Supplementary Information

Thrombopoietin Receptor Agonists for Chemotherapy-Induced Thrombocytopenia: A Systematic Review and Network Meta-analysis

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Table S1. Database-specific search strategies and records retrieved for trials of chemotherapy-induced thrombocytopenia

Database	Search strategy	Records retrieved
PubMed	"chemotherapy-induced thrombocytopenia" OR "chemotherapy induced thrombocytopenia" OR (thrombocytopenia AND (chemotherapy OR chemotherapeutic OR antineoplastic)) AND (romiplostim OR eltrombopag OR avatrombopag OR hetrombopag OR lusutrombopag OR "thrombopoietin receptor agonist" OR "thrombopoietin receptor agonists" OR "thrombopoietin mimetic" OR "thrombopoietin mimetics" OR thrombopoietin) AND (randomized OR randomised OR placebo OR trial	709
Embase	('chemotherapy induced thrombocytopenia'/exp OR 'chemotherapy induced thrombocytopenia':ti,ab,kw OR 'chemotherapy-induced thrombocytopenia':ti,ab,kw OR (thrombocytopenia:ti,ab,kw AND (chemotherapy:ti,ab,kw OR chemotherapeutic*:ti,ab,kw OR antineoplastic*:ti,ab,kw)) AND (romiplostim:ti,ab,kw OR eltrombopag:ti,ab,kw OR avatrombopag:ti,ab,kw OR hetrombopag:ti,ab,kw OR lusutrombopag:ti,ab,kw OR 'thrombopoietin receptor agonist':ti,ab,kw OR 'thrombopoietin receptor agonists':ti,ab,kw OR 'thrombopoietin mimetic':ti,ab,kw OR 'thrombopoietin mimetics':ti,ab,kw OR thrombopoietin:ti,ab,kw) AND ('randomized controlled trial'/exp OR random*:ti,ab,kw OR placebo:ti,ab,kw OR trial:ti,ab,kw) AND [humans]/lim	605
Cochrane CENTRAL	#1 ("chemotherapy-induced thrombocytopenia" OR "chemotherapy induced thrombocytopenia" OR (thrombocytopenia AND (chemotherapy OR chemotherapeutic* OR antineoplastic*)):ti,ab,kw #2 (romiplostim OR eltrombopag OR avatrombopag OR hetrombopag OR lusutrombopag OR "thrombopoietin receptor agonist" OR "thrombopoietin receptor agonists" OR "thrombopoietin mimetic" OR "thrombopoietin mimetics" OR thrombopoietin):ti,ab,kw #3 (random* OR placebo OR trial):ti,ab,kw #4 #1 AND #2 AND #3	144
Web of Science	("chemotherapy-induced thrombocytopenia" OR "chemotherapy induced thrombocytopenia" OR (thrombocytopenia NEAR/5 (chemotherapy OR chemotherapeutic* OR antineoplastic*)) AND (romiplostim OR eltrombopag OR avatrombopag OR hetrombopag OR lusutrombopag OR "thrombopoietin receptor agonist" OR "thrombopoietin receptor agonists" OR "thrombopoietin mimetic" OR "thrombopoietin mimetics" OR thrombopoietin) AND (random* OR placebo OR trial)	113

Table S2. Risk ratios for thrombocytopenia in the network meta-analysis

Avatrombopag	0.56 [0.30; 1.07]	.	.	.	.
0.56 [0.30; 1.07]	Placebo	.	0.97 [0.51; 1.86]	0.62 [0.23; 1.71]	0.30 [0.01; 7.11]
0.55 [0.22; 1.39]	0.97 [0.50; 1.91]	Observation	1.00 [0.83; 1.21]	.	.
0.55 [0.22; 1.36]	0.97 [0.51; 1.86]	1.00 [0.83; 1.21]	Romiplostim	.	.
0.35 [0.11; 1.16]	0.62 [0.23; 1.71]	0.64 [0.19; 2.16]	0.64 [0.19; 2.13]	Eltrombopag	.
0.17 [0.01; 4.27]	0.30 [0.01; 7.11]	0.31 [0.01; 7.85]	0.31 [0.01; 7.80]	0.48 [0.02; 13.34]	Hetrombopag

Table S3. CINeMA assessment of certainty of evidence for direct comparisons of TPO-RAs versus placebo

