Romiplostim for Chemotherapy-Induced Thrombocytopenia in Colorectal, Gastroesophageal, and Pancreatic Cancers: A Global, Phase 3, Randomized, Placebo-Controlled Trial

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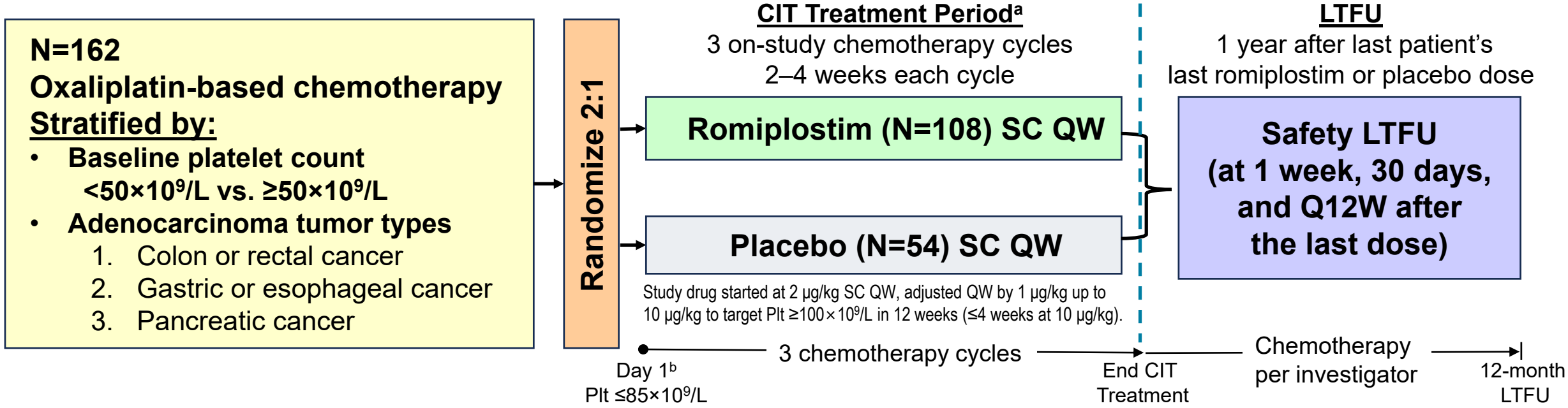
CIT Occurs Frequently in Cancer Treatment and Compromises Patient Outcomes

- Full-dose on-time chemotherapy correlates with improved outcomes.[1]
- CIT is often managed by chemotherapy changes that lower RDI, possibly compromising outcomes.[2-4]
  - There are no widely available approved agents for CIT.
  - Platelet transfusions have limited availability, transient benefits, and infusion risks.
- The TPO-RA romiplostim has demonstrated acceptable safety and efficacy for CIT.
  - Randomized phase 2 trial: Increased platelet correction rate (93% romiplostim vs. 13% untreated observation)[5]
  - Observational study: 71% platelet response rate[6]
- RECITE is the first phase 3 RCT of romiplostim in persistent CIT in patients with GI cancers being treated with oxaliplatin-based multiagent cytotoxic chemotherapy (NCT03362177).

CIT, chemotherapy-induced thrombocytopenia; GI, gastrointestinal; RCT, randomized controlled trial; RDI, relative dose intensity; TPO-RA, thrombopoietin receptor agonist.

1 Havrilesky LJ et al *Crit Rev Oncol Hematol.* 2015;93:203-210; 2 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Hematopoietic Growth Factors. 2025; 3 Wu Y et al *Clin Ther.* 2009;31:2416-2432; 4 Al-Samkari H, Soff GA. *Expert Rev Hematol.* 2021;14:437-448; 5 Soff GA et al *J Clin Oncol.* 2019;37:2892-2898; 6 Al-Samkari H et al *Haematologica.* 2021;106:1148-1157.

