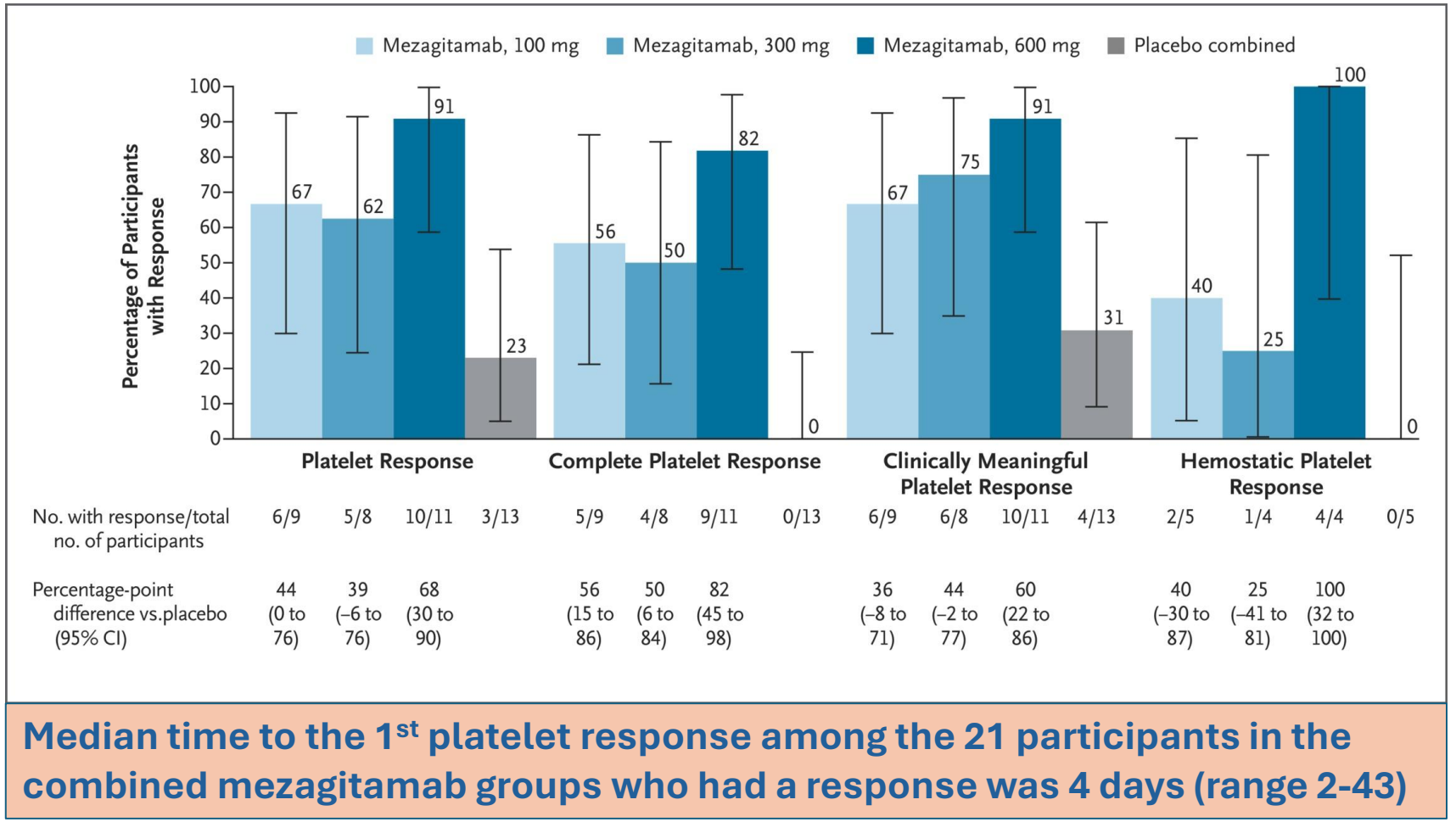
ORIGINAL ARTICLE

A Phase 2 Randomized Trial of Mezagitamab in Primary Immune Thrombocytopenia



Kuter DJ et al. N Engl J Med2026;394:1388-1398

Platelet Responses at Week 16



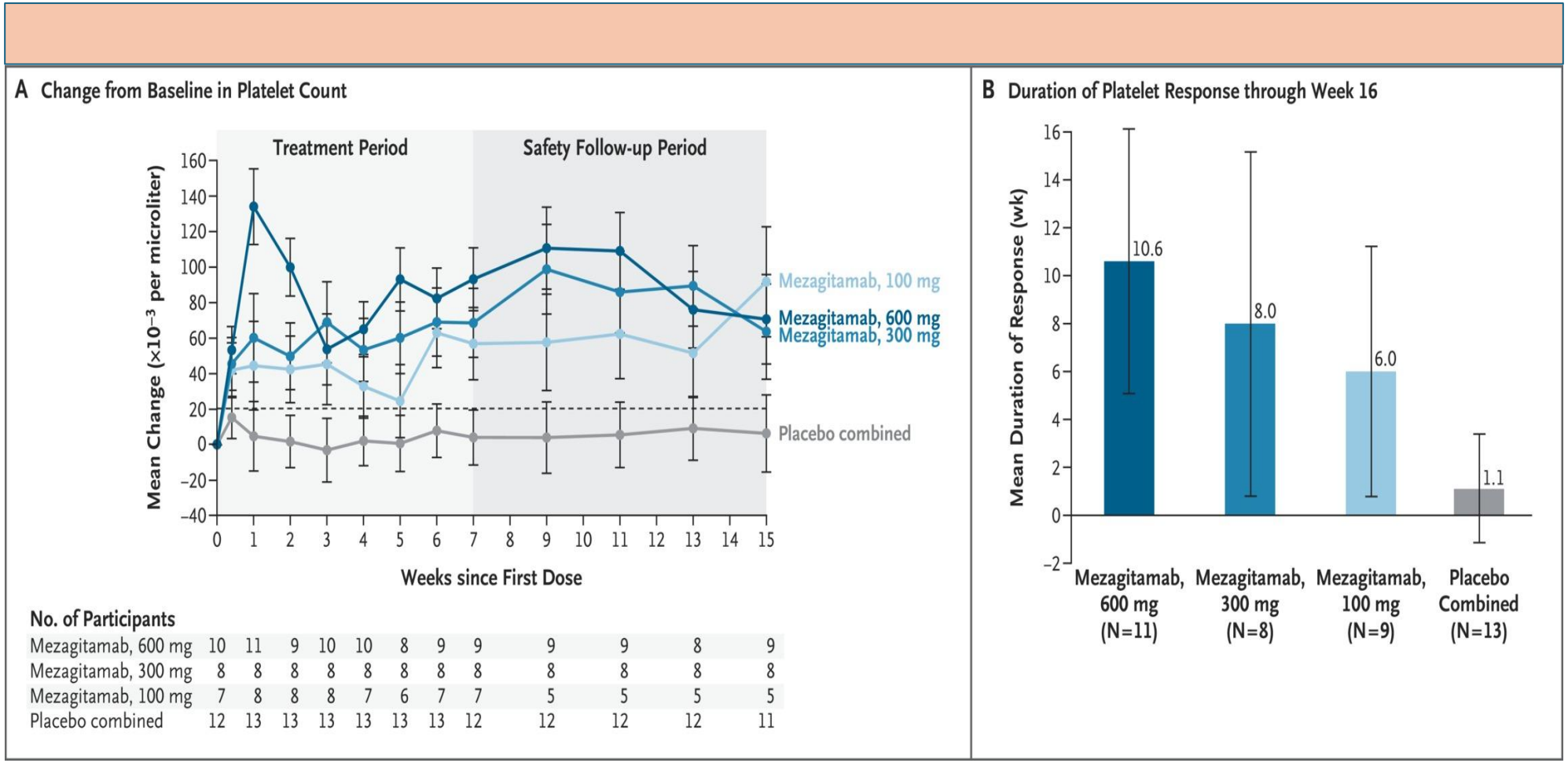
	Platelet Response				Complete Platelet Response				Clinically Meaningful Platelet Response				Hemostatic Platelet Response			
No. with response/total no. of participants	6/9	5/8	10/11	3/13	5/9	4/8	9/11	0/13	6/9	6/8	10/11	4/13	2/5	1/4	4/4	0/5
Percentage-point difference vs.placebo (95% CI)	44 (0 to 76)	39 (–6 to 76)	68 (30 to 90)		56 (15 to 86)	50 (6 to 84)	82 (45 to 98)		36 (–8 to 71)	44 (–2 to 77)	60 (22 to 86)		40 (–30 to 87)	25 (–41 to 81)	100 (32 to 100)	

