Supplementary

Appendix 1 Full search strategy for each database.

(A) PubMed

(A) PubMed†
(“Datopotamab deruxtecan” OR “dato-DXd” OR “DS-1062”) AND (lung)

†No filters were selected in this database

(B) Cochrane

(B) Cochrane†
(“Datopotamab deruxtecan” OR “ dato-DXd” OR ”DS-1062”)

†No filters were selected in this database

(C) Embase

(C) Embase†
(‘datopotamab deruxtecan’/exp OR ‘datopotamab deruxtecan’ OR ‘dato-dxd’/exp OR ‘dato-dxd' OR ‘ds-1062’/exp OR ‘ds-1062’) AND (‘lung’/exp OR lung)

†No filters were selected in this database

(D) ESMO

(D) ESMO†
“Dato-DXd”

†No filters were selected in this database

(E) ASCO

(E) ASCO†
“Datopotamab deruxtecan”

†No filters were selected in this database

https://dx.doi.org/10.21037/jtd-2025-583

Table S1 Main adverse events reported in each study

Study	Toxicity assessment criteria	N	Most common AEs	All grade, N (%)	Grade ≥3, N (%)
TROPION-PanTumor01 (I)	CTCAE v4.03	50[a]	Nausea	24 (48)	0
		50[b]	Nausea	32 (64)	2 (4)
		80[c]	Stomatitis	44 (55)	4 (5)
TROPION-PanTumor02 (II)	NA	40	Nausea	25 (62.5)	NA
			Stomatitis	23 (57.5)	
			Anemia	23 (57.5)	
TROPION-Lung01 (III)	NA	297	Stomatitis	160 (54)	19 (6)
			Nausea	101 (34)	7 (2)
TROPION-Lung02 (IV)	NA	120	Nausea	54 (45)	NA
			Stomatitis	54 (45)	
TROPION-Lung04 (V)	NA	19[d]	Constipation	11 (57.9)	0
		14[e]	Stomatitis	9 (64.3)	1 (7.1)
TROPION-Lung05 (VI)	CTCAE v4.03	137	Nausea	60 (43.7)	2 (1.4)
			Stomatitis	59 (43)	10 (7.2)
			Alopecia	52 (37.9)	0
ICARUS-Lung01 (VII)	NA	100	Stomatitis	49 (49)	10 (10)
			Nausea	45 (45)	0

[a], represents a subgroup on 4 mg/kg Q3W; [b], 6 mg/kg Q3W; [c], 8 mg/kg Q3W; [d], represents cohorts that use datopotamab-deruxtecan (dato-DXd) on 4 mg/kg Q3W; [e], represents cohorts that use dato-DXd on 6 mg/kg.

Table S2 Quality assessment for studies included in this systematic review and meta-analysis using: risk of bias summary for non-randomized studies (ROBINS-I) tool for retrospective cohorts and prospective studies

Study/author	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias judgment
TROPION-PanTumor01	Moderate[a]	Low	Low	Low	Low	Low	Low	Moderate
TROPION-PanTumor02[†]	Moderate[a]	Moderate[b]	Low	Low	Low	Low	Low	Moderate
TROPION-Lung02[†]	Moderate[a]	Low	Low	Low	Low	Low	Low	Moderate
TROPION-Lung04[†]	Moderate[a]	Moderate[b]	Low	Low	Low	Low	Low	Moderate
TROPION-Lung05[†]	Moderate[a]	Low	Low	Low	Low	Low	Low	Moderate
ICARUS-Lung01[†]	Moderate[a]	Low	Low	Low	Low	Low	Low	Moderate

[†], abstract or conference presentations. [a], All non-randomized studies are subject to bias due to confounding factors; [b], Moderate due to limited number of patients.

https://dx.doi.org/10.21037/jtd-2025-583

Table S3 Quality assessment for studies included in this systematic review and meta-analysis using risk-of-bias 2 tool for randomized clinical trials (RoB 2)