RECITE: A Global, Phase 3, Randomized, Placebo-Controlled Trial of Romiplostim for CIT



Eligible adults in this phase 3 RCT had ≥3 remaining planned chemotherapy cycles[c] and:

- Any stage or line of therapy in adjuvant or advanced setting
- Persistent CIT: platelet count ≤85×10⁹/L on study day 1[b]

Excluded were patients with:

- Thrombocytopenia from other causes
- Hemoglobin <8 g/dL or ANC <1×10⁹/L on study day 1
- Past / current hematological malignancy
- Past arterial thrombosis or cardiac / CV abnormalities in the past 4 months

ANC, absolute neutrophil count; CIT, chemotherapy-induced thrombocytopenia; CV, cardiovascular; LTFU, long-term follow-up; Plt, platelet count; QW, weekly; Q12W, every 12 weeks; RCT, randomized controlled trial; SC, subcutaneous. [a]Patients not achieving platelet counts deemed safe to proceed with chemotherapy after 12 doses were taken off treatment and entered LTFU. [b]At end of a chemotherapy cycle despite time to recover; previous cycle day 14-21 depending on regimen. [c]5-fluorouracil or capecitabine and oxaliplatin, ie, FOLFOX, CAPEOX, FOLFIRINOX, or FOLFOXIRI.

Study Endpoints and Hierarchical Evaluation

Hypothesis: Romiplostim will raise platelet counts faster than placebo, resulting in more full-dose on-time chemotherapy delivery in patients with CIT and decreasing bleeding and platelet transfusions.

Primary endpoint: no dose modification (reduction, delay, omission, or discontinuation) of any myelosuppressive agent due to CIT in second and/or third planned chemotherapy cycles; CIT defined as platelet counts $<100\times10^9$/L per independent blinded adjudication committee (oncologists, biostatistician).

- Secondary efficacy endpoints hierarchical evaluation[a]:
  1) Platelet nadir while on study treatment
  2) Time to platelet response ($\geq100\times10^9$/L, no platelet transfusions the preceding 7 days)
  3) Duration-adjusted rate of grade ≥2 bleeding events per CTCAE v5.0
  4) Overall survival
  5) Platelet transfusion
  6) Platelet response day 1 to week 4
- Secondary safety endpoints

CIT, chemotherapy-induced thrombocytopenia; CTCAE, Common Terminology Criteria for Adverse Events.
[a]Hierarchical evaluation was to preserve significance: if romiplostim demonstrated superiority for the primary endpoint, then the first secondary endpoint was tested, then the second, etc.

Baseline Demographics

Characteristic	Placebo (N = 56)				Romiplostim (N = 109)			
Sex, male	36 (64)				63 (58)			
Age, median (min, max), years	62 (35, 81)				64 (34, 84)			
Race								
Caucasian	54 (96)				94 (86)			
Black	2 (4)				4 (4)			
Other[a]	0 (0)				11 (10)			
Ethnicity, Hispanic	11 (20)				28 (26)			
Platelet count, median (min, max) $\times 10^9$/L	67 (8, 84)				70 (16, 85)			
Platelet count								
$<50\times10^9$/L	6 (11)				12 (11)			
$\geq50\times10^9$/L	50 (89)				97 (89)			
Thrombocytopenia grade	Gr 1	Gr 2	Gr 3	Gr 4	Gr 1	Gr 2	Gr 3	Gr 4
% of patients	14	75	7	4	30	59	9	2
Prior bleeding	3 (5)				6 (6)			

Gr, grade. Data are n (%) unless indicated otherwise. [a]Other was reported as mestizo/mixed race (n = 7), Hispanic (n = 2), and Latin (n = 1).