Outcome	Comparison	RR (95% CI)	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Overall certainty
Chemotherapy delay or dose reduction	Romiplostim vs placebo	0.26 (0.13–0.51)	Some concerns	Undetected	No concerns	No concerns	Not estimable	Not estimable	Moderate
	Eltrombopag vs placebo	0.57 (0.39–0.82)	Some concerns	Undetected	No concerns	No concerns	Not estimable	Not estimable	Moderate
	Hetrombopag vs placebo	0.53 (0.32–0.88)	Some concerns	Undetected	No concerns	Some concerns	Not estimable	Not estimable	Low
	Avatrombopag vs placebo	0.92 (0.46–1.84)	Some concerns	Undetected	No concerns	Major concerns	Not estimable	Not estimable	Low
Platelet transfusion	Romiplostim vs placebo	0.12 (0.04–0.40)	Some concerns	Undetected	No concerns	Some concerns	Not estimable	Not estimable	Moderate
	Hetrombopag vs placebo	0.29 (0.13–0.68)	Some concerns	Undetected	No concerns	Some concerns	Not estimable	Not estimable	Low
	Eltrombopag vs placebo	0.99 (0.39–2.53)	Some concerns	Undetected	No concerns	Major concerns	Not estimable	Not estimable	Low
	Avatrombopag vs placebo	0.77 (0.22–2.74)	Some concerns	Undetected	No concerns	Major concerns	Not estimable	Not estimable	Low
Any adverse event	Romiplostim vs placebo	0.69 (0.49–0.96)	Some concerns	Undetected	Some concerns	Some concerns	Not estimable	Not estimable	Low
	Eltrombopag vs placebo	0.99 (0.82–1.20)	Some concerns	Undetected	Some concerns	Some concerns	Not estimable	Not estimable	Low
	Hetrombopag vs placebo	1.00 (0.76–1.30)	Some concerns	Undetected	Some concerns	Some concerns	Not estimable	Not estimable	Low
	Avatrombopag vs placebo	0.96 (0.72–1.28)	Some concerns	Undetected	Some concerns	Some concerns	Not estimable	Not estimable	Low
Serious adverse event	Romiplostim vs placebo	0.25 (0.08–0.81)	Some concerns	Undetected	Some concerns	Some concerns	Not estimable	Not estimable	Low
	Eltrombopag vs placebo	0.63 (0.37–1.07)	Some concerns	Undetected	Some concerns	Some concerns	Not estimable	Not estimable	Low
	Avatrombopag vs placebo	0.91 (0.42–1.98)	Some concerns	Undetected	Some concerns	Major concerns	Not estimable	Not estimable	Low
	Hetrombopag vs placebo	0.37 (0.04–3.35)	Some concerns	Undetected	Some concerns	Major concerns	Not estimable	Not estimable	Very low
Thrombocytopenia	Romiplostim vs placebo	0.55 (0.22–1.36)	Some concerns	Undetected	Some concerns	Major concerns	Not estimable	Not estimable	Low
	Avatrombopag vs placebo	0.56 (0.30–1.07)	Some concerns	Undetected	Some concerns	Some concerns	Not estimable	Not estimable	Low

Table S4. CINeMA assessment of certainty of evidence for indirect comparisons among TPO-Ras

Outcome	Comparisons	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Overall certainty
Chemotherapy delay or dose reduction	All available active-agent comparisons	Some concerns	Undetected	Major concerns	Major concerns	Not estimable	Not assessable	Very low
Platelet transfusion	All available active-agent comparisons	Some concerns	Undetected	Major concerns	Major concerns	Not estimable	Not assessable	Very low
Any adverse event	All available active-agent comparisons	Some concerns	Undetected	Major concerns	Major concerns	Not estimable	Not assessable	Very low
Serious adverse event	All available active-agent comparisons	Some concerns	Undetected	Major concerns	Major concerns	Not estimable	Not assessable	Very low
Thrombocytopenia	All available active-agent comparisons	Some concerns	Undetected	Major concerns	Major concerns	Not estimable	Not assessable	Very low