Study	Bias from randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the outcomes	Bias in selection of the reported result	Overall risk of bias
TROPION-Lung01	Low	Low	Low	Low	Low	Low

https://dx.doi.org/10.21037/jtd-2025-583

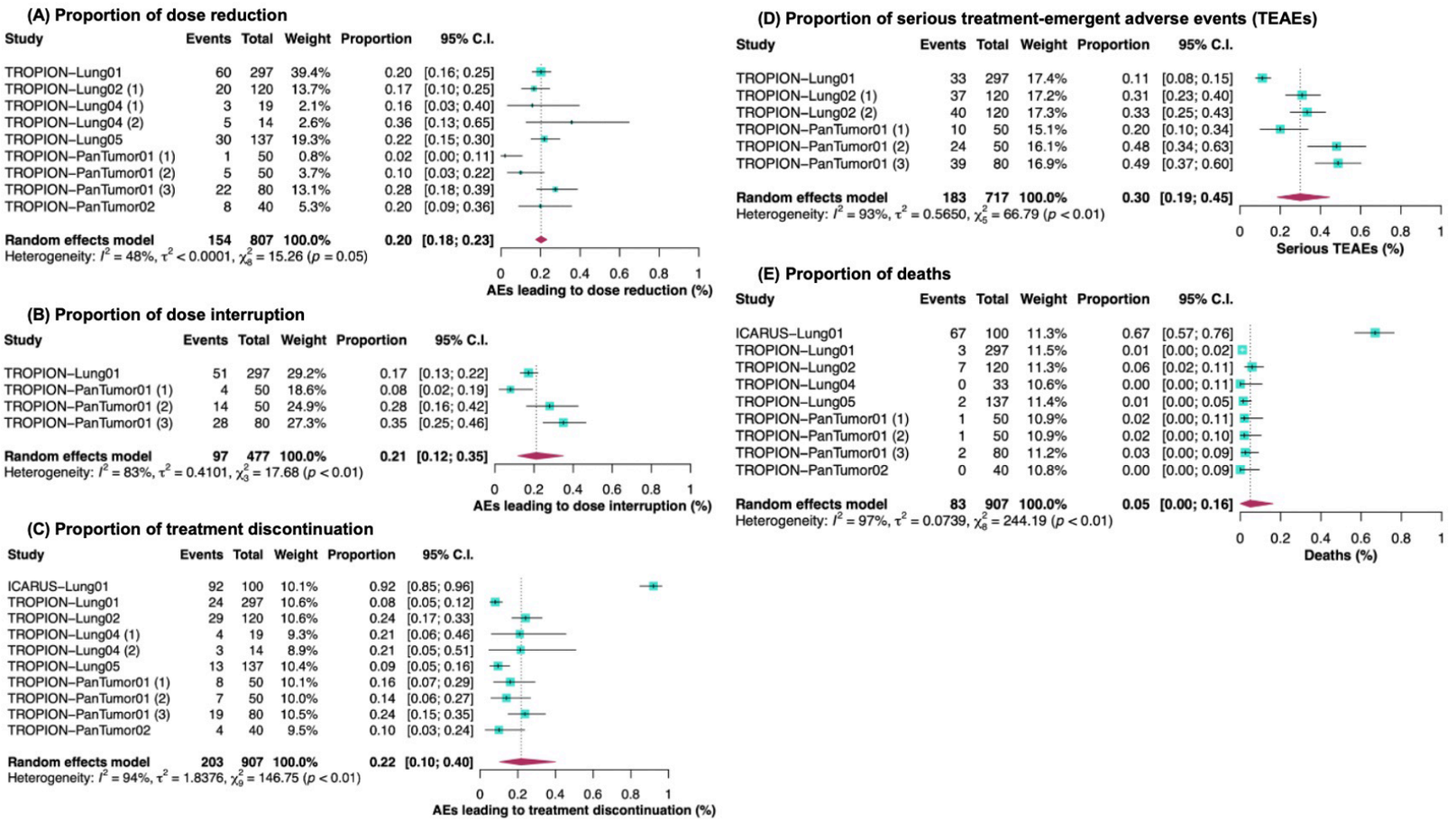

Figure S1 Dose adjustments. (A) Proportion of dose reduction; (B) Proportion of dose interruption; (C) Proportion of treatment discontinuation; (D) Proportion of serious treatment-emergent adverse events (TEAEs); (E) Proportion of deaths.