Median time to the 1st platelet response among the 21 participants in the combined mezagitamab groups who had a response was 4 days (range 2-43)

Platelet response was defined as on at least two visits at any time through week 16: a platelet count of ≥50 x10^9/L and ≥20 x10^9/L above the baseline value/ complete platelet response defined by a platelet count of ≥100 x10^9/L / a clinically meaningful platelet response defined by a platelet count of ≥20 x10^9/L above the baseline value/ and a hemostatic platelet response defined by a platelet count of ≥30 and ≥20 x10^9/L above the baseline value, with a baseline platelet count of <15 x10^9/L.

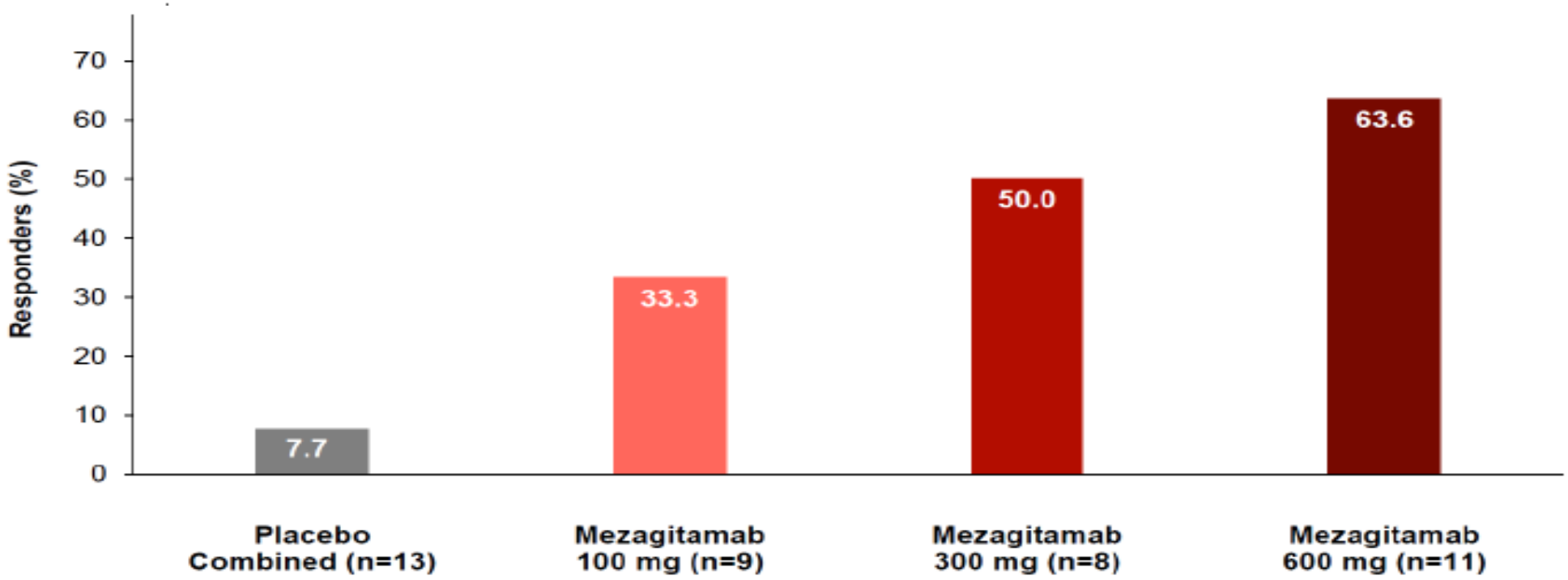
Kuter DJ et al. N Engl J Med2026;394:1388-1398

