Figure S1. A leave-one-out sensitivity of progression-free survival in immunotherapy-based regimens compared with chemo-therapy in EC/GC/GEJC. IPI, ipilimumab; NIVO, nivolumab; CT, chemotherapy; SE, standard error; df, degrees of freedom; CI, confidence interval.

Study or subgroup	Log [hazard ratio]	SE	Weight	Hazard ratio IV, Random, 95% CI	Hazard ratio IV, Random, 95% CI	
ATTRACTION-4 2022	-0.386	0.145	10.1%	0.68 (0.51, 0.90)		
CHECKMATE-648 2022 NIVO + CT arm	-0.211	0.124	12.0%	0.81 [0.64, 1.03]		
CHECKMATE-648 2022 NIVO + IPI arm	0.231	0.097	0.0%	1.26 [1.04, 1.52]		
CHECKMATE-649 2021	-0.261	0.063	19.4%	0.77 [0.68, 0.87]	+	
ESCORT-1st 2021	-0.58	0.1	14.7%	0.56 [0.46, 0.68]	+	
JUPITER-06 2022	-0.545	0.121	12.3%	0.58 [0.46, 0.74]		
KEYNOTE-590 2021	-0.431	0.083	16.8%	0.65 [0.55, 0.76]	+	
ORIENT-15 2022	-0.58	0.1	14.7%	0.56 [0.46, 0.68]		
Total (95% CI)			100.0%	0.65 [0.58, 0.74]	•	
Heterogeneity: Tau ² = 0.01; Chi ² = 15.25,	$df = 6 (P = 0.02); I^2 = 0$	61%				
Test for overall effect: Z = 7.06 (P < 0.0000)1)				0.01 0.1 1 10 Favours (experimental) Favours (control)	100

Figure S2. A leave-one-out sensitivity of disease control rate in immunotherapy-based regimens compared with chemotherapy in EC/GC/GEJC. IPI, ipilimumab; NIVO, nivolumab; CT, chemotherapy; SE, standard error; df, degrees of freedom; CI, confidence interval; M-H, Mantel-Haenszel.

	Experimental Control		Control		perimental Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl		
CHECKMATE-648 2022 NIVO+CT	255	321	235	324	11.1%	1.10 [1.00, 1.19]	•		
ESCORT-1st 2021	272	298	265	298	29.7%	1.03 [0.97, 1.08]	•		
JUPITER-06 2022	229	257	211	257	16.5%	1.09 [1.01, 1.17]	•		
KEYNOTE-811 2021	128	133	117	131	18.1%	1.08 [1.01, 1.15]	•		
ORIENT-15 2022	295	327	280	332	24.6%	1.07 [1.01, 1.13]			
Total (95% CI)		1336		1342	100.0%	1.06 [1.03, 1.09]			
Total events	1179		1108						
Heterogeneity: Tau ² = 0.00; Chi ² = 2	.74, df = 4 (P = 0.6	0); I ² = 09	6					
Test for overall effect: Z = 4.15 (P < 0	0.0001)						Favours [experimental] Favours [control]		

Figure S3. Subgroup analysis of OS in patients with PD-L1 CPS ≥ 10 and CPS < 10 groups. CI, confidence interval; CPS, combined positive score; SE standard error; df, degrees of freedom; CI, confidence interval; M-H, Mantel-Haenszel.

Study or subgroup	Log [hazard ratio]	SE	Weight	Hazard ratio IV, Fixed, 95% C	Hazard ratio IV, Fixed, 95% CI	
1.2.1 PD-1 CPS ≥10 OS						
JUPITER-06 2022	-0.446	0.241	5.2%	0.64 [0.40, 1.03]		
KEYNOTE-062 2020 Pembrolizumab	-0.371	0.174	10.0%	0.69 [0.49, 0.97]		
KEYNOTE-062 2020 Pembrolizumab+CT	-0.163	0.162	11.5%	0.85 [0.62, 1.17]	-++	
KEYNOTE-590 2021	-0.478	0.119	21.3%	0.62 [0.49, 0.78]	-	
ORIENT-15 2022	-0.446	0.146	14.1%	0.64 [0.48, 0.85]	-	
Subtotal (95% CI)			62.1%	0.68 [0.59, 0.77]	•	
Heterogeneity: Chi ² = 2.72, df = 4 (P = 0.61);	I ² = 0%					
Test for overall effect: $Z = 5.63$ (P < 0.00001)						
1.2.2 PD-L1 CPS<10 OS						
JUPITER-06 2022	-0.494	0.215	6.5%	0.61 [0.40, 0.93]		
KEYNOTE-590 2021	-0.151	0.123	19.9%	0.86 [0.68, 1.09]		
ORIENT-15 2022	-0.478	0.162	11.5%	0.62 [0.45, 0.85]		
Subtotal (95% CI)			37.9%	0.73 [0.62, 0.87]	◆	
Heterogeneity: Chi ² = 3.48, df = 2 (P = 0.18);	I ² = 43%					
Test for overall effect: $Z = 3.47$ (P = 0.0005)						
Total (95% CI)			100.0%	0.70 [0.63, 0.78]	•	
Heterogeneity: Chi ² = 6.75, df = 7 (P = 0.46);	l ² = 0%			• • •		
Test for overall effect: Z = 6.57 (P < 0.00001)					0.01 0.1 1 10	
Test for subaroup differences: Chi² = 0.55. d		0%			Favours [experimental] Favours [contr	oij