Figure S1. Flow diagram of study selection

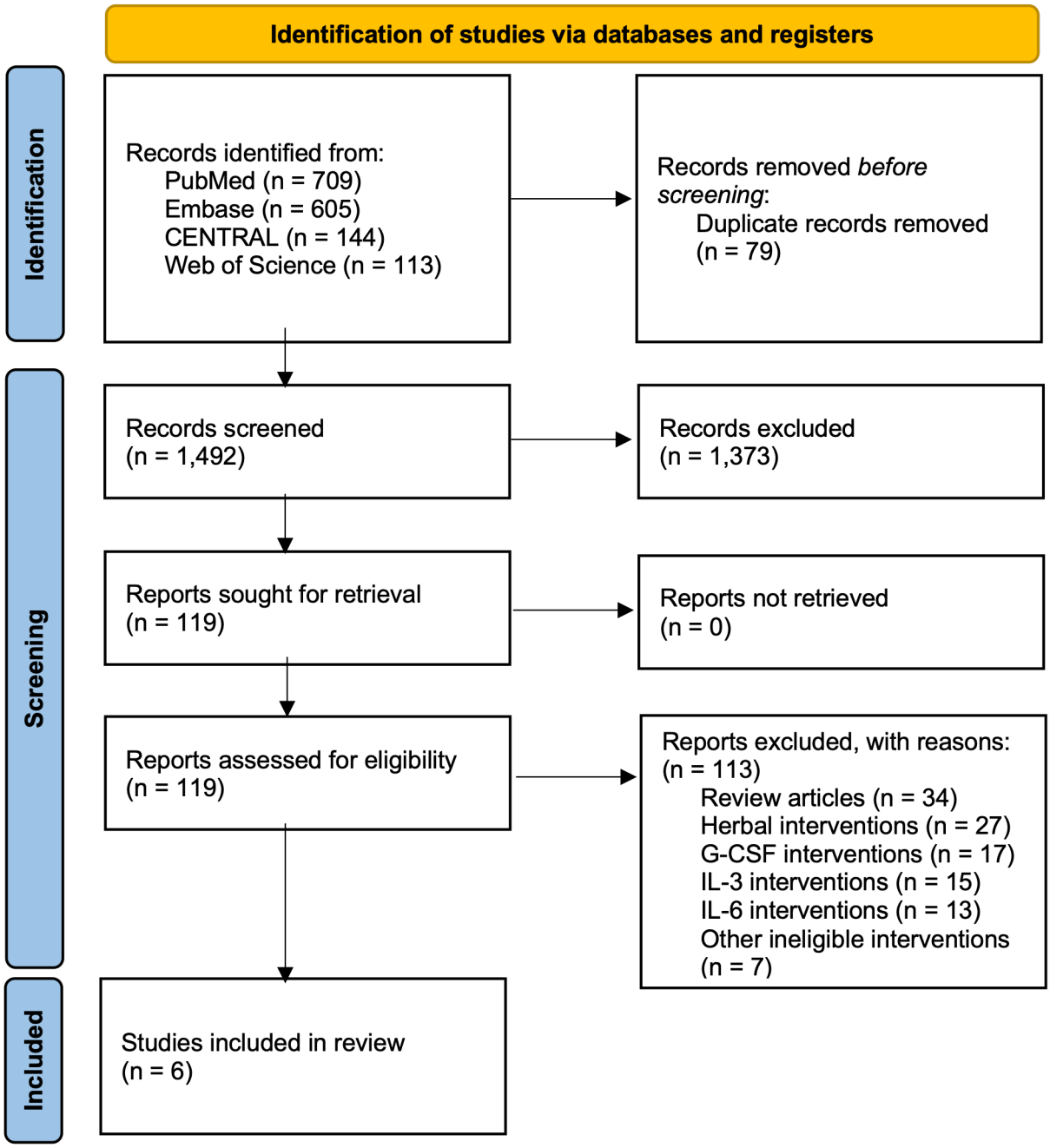


Figure S2. Direct pairwise comparisons for thrombocytopenia

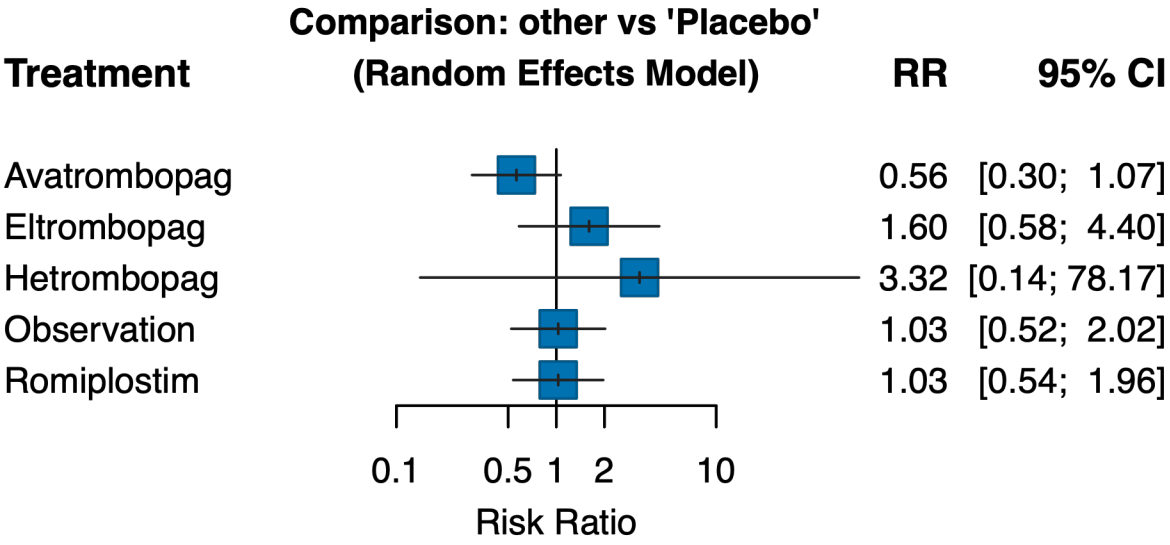


