

REVIEW - SUPPLEMENTARY MATERIAL

Predicting outcomes with pembrolizumab: A meta-analysis of pre-treatment hematological and clinical prognostic factors in advanced/metastatic urothelial carcinoma

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SUPPLEMENTARY METHODS

Table S1.

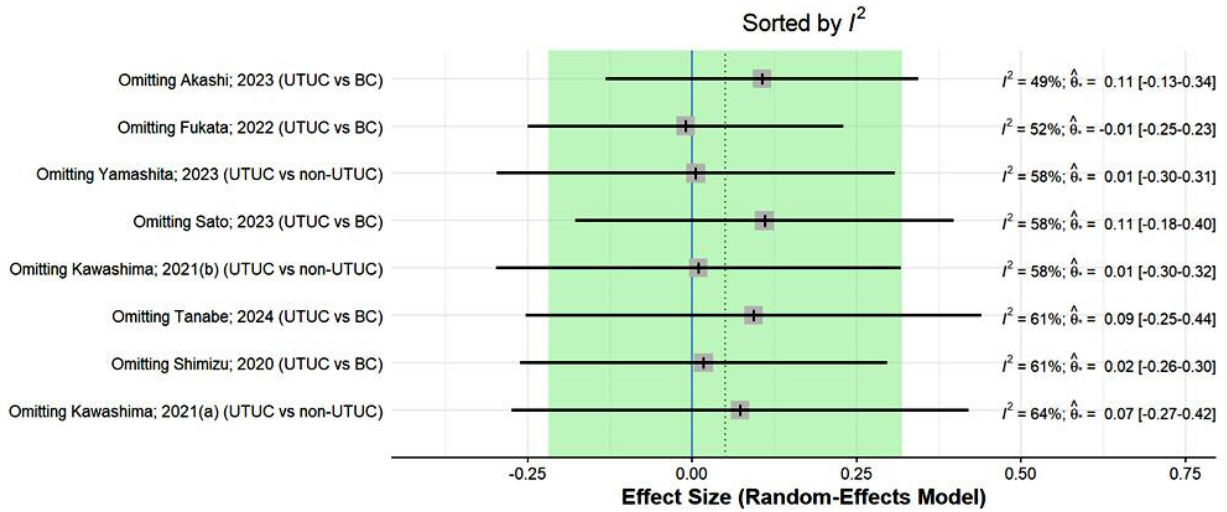
Search strategies.

Database	Keywords
PubMed	#1 (((pembrolizumab) OR (nivolumab)) OR (atezolizumab)) OR (durvalumab) OR (avelumab) #2 (((((((hemoglobins[MeSH Terms]) OR (c reactive protein[MeSH Terms])) OR (lactate dehydrogenase[MeSH Terms])) OR (neutrophil) OR (platelet)) OR (lymphocyte)) OR (hemoglobin)) OR ("NLR")) OR ("PLR")) #3 (urothelial carcinoma) OR (urinary bladder neoplasms[MeSH Terms]) #4 ((#1) AND (#2)) AND (#3))
CENTRAL	#1 MeSH descriptor: [hemoglobins] explode all trees #2 MeSH descriptor: [c reactive protein] explode all trees #3 MeSH descriptor: [lactate dehydrogenase] explode all trees #4 MeSH descriptor: [urinary bladder neoplasms] explode all trees #5 ("pembrolizumab" OR "nivolumab" OR "atezolizumab" OR "durvalumab" OR "avelumab"):ti,ab,kw #6 (("neutrophil" OR "platelet" OR "lymphocyte" OR "NLR" OR "PLR")):ti,ab,kw #7 (("bladder" OR "upper urinary tract" OR "UTUC")):ti,ab,kw #8 #1 OR #2 OR #3 OR #4 #9 #4 OR 7 #10 #5 AND #8 AND #9
ProQuest	("pembrolizumab" OR "nivolumab" OR "atezolizumab" OR "durvalumab" OR "avelumab") AND (MESH("hemoglobins" OR "c reactive protein" OR "lactate dehydrogenase") OR "neutrophil" OR "platelet" OR "lymphocyte" OR "hemoglobin" OR "NLR" OR "PLR") AND ("urothelial carcinoma" OR MESH("urinary bladder neoplasms"))
CINAHL, MEDLINE (via EBSCO)	S1 ("pembrolizumab" OR "nivolumab" OR "atezolizumab" OR "durvalumab" OR "avelumab") S2 ("hemoglobin" OR "c reactive protein" OR "lactate dehydrogenase" OR "neutrophil" OR "platelet" OR "lymphocyte" OR "NLR" OR "PLR") S3 ("urothelial carcinoma" OR "bladder" OR "UTUC" OR "upper urinary tract")
Scopus	(TITLE-ABS-KEY("pembrolizumab" OR "nivolumab" OR "atezolizumab" OR "durvalumab" OR "avelumab")) AND (TITLE-ABS-KEY("hemoglobin" OR "c reactive protein" OR "lactate dehydrogenase" OR "neutrophil" OR "platelet" OR "lymphocyte" OR "NLR" OR "PLR")) AND (TITLE-ABS-KEY("urothelial carcinoma" OR "bladder" OR "UTUC" OR "upper urinary tract"))