Change from Baseline in Platelet Count and Duration of Platelet Response through Week 16



Kuter DJ et al. N Engl J Med2026;394:1388-1398

Durable platelet response at week 24



Durable platelet response: participants achieving platelet counts ≥50 x109/L for ≥4 of the last 6 visits between Weeks 10 and 24 of the main study period for the mezagitamab groups and for ≥2 of the last 3 visits between Weeks 12 and 16 for the placebo group

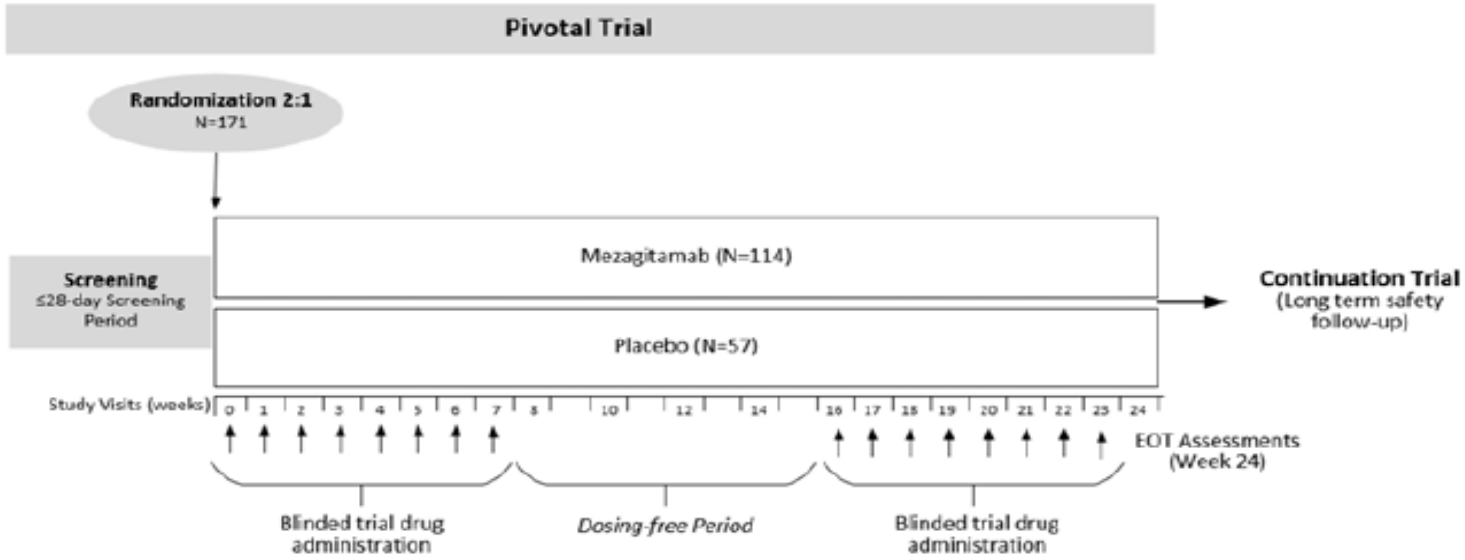
Kuter DJ et al. N Engl J Med2026;394:1388-1398

Ongoing phase 3 trial

Phase 3 ITP Pivotal Study: Powered to Provide a Highly Statistically Persuasive Result

Population: Chronic ITP patients with insufficient response or intolerance to at least 2 prior ITP treatments

Primary Endpoint: Durable platelet response over Weeks 19 – 24



CM313

ORIGINAL ARTICLE

A Novel Anti-CD38 Monoclonal Antibody for Treating Immune Thrombocytopenia

- **Phase 1–2, study to evaluate the safety and efficacy of CM313 in adults with ITP**.
- CM313 administered IV at a dose of 16 mg /kg weekly for 8 weeks, followed by a 16- week follow-up period.