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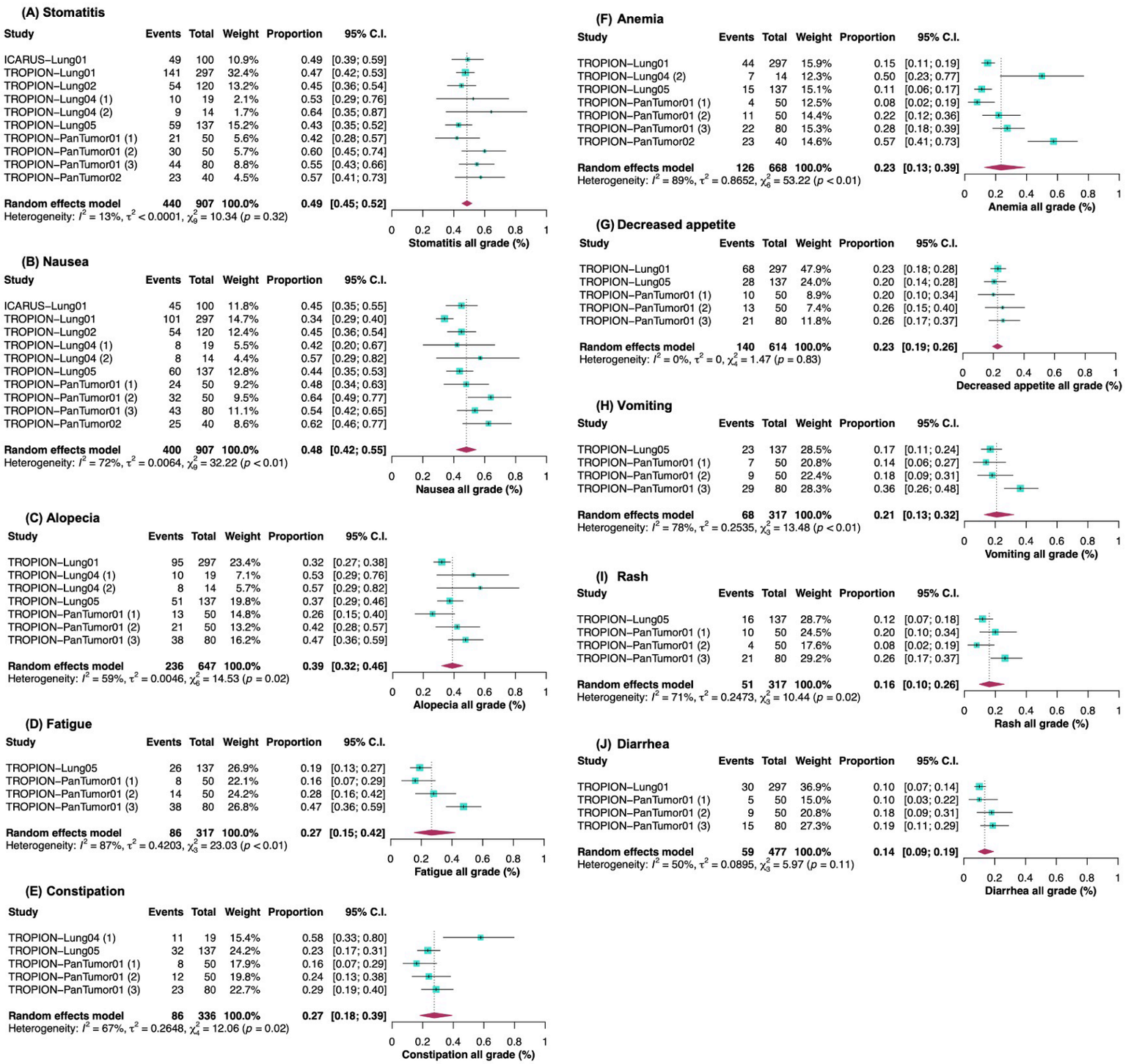

Figure S2 Incidence of all grade adverse events (AEs). (A) Stomatitis; (B) Nausea; (C) Alopecia; (D) Fatigue; (E) Constipation; (F) Anemia; (G) Decreased appetite; (H) Vomiting; (I) Rash; (J) Diarrhea.