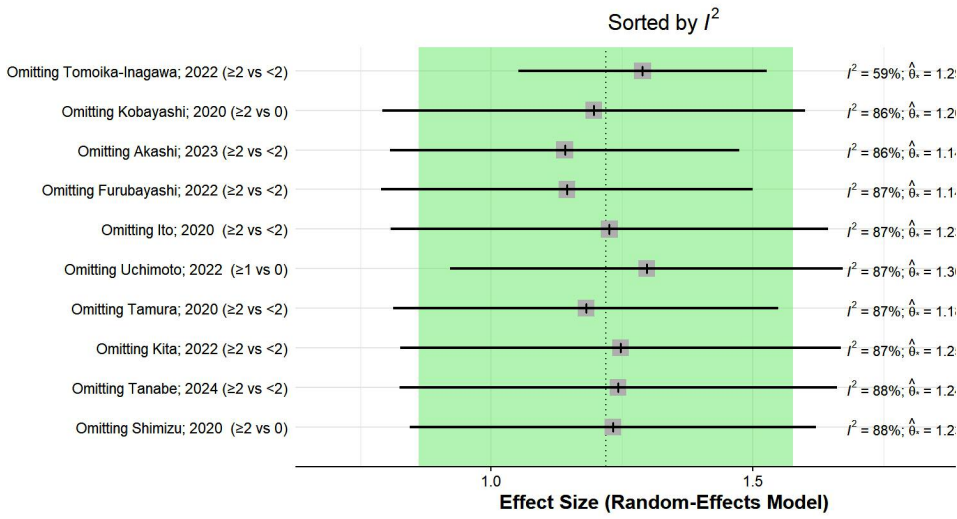
SUPPLEMENTARY RESULTS

Figure S1.

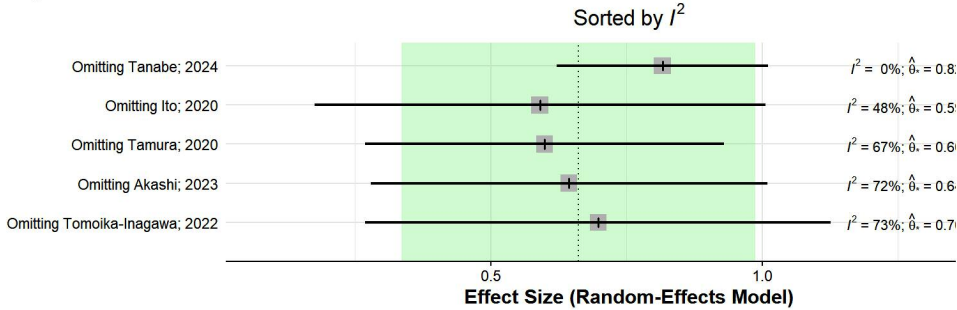
Leave-one-out sensitivity analysis for primary tumor site on Progression Free Survival (PFS).