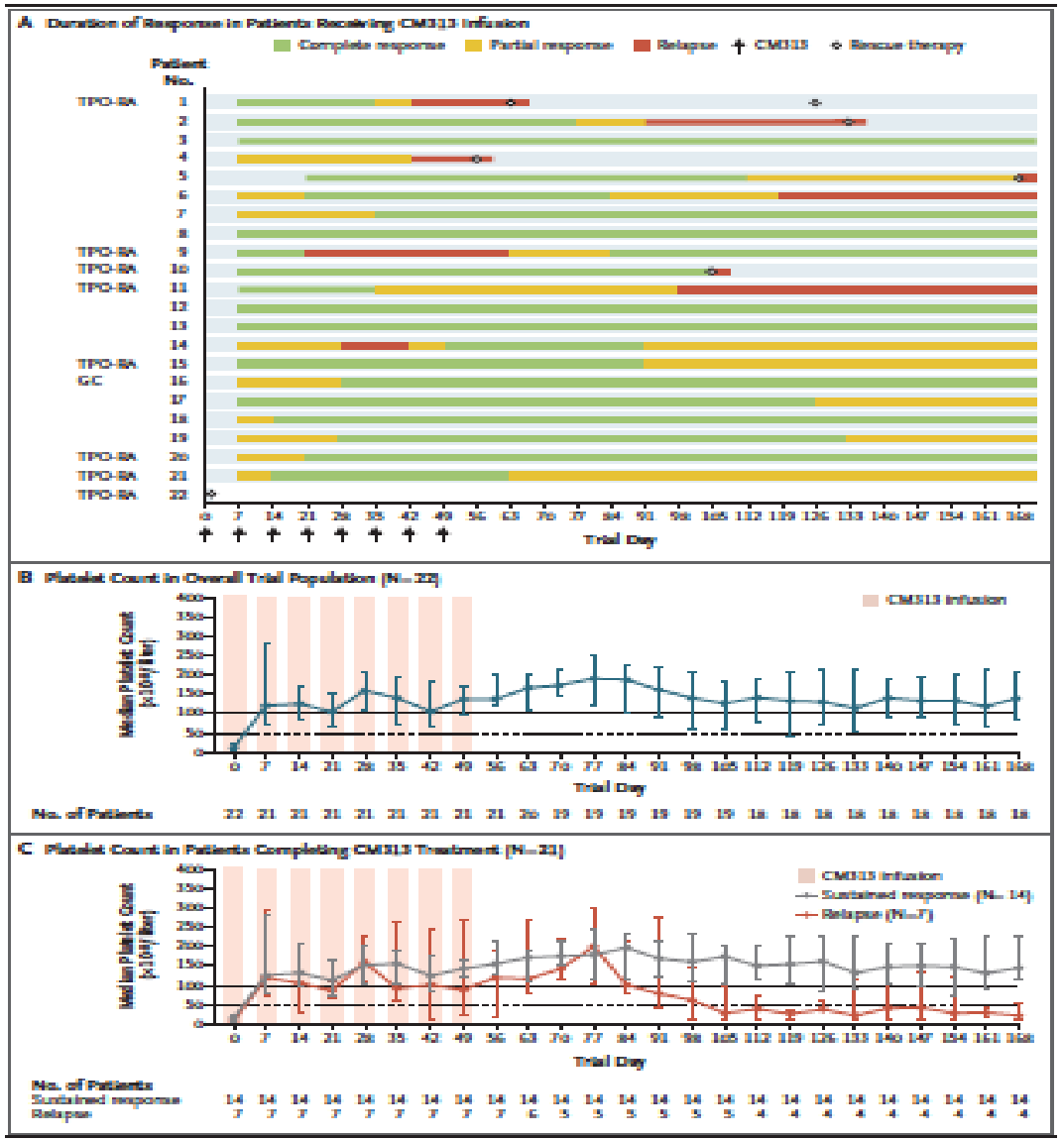
Primary outcomes:

- **Safety** and side effects profile
- **Efficacy: ≥2** consecutive platelet counts (separated by ≥1 day) of at least 50×10^9 /L within 8 weeks after receiving the 1st CM313 dose.

Chen et al. N Engl J Med 2024;390:2178-90

Results

- **95%** had 2 consecutive platelet counts >50X10^9 during the treatment period
- **Median time to1st plt ≥ 50X10^9 =1 week** (1-3)
- **Overall response:**
  - **82%** (n=18) at week 8
  - **86%** (n=19) at week 12
  - **64%** (n=14) at week 24
- **Most common AE**
  - infusion-related reaction in 32%
  - upper respiratory tract infection (32%).



Chen et al. N Engl J Med 2024;390:2178-90

A Randomized, Double-blind, Placebo-controlled, and Multi-center Clinical Study of CM313 in the Treatment of ITP (NCT06199089)

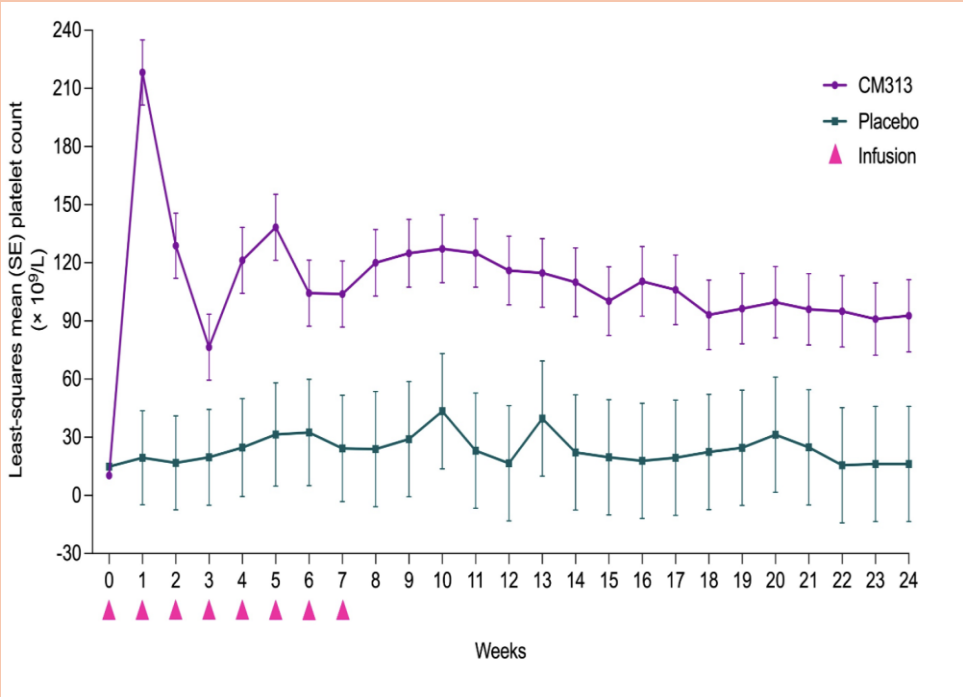
- Multicenter, double-blind, placebo-controlled, phase 2
- Persistent /chronic primary ITP
- Failed or relapsed after CS
- Previously responded to standard first-line therapy (CS or/and IVIG)