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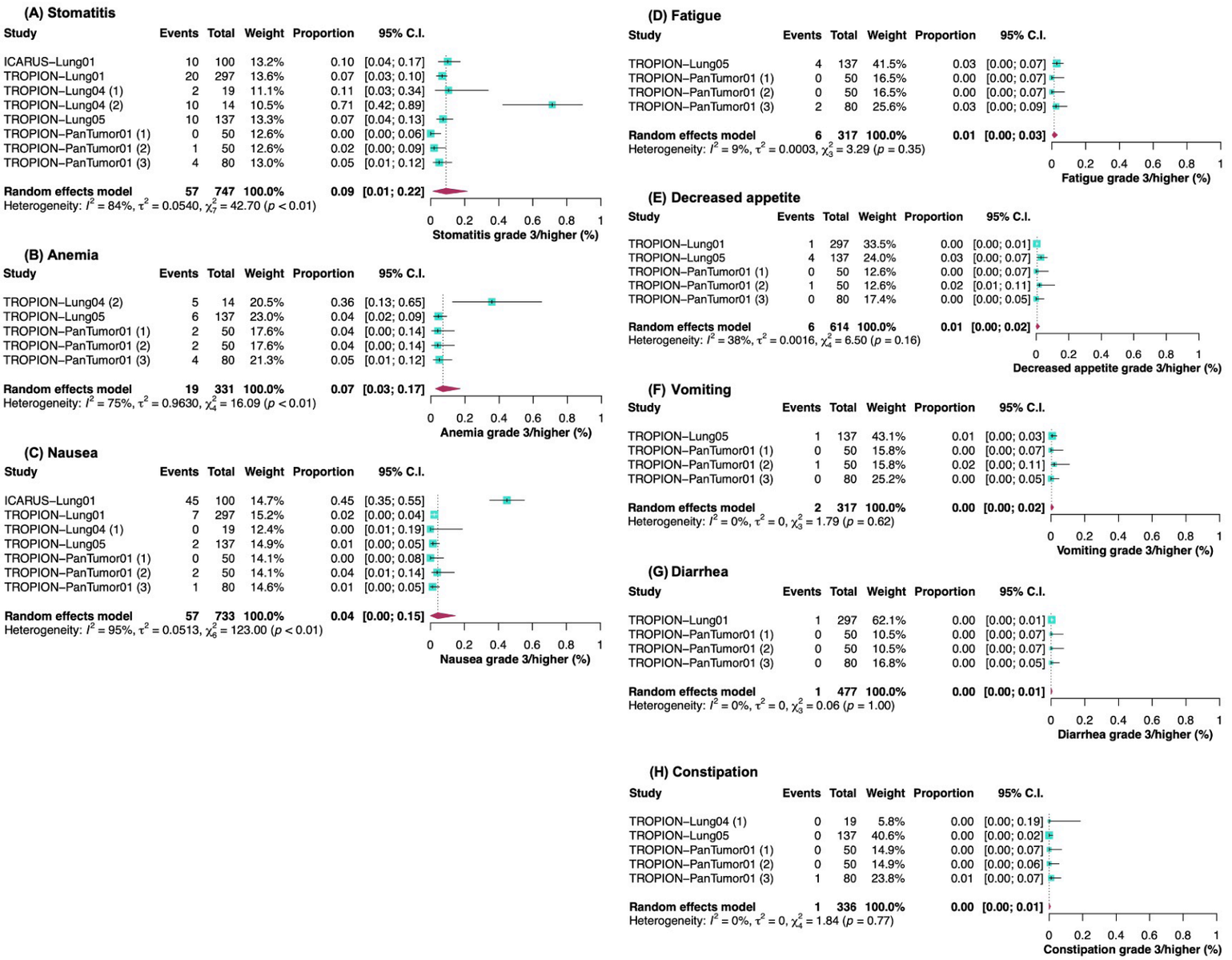

Figure S3 Incidence of Severe Adverse Events (AEs). (A) Stomatitis; (B) Anemia; (C) Nausea; (D) Fatigue; (E) Decreased appetite; (F) Vomiting; (G) Diarrhea; (H) Constipation.