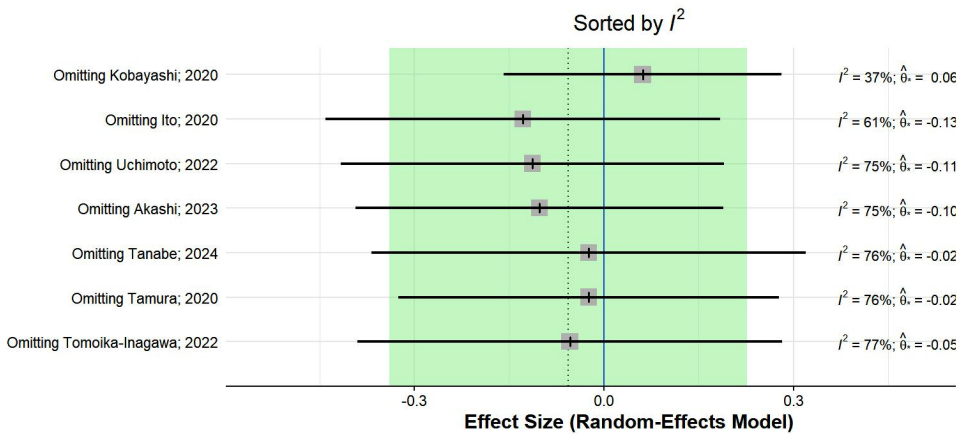
A) Overall Survival: ECOG-PS ≥ 2



B) Overall Survival: Bone Metastasis



C) Overall Survival: Lymph Node Metastasis



D) Overall Survival: C-reactive protein

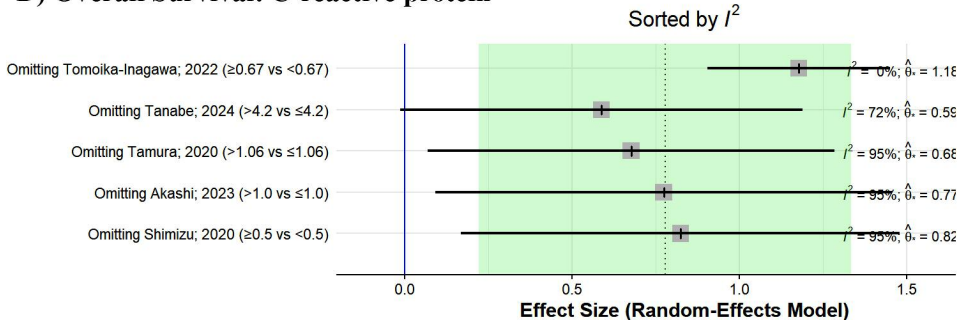
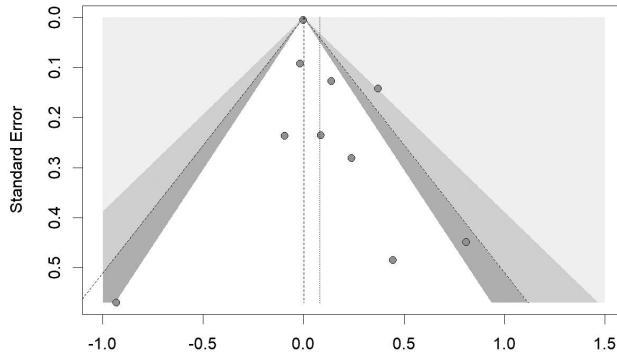


Figure S2. Leave-one-out sensitivity analysis for (A) ECOG-PS ≥ 2 , (B) bone metastasis, (C) lymph node metastasis, and (D) C-reactive protein on Overall Survival (OS).