- **Randomization: 2:1 to CM313 (n=30) or placebo (n=15)**
- Standard premedication (CS, antihistamins acetaminophen)
- **CM313 group:**
  - 30 included
  - 1 discontinued due to AE
  - 29 completed treatment
  - 30 included in statistical analysis
- **Placebo group**:
  - 15 completed treatment and included in statistical analysis

Presented at EHA 2025, **Abstract:** LB4004

Results

- **Improvement in platelet counts**
  - Overall response at week 8 = **83% vs 20%**
  - Median time to plt ≥50x10^9/L in CM313 group = 1 week
  - Median cumulative duration of plt≥50x10^9/L: 18 weeks vs 3 weeks
- **Improvement in bleeding from baseline to w24:**
  - CM313 : decreased from 37% to 13%
  - Placebo: increased from 27% to 33%
- **Safety:**
  - TEA occurred in 83% of participants in the CM313 group vs 80% in the placebo
  - The most commonly reported events were infusion-related reactions and petechiae, with no unexpected safety signals observed.



Presented at EHA 2025, **Abstract:** LB4004

The biological changes associated with anti CD38

Are we close to finding a biomarker?

Paul Cezanne
Nature morte à la bouilloire

It does not seem to be an association between response to antiCD38 and the presence /absence of anti-platelet GP antibodies neither at baseline nor after treatment

CM313

- 67% of the patients who were positive for Ib/IX antibodies had a relapse
- 29% of the patients who were negative for Ib/IX but positive for anti–GP IIb/IIIa also had a relapse