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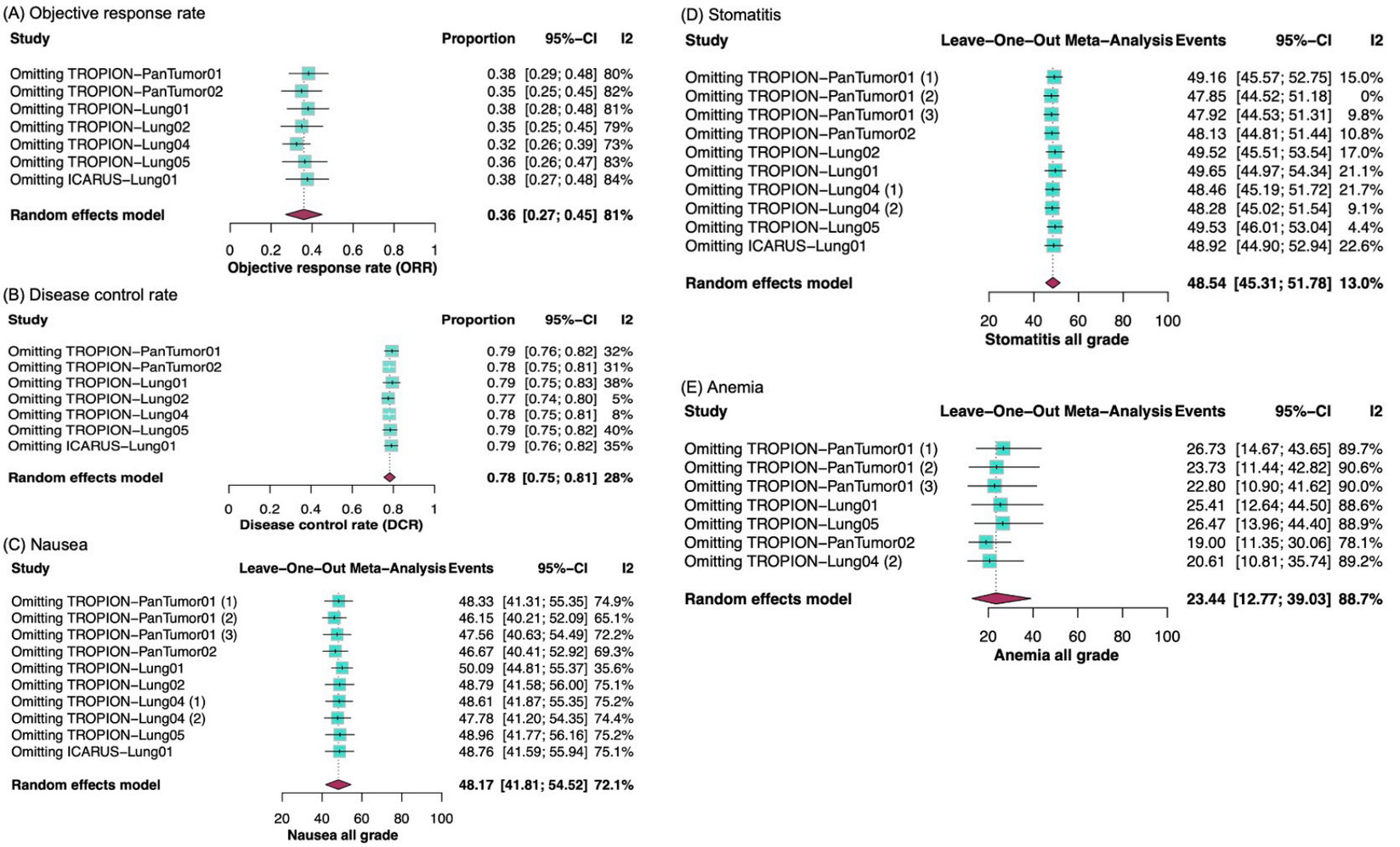