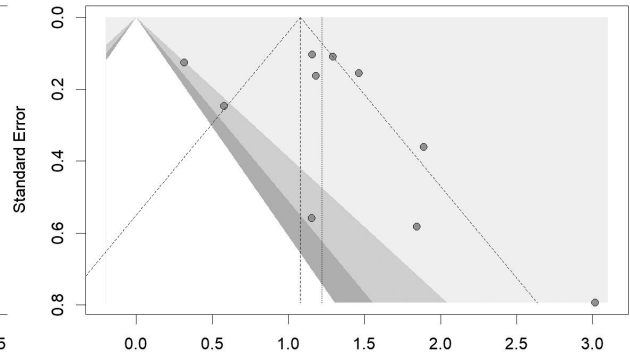
Figure S3.

Contour-enhanced funnel plot with pseudo 95% confidence interval indicating evidence of publication bias (as shown by asymmetry) for (A) Age, (B) Gender, (C) Liver Metastasis, (D) ECOG-PS ≥ 2 , (E) Primary Site on Overall Survival (OS).

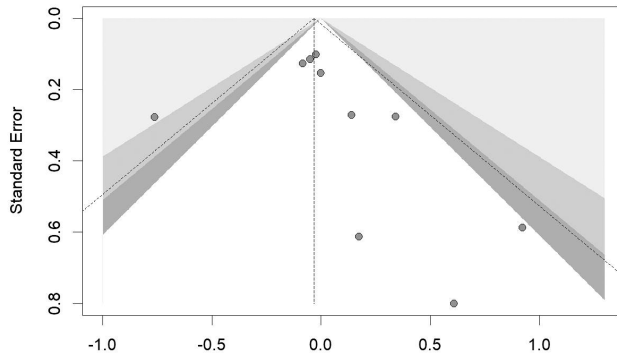
A) Overall Survival: Age



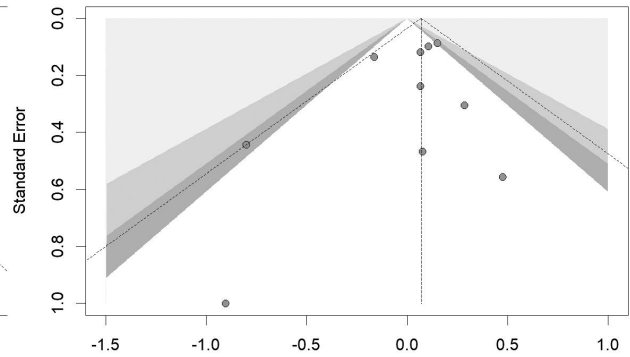
D) ECOG-PS ≥ 2



B) Overall Survival: Gender



E) Overall Survival: Primary Site



C) Overall Survival: Liver Metastasis

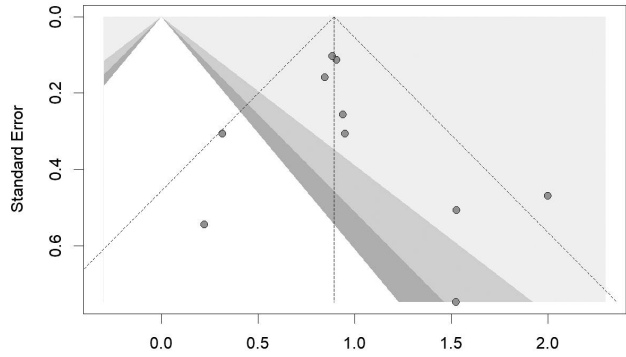


Table S2.

Egger's test result for risk factors with sufficient number of studies on outcome.

Factors	Definition	Number of studies	Hazard ratio (95%CI)	Heterogeneity		Overall effect		Egger's test	
				I ²	p-value	Z-score	p-value	Z-score	p-value
Overall Survival									
Demographic factors									
Age	≥ 70-75 years old	10	1.00 (0.99-1.01)	43	0.07	0.16	0.87	0.616	0.19
Gender	Male vs. female	10	0.97 (0.87-1.08)	30	0.17	-0.58	0.57	0.685	0.371
Clinical factors									
Liver metastasis	Yes vs. no	10	2.44 (2.16-2.76)	31	0.16	14.39	<0.01	0.474	0.522
ECOG-PS	≥2 vs. <2	10	3.38 (2.17-5.28)	86	<0.01	6.68	<0.01	1.478	0.405
Primary site	UTUC vs BC	10	1.07 (0.97-1.18)	7	0.38	1.36	0.17	-0.582	0.343

Table S3.