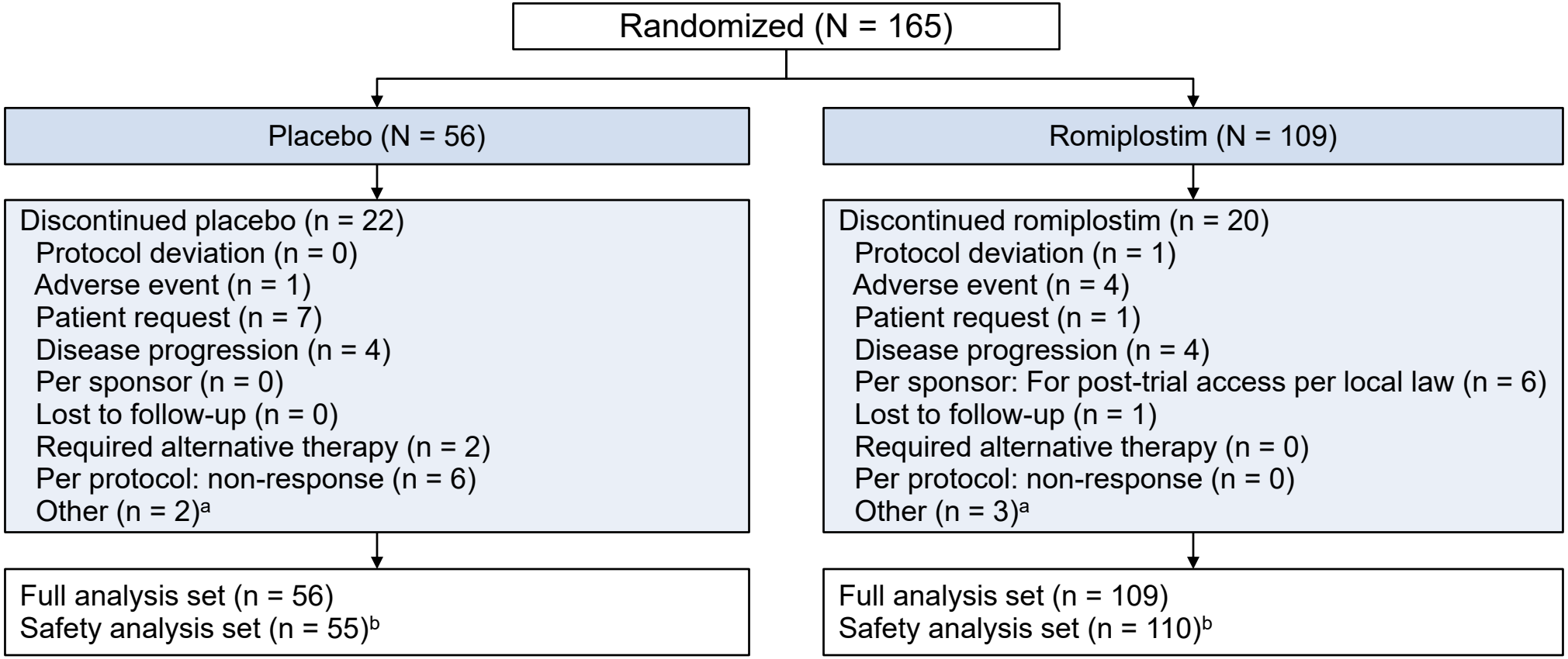
Baseline Disease Characteristics

Characteristic	Categories	Placebo (N = 56)	Romiplostim (N = 109)
Tumor type	Colorectal	42 (75)	82 (75)
	Gastroesophageal	7 (13)	14 (13)
	Pancreatic	7 (13)	13 (12)
Disease stage	1	0 (0)	1 (1)
	2	4 (7)	4 (4)
	3	14 (25)	23 (21)
	4	**34 (61)**	**78 (72)**
	Recurrent	4 (7)	2 (2)
Chemotherapy regimen	CAPEOX	10 (18)	23 (21)
	FOLFIRINOX / FOLFOXIRI	7 (13)	15 (14)
	FOLFOX	37 (66)	71 (65)
Eastern Cooperative Oncology Group (ECOG) PS			
0		33 (59)	51 (47)
1		**23 (41)**	**58 (53)**
Line of chemotherapy			
<2		43 (77)	78 (72)
≥2		**12 (21)**	**30 (28)**
Cycles of chemotherapy			
≤2		7 (13)	15 (14)
>2		48 (86)	91 (84)
Prior bevacizumab use		**11 (20)**	**38 (35)**
Concurrent bevacizumab use		**8 (14)**	**27 (25)**

CIT, chemotherapy-induced thrombocytopenia; PS, performance status. Data are n (%).

- A higher proportion of patients receiving romiplostim vs. placebo had stage 4 disease, ECOG PS >0, ≥2 prior lines, and prior or concurrent bevacizumab use.
- These observed differences are more closely associated with impact on overall cancer outcomes than impact on CIT.