Figure S4 Leave-one-out sensitivity analysis for the ORR, DCR, Nausea, Stomatitis and Anemia. (A) Objective response rate; (B) Disease control rate; (C) Nausea; (D) Stomatitis; (E) Anemia. Proportions of the ORR leaving each study out are represented by a square and the horizontal line crossing the squares indicates the 95% CI. The diamond represents the estimated overall effect of the meta-analysis based on random effects. CI, confidence interval; DCR, disease control rate; ORR, objective response rate.

https://dx.doi.org/10.21037/jtd-2025-583

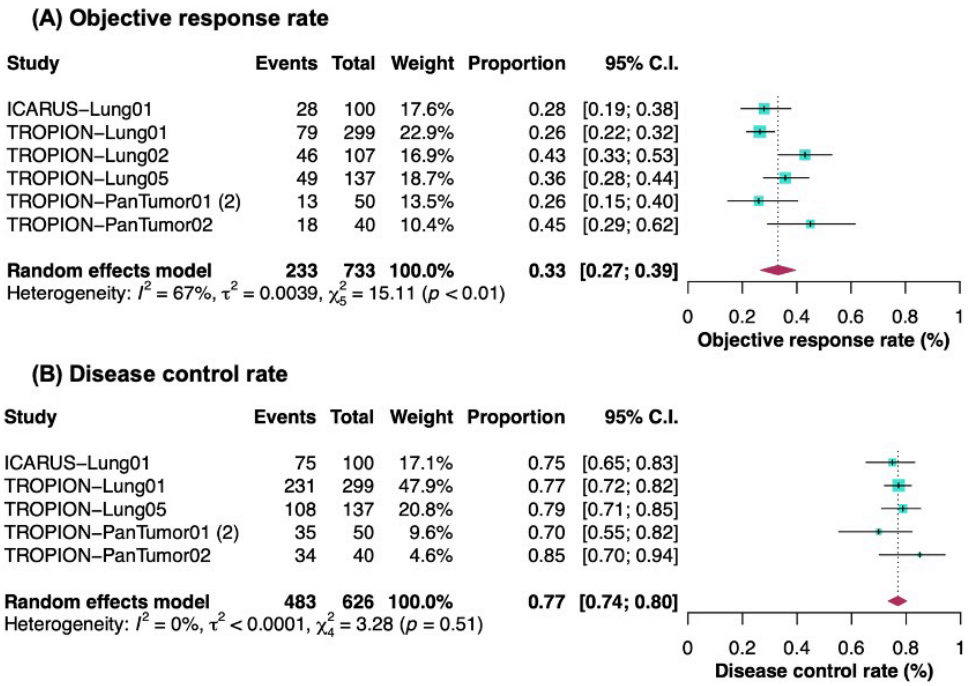

Figure S5 Efficacy of Dato-DXd considering only 6 mg/kg dosing.

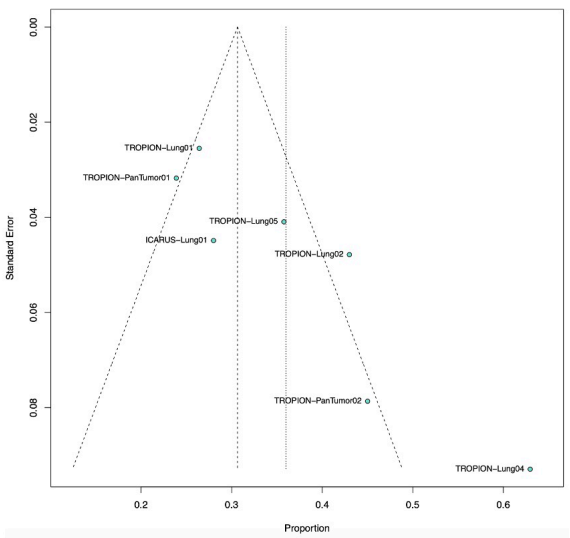

Figure S6 Funnel plot analysis for objective response rate (ORR). The dots represent individual studies, the effect size is represented in the x-axis, and their corresponding error in the y-axis. The central line represents the summary effect estimate; ORR, objective response rate.

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