Figure S3. Treatment rankings for thrombocytopenia based on P-scores

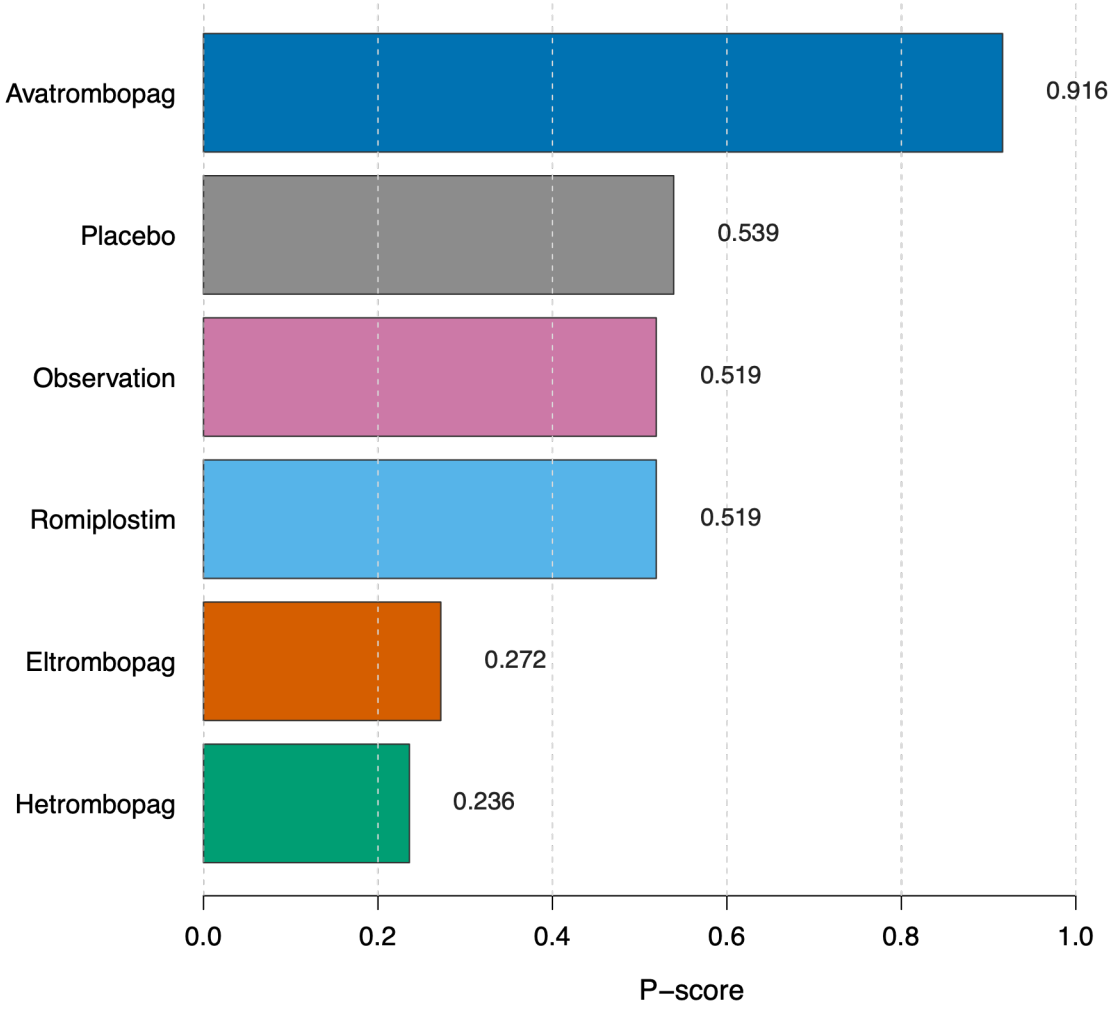


Figure S4. Risk-of-bias assessment by outcome