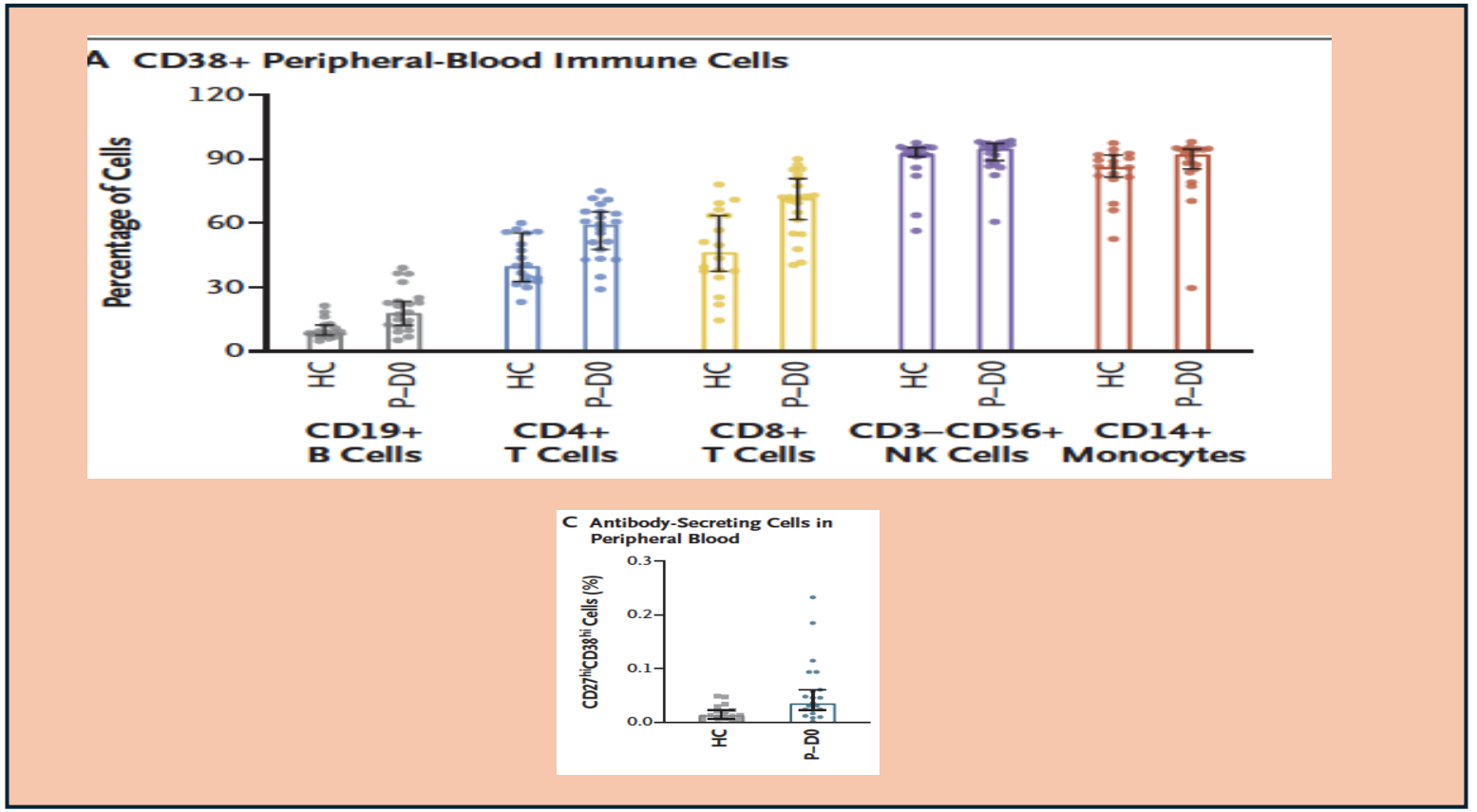
Daratumumab

- Platelet autoantibodies were detectable in 38% patients tested at baseline
- 43% of the responders, and 44% of the non-responders had anti platelet antibodies measured by direct MAIPA

Chen et al. N Engl J Med 2024;390:2178-90

Tsykunova - Ghanima . Et al BloodAdv 2025

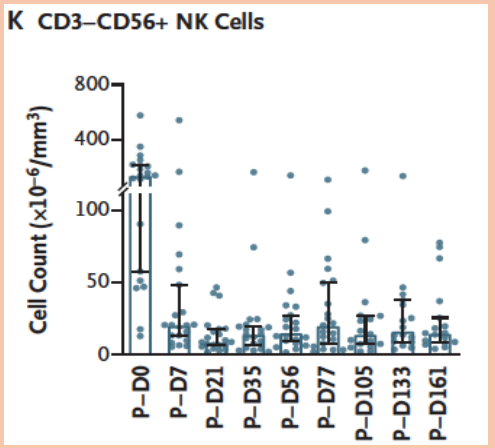
CD38 expressing cells in ITP compared to healthy controls (HC)

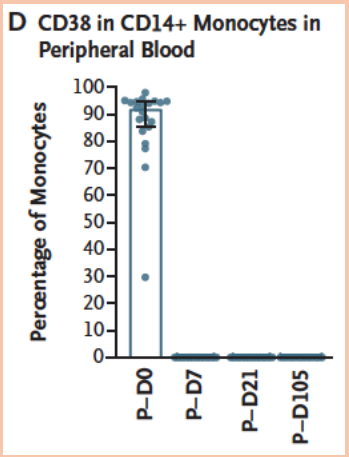


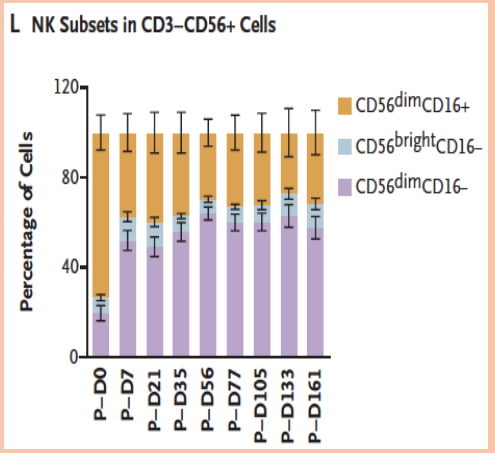
Before treatment with CM313, patients had substantially higher CD38 expression on various immune cells (T- lymphocytes, B lymphocytes, monocytes, and NK cells), along with a higher percentage of antibody-secreting cells in peripheral blood, than healthy controls

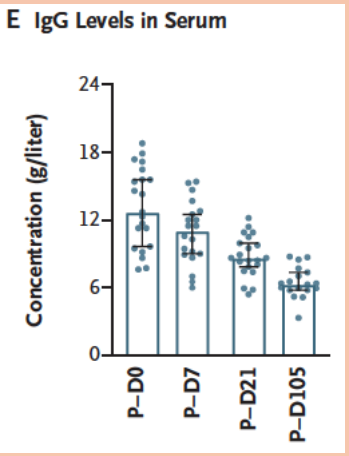
Chen et al. N Engl J Med 2024;390:2178-90

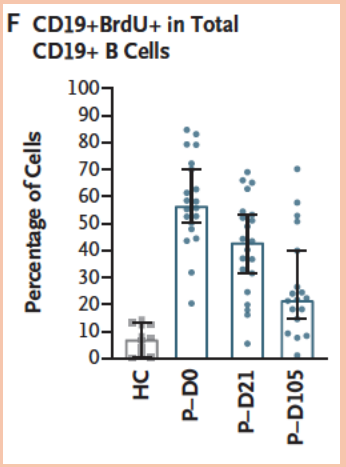
CD38 expressing cells decreased after treatment with CM313