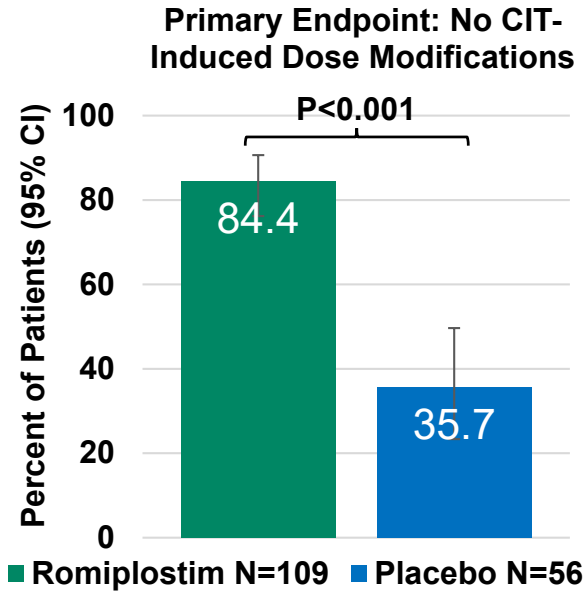
Patient Flow and Disposition

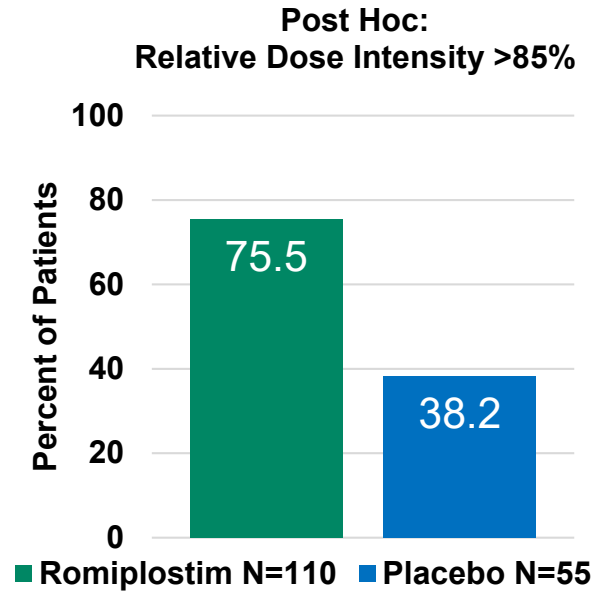


- Study drug completion rate was higher with romiplostim than with placebo (82% vs. 61%).
- Frequent reasons for discontinuation included per patient (romiplostim: 1%, placebo: 13%) and non-response (0% vs. 11%).

[a]Other: for placebo consent withdrawn (n=1), COVID-19 control measures (n=1), for romiplostim: per investigator (n=1), on commercial supply (n=1), and hospitalization (n=1). [b]Two patients randomized to romiplostim also received placebo and one patient randomized to placebo also received romiplostim; all three patients are included in the romiplostim safety analysis set of 110.

RECITE Met its Primary Endpoint: Romiplostim Reduced Chemotherapy Modifications Due to CIT





Primary Endpoint: Chemotherapy dose modifications were reduced with romiplostim (84.4% vs. 35.7%, **OR 10.2**; 95% CI 4.44–23.72; P<0.001).

Post Hoc: More romiplostim-treated patients achieved RDI >85%, which is associated with improved outcomes.[1]

- Median (IQR) **RDI was 98% (88–100) with romiplostim vs. 77% (56–98) with placebo** across the 3 planned cycles.

CI, confidence interval; CIT, chemotherapy-induced thrombocytopenia; IQR, interquartile range; OR, odds ratio; RDI, relative dose intensity. In these post hoc analyses over all 3 cycles, RDI was defined as actual dose intensity (actual dose received / actual dose duration) / planned dose intensity (planned dose / planned dose duration). 1 Havrilesky LJ et al *Crit Rev Oncol Hematol.* 2015;93:203-210.