Meta-regression results for ECOG-PS ≥ 2 on Overall Survival.

Covariates	Number of studies	Total sample size	Coefficient	95%CI	p-value
Year of publication	10	2890	-0.04	-0.4; 0.32	0.79
% male	10	2890	0.05	0.03; 0.08	0.001
Sample size	10	2890	-0.0003	-0.002; 0.002	0.76
Mean age	10	2890	0.05	-0.38; 0.49	0.78
% UTUC	10	2890	0.02	-0.01; 0.06	0.16
Follow up duration	10	2890	0.01	-0.05; 0.06	0.79

Figure S4.

Meta-regression plot of percentage of male and overall survival hazard ratios (HRs) for ECOG-PS ≥ 2 .

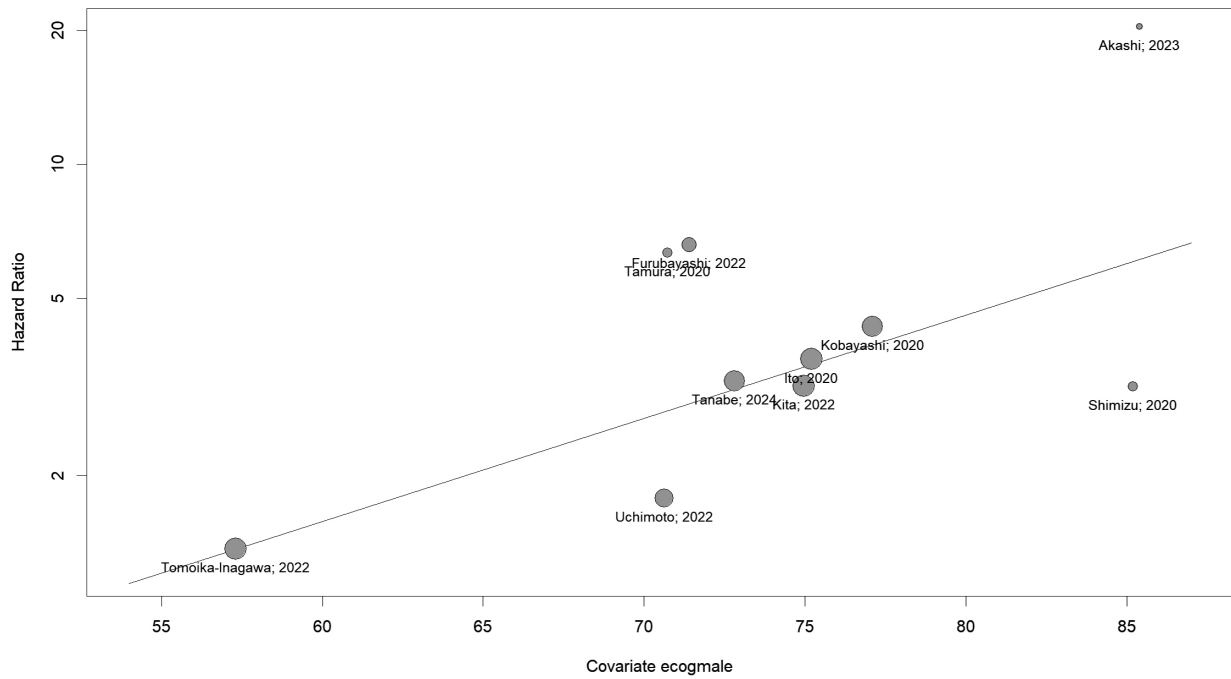


Figure S5.

Forest plot of subgroup analysis for ECOG-PS ≥ 2 on Overall Survival.