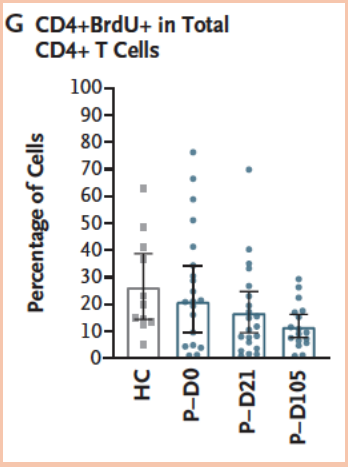


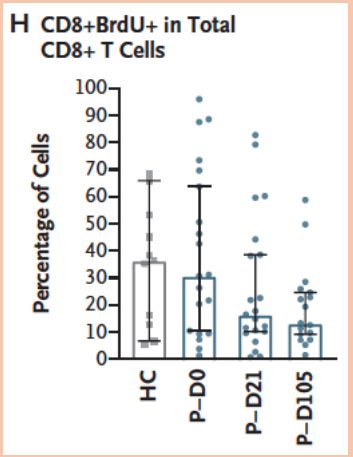


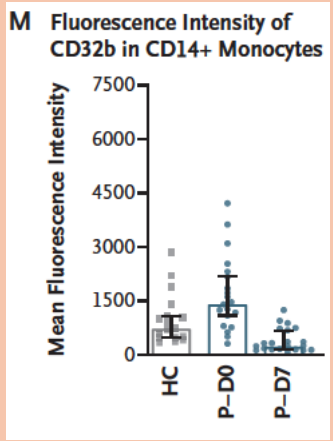










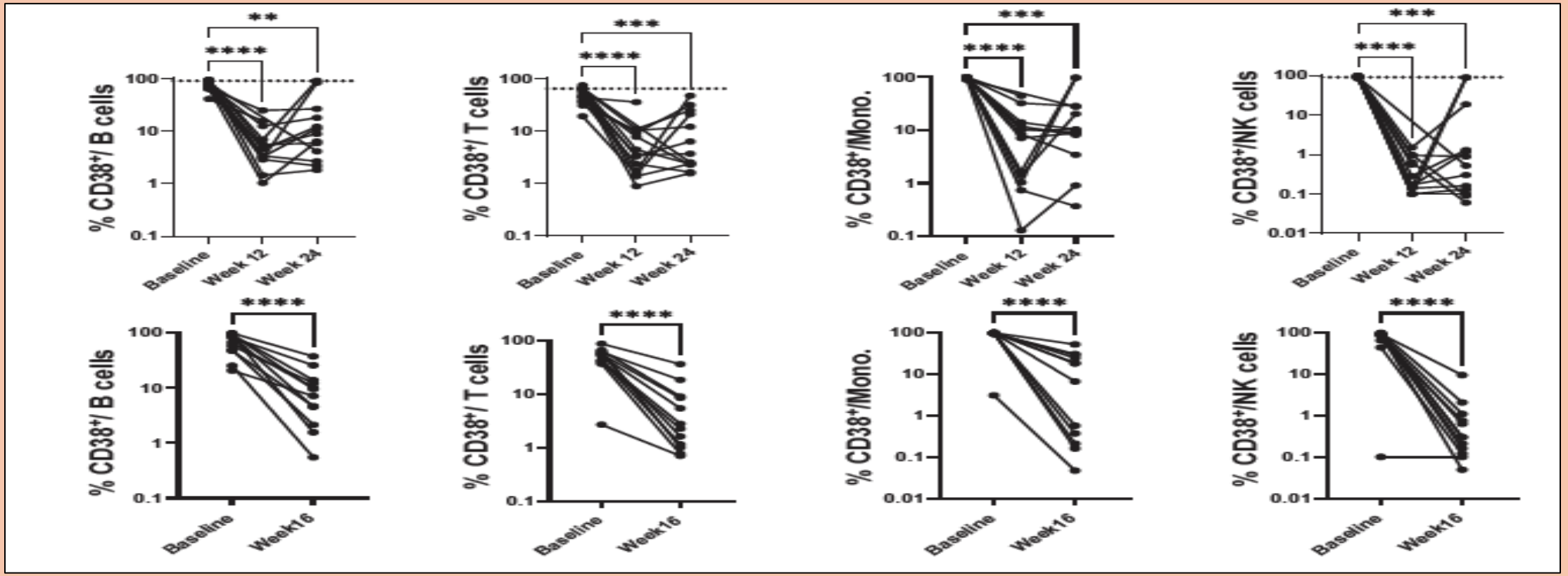


After treatment the surface expression of CD38 on immune cells decreased markedly

The expression of CD32b (an inhibitory Fcγ Receptor) on the remaining monocytes was substantially lower after the first treatment than before treatment

Chen et al. N Engl J Med 2024;390:2178-90

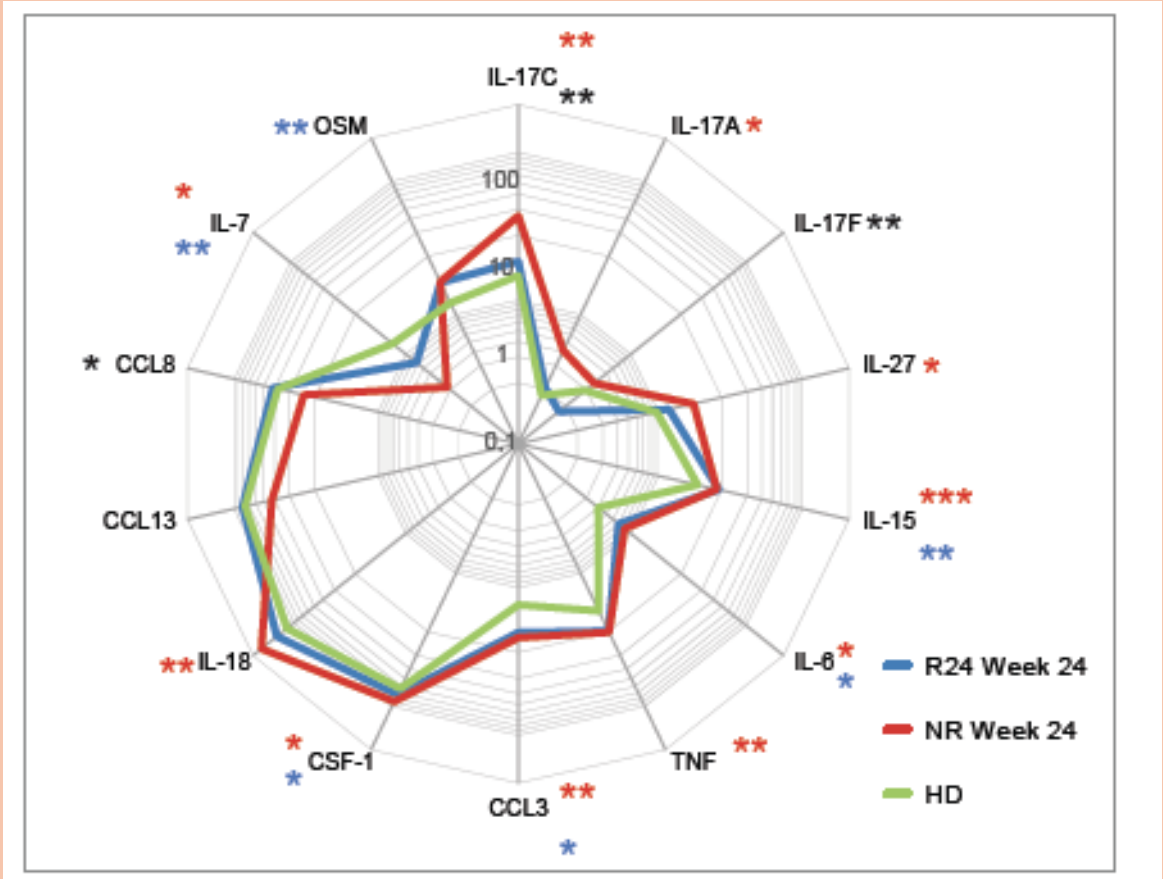
Depletion and re-emergence of CD38+cells after treatment with daratumumab