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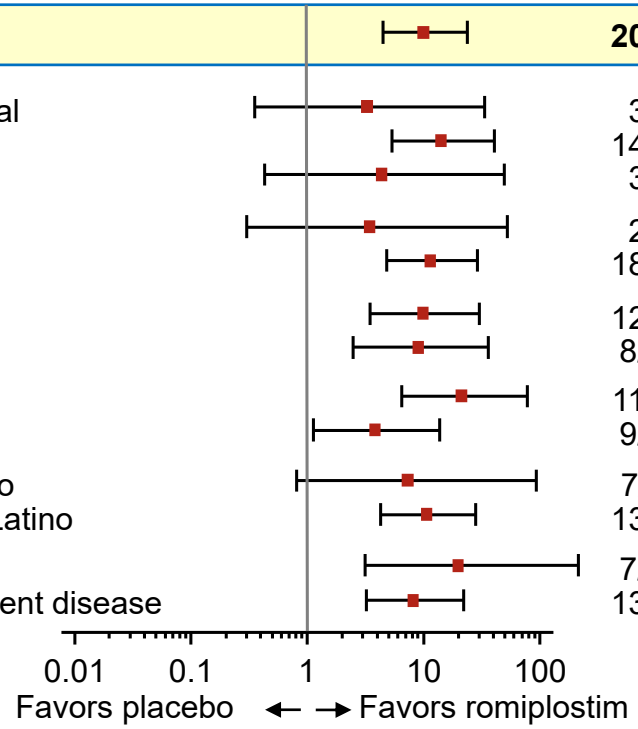
Romiplostim Reduced CIT-Induced Chemotherapy Dose Modifications Across Relevant Subgroups Consistent with the Primary Endpoint



Subgroup		Placebo N = 56	Romiplostim N = 109	Odds Ratio	95% CI	
All patients		**20/56 (35.7)**	**92/109 (84.4)**	**10.2**	**4.44–23.72**	**P<0.001**
Stratification: Tumor type	Gastroesophageal	3/7 (42.9)	10/14 (71.4)	3.3	0.35–33.02	
	Colorectal	14/42 (33.3)	72/82 (87.8)	14.4	5.26–40.39	
	Pancreatic	3/7 (42.9)	10/13 (76.9)	4.4	0.42–48.69	
Stratification: Platelet count	<50×10^9/L	2/6 (33.3)	7/11 (63.6)	3.5	0.30–51.98	
	≥50×10^9/L	18/50 (36.0)	85/98 (86.7)	11.6	4.76–28.81	
Age group	≤65 years	12/34 (35.3)	55/65 (84.6)	10.1	3.45–30.07	
	>65 years	8/22 (36.4)	37/44 (84.1)	9.3	2.45–35.98	
Sex	Male	11/36 (30.6)	57/63 (90.5)	21.6	6.46–77.08	
	Female	9/20 (45.0)	35/46 (76.1)	3.9	1.11–13.64	
Ethnicity	Hispanic or Latino	7/11 (63.6)	26/28 (92.9)	7.4	0.81–91.99	
	Not Hispanic or Latino	13/45 (28.9)	66/81 (81.5)	10.8	4.27–27.90	
Disease stage	Stage 1-3	7/18 (38.9)	26/28 (92.9)	20.4	3.11–212.26	
	Stage 4 or recurrent disease	13/38 (34.2)	65/80 (81.3)	8.3	3.20–21.96	

Benefit was consistent in relevant subgroups, including those shown and by treatment line (<2, ≥2), number of previous chemotherapy cycles (≤2, >2), chemotherapy regimens, and prior or concurrent bevacizumab use (yes or no).

CI, confidence interval; CIT, chemotherapy-induced thrombocytopenia. Data in placebo and romiplostim columns are n/N (%).

Hierarchical Analysis of Secondary Endpoints

	Placebo (N = 56)	Romiplostim (N = 109)	P-value
Platelet count nadir, median (min, max), $\times 10^9$/L	58 (22, 95)	87 (14, 167)	0.005
Platelet response rate, n (%)	43 (77)	106 (97)	
Median time to response, median (95% CI), weeks	2.1 (1.1–3.0)	1.1 (NE)	<0.001
Duration-adjusted grade ≥2 bleeding events per 100 patient-years	7.6	4.0	
Hazard ratio for romiplostim vs. placebo (95% CI)	0.53 (0.04–6.77)		0.63

- With romiplostim, there was a significantly higher platelet count nadir and faster median to time to response.
- Patients on the romiplostim arm had a numerically lower duration-adjusted grade ≥2 bleeding rate, but the difference was not statistically significant, so no further testing could be performed.[a]

Descriptive results not evaluated for statistical significance[a]	Placebo (N = 56)	Romiplostim (N = 109)
OS: Events through 12 months of long-term follow-up	44.6% (25/56)	53.2% (58/109)
Platelet transfusion rates	0%	1.8%
Platelet response by week 4	66.1%	96.3%

CI, confidence interval; NE, not estimable; OS, overall survival. Platelet response = platelet count ≥100×10^9/L without platelet transfusions past 7 days.
[a]Based on per-protocol hierarchical testing of endpoints.