From the DART study - unpublished

Daratumumab non-responders demonstrated a pro-inflammatory environment characterized by elevated Th17 cytokines

- NR patients exhibited a pronounced pro-inflammatory signature (IL-6, IL-18, TNF, IL-27, IL-15, and CSF-1, a nd Th17-related cytokines.
- IL-17F and IL-17C distinguished NR from R24 at baseline

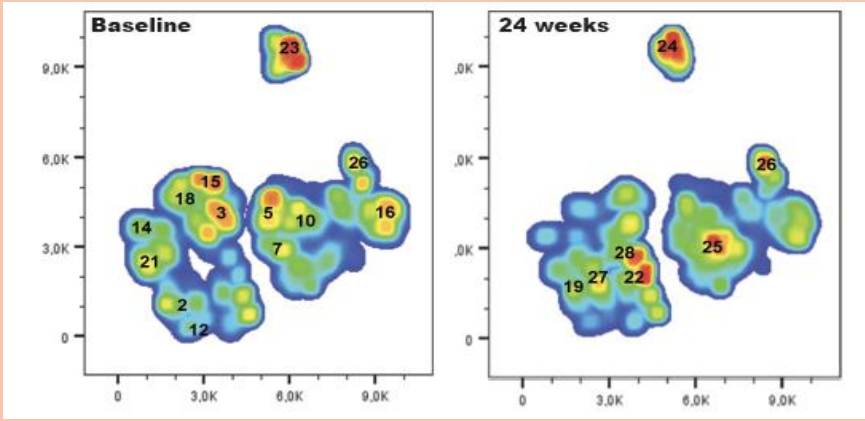


From the DART study - unpublished

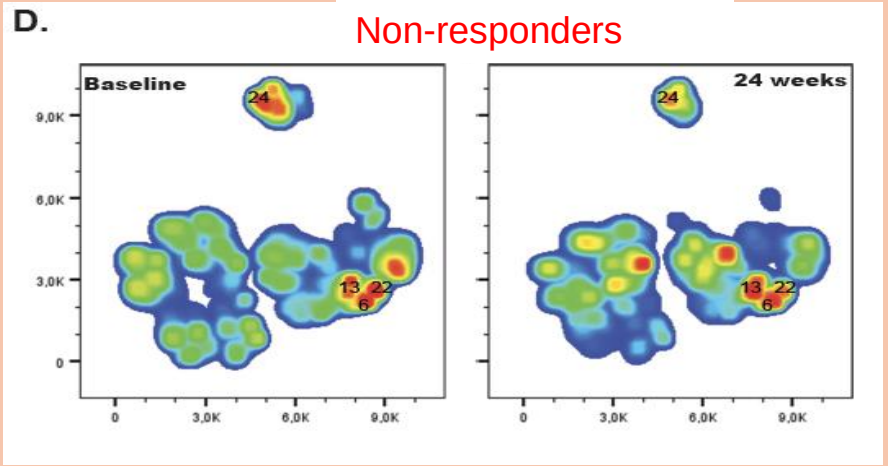
A specific B-cell signatures suggest the persistence of auto-reactive memory B cells in non-responders

- Cluster 24, defined by high CD10 and CD24 expression with low CD20 and CD21 levels, corresponded to immature B cells was present at baseline in NR
- The lack of CD38 expression in cluster 24 may render them resistant to daratumumab

Responders



- Clusters 6, 13, and 22, which were enriched in NR
- Expression of CD27, CD138, and IgG in these clusters suggests a memory antibody-secreting cell phenotype



From the DART study - unpublished

High-dimensional analysis by spectral flow cytometry of B cells

Summary of anti-CD38

- Effective and well tolerated.
- Rapid response
- Response rates during treatment or following the last injection ranges between 60-95%.
- Long-term response remains unknown.
- Optimal number of infusions need to be explored.
- Several biological changes have been identified.
- We might be close to identifying a biomarker!

Renoir: Bal du Moulin de la Galette