No New Safety Signals; Adverse Events were Consistent with Chemotherapy

Adverse events, n (%)	Placebo (N = 55)[a]		Romiplostim (N = 110)[a]	
	All	Treatment Related	All	Treatment Related
All	34 (62)	4 (7)	96 (87)	13 (12)
Grade ≥3	12 (22)	2 (4)	41 (37)	3 (3)
Serious	3 (6)	0 (0)	23 (21)	0 (0)
Leading to D/C of study drug	1 (2)	0 (0)	3 (3)	0 (0)
Leading to D/C of chemotherapy	1 (2)	0 (0)	7 (6)	0 (0)
Fatal	0 (0)	0 (0)	2 (2)	0 (0)
Most common	All	Grade ≥3	All	Grade ≥3
Thrombocytopenia	11 (20)	4 (7)	22 (20)	9 (8)
Neutropenia	8 (15)	4 (7)	21 (19)	9 (8)
Anemia	5 (9)	1 (2)	16 (15)	6 (6)
Most frequent treatment-related				
Nausea	1 (2)		2 (2)	
Headache	0 (0)		2 (2)	
Thromboembolic events	0 (0)		2 (2)[b]	
Myelodysplastic syndrome	0 (0)		1 (1)	
Secondary malignancies	3 (6)		2 (2)	

AE, adverse event; D/C, discontinuation. Data are n (%). Most common ≥15% any group. [a]Two patients randomized to romiplostim also received placebo and one patient randomized to placebo also received romiplostim; all three patients are included in the romiplostim safety analysis set of 110. [b]Both patients with thromboembolic events had colorectal cancer: one had portal vein thrombosis and one had splenic infarct.

- **No treatment-related serious AEs or treatment-related AEs leading to death or D/C of romiplostim, placebo, or chemotherapy were observed in either arm.**
- The AE profile was consistent with the chemotherapy regimens patients received.

Study Limitations

- This study was primarily designed to evaluate the impact of romiplostim on chemotherapy dose modifications by treating CIT during 3 chemotherapy cycles. Treatment during LTFU with chemotherapy and other agents was per investigator and not recorded.
- The study population spanned tumor types, stages, and treatment lines, all factors that may impact chemotherapy outcomes. Stratification by baseline platelet count and tumor type was to evaluate chemotherapy modification (ie, primary endpoint).
- Infrequency of grade ≥2 bleeding events in both arms limited the ability to detect a statistically significant difference.

CIT, chemotherapy-induced thrombocytopenia; LTFU, long-term follow-up.

RECITE Phase 3 RCT of Romiplostim for CIT in GI Cancers

- This study met its primary endpoint: **more patients avoided chemotherapy dose modifications** with romiplostim vs. placebo (**84.4% vs. 35.7%, OR 10.2**; 95% CI 4.44-23.72; P<0.001).
- Romiplostim resulted in significantly **higher platelet count nadirs** and **faster median time to response**, along with a numerically lower rate of grade ≥2 bleeding.
- More patients receiving romiplostim had **RDI >85%: 75.5% vs. 38.2%** in a post hoc analysis.
- Romiplostim was **well tolerated in a highly comorbid population**, with no treatment-related serious AEs or treatment-related AEs leading to death or D/C of romiplostim or chemotherapy.

Romiplostim may be considered for the treatment of CIT in patients receiving oxaliplatin-based chemotherapy for GI malignancies to support full-dose on-time chemotherapy.

The phase 3 PROCLAIM study of romiplostim for CIT in NSCLC, breast, and ovarian cancer is ongoing (NCT03937154).

AE, adverse event; CI, confidence interval; CIT, chemotherapy-induced thrombocytopenia; D/C, discontinuation; GI, gastrointestinal; NSCLC, non-small cell lung cancer; OR, odds ratio; RCT, randomized controlled trial; RDI, relative dose intensity. RDI is calculated as percent of intended chemotherapy, ie actual / planned chemotherapy.

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