Figure S4. A leave-one-out sensitivity analysis of progression-free survival in patients with PD-L1 CPS \geq 10. IPI, ipilimumab; NIVO, nivolumab; CT, chemotherapy; SE, standard error; df, degrees of freedom; CI, confidence interval; CPS, combined positive score.

				Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
JUPITER-06 2022	-0.431	0.182	18.7%	0.65 [0.45, 0.93]	
KEYNOTE-590 2021	-0.673	0.118	44.6%	0.51 [0.40, 0.64]	➡
ORIENT-15 2022	-0.545	0.13	36.7%	0.58 [0.45, 0.75]	-
Total (95% CI)			100.0%	0.56 [0.48, 0.65]	•
Heterogeneity: Tau² = 0 Test for overall effect: Z			0.51); I² =	0%	0.01 0.1 1 10 100 Favours [experimental] Favours [control]

Figure S5. A leave-one-out sensitivity analysis of progression-free survival in patients with PD-L1 CPS <10. EC, oesophageal cancer; IPI, ipilimumab; NIVO, nivolumab; CT, chemotherapy; SE, standard error; df, degrees of freedom; CI, confidence interval; CPS, combined positive score.

Churche on Culture out	le «fillement Detiel	er.	Mainht	Hazard Ratio	Hazar		
Study or Subgroup	log[Hazard Ratio]	SE	weight	IV, Fixed, 95% Cl	IV, Fixed	1,95% CI	
JUPITER-06 2022	-0.58	0.164	44.2%	0.56 [0.41, 0.77]	-		
ORIENT-15 2022	-0.635	0.146	55.8%	0.53 [0.40, 0.71]			
Total (95% CI)				0.54 [0.44, 0.67]	•		
Heterogeneity: Chi ² = Test for overall effect:			%		0.01 0.1 Favours [experimental]	10 Favours (control)	100

Figure S6. Subgroup analysis of progression-free survival in patients with PD-L1 CPS \geq 10 and CPS <10 groups. CI, confidence interval; CPS, combined positive score; SE standard error.

Study or subgroup	Log [hazard ratio]	SE	Weight	Hazard ratio IV, Random, 95% C	Hazard ratio IV, Random, 95% CI
1.3.1 PD-L1 CPS ≥ 10 PFS					
JUPITER-06 2022	-0.431	0.182	12.2%	0.65 (0.45, 0.93)	
KEYNOTE-062 2020 Pembrolizumab	0.095	0.165	13.2%	1.10 [0.80, 1.52]	+
KEYNOTE-590 2021	-0.673	0.118	15.9%	0.51 [0.40, 0.64]	-
ORIENT-15 2022	-0.545	0.13	15.2%	0.58 [0.45, 0.75]	
Subtotal (95% CI)			56.5%	0.67 [0.49, 0.92]	\bullet
Heterogeneity: Tau ² = 0.08; Chi ² = 15.0	02, df = 3 (P = 0.002); l	r= 809	6		
Test for overall effect: Z = 2.46 (P = 0.0					
1.3.2 PD-L1 CPS<10 PFS					
JUPITER-06 2022	-0.58	0.164	13.2%	0.56 [0.41, 0.77]	
KEYNOTE-590 2021	-0.223	0.116	16.0%	0.80 (0.64, 1.00)	
ORIENT-15 2022	-0.635	0.146	14.3%	0.53 (0.40, 0.71)	
Subtotal (95% Cl)			43.5%	0.63 [0.48, 0.83]	\bullet
Heterogeneity: Tau ² = 0.04; Chi ² = 5.99	3, df = 2 (P = 0.05); l ² =	67%			
Test for overall effect: Z = 3.29 (P = 0.0	010)				
Total (95% CI)			100.0%	0.65 [0.53, 0.79]	◆
Heterogeneity: Tau ² = 0.05; Chi ² = 21.0	07, df = 6 (P = 0.002); l	l² = 729	6	- / -	
Test for overall effect: Z = 4.29 (P < 0.0					0.01 0.1 1 10 100
Test for subaroup differences: Chi ² = 0	•	I ^z = 0%			Favours (experimental) Favours (control)

Figure S7. Subgroup analysis of overall survival in Asian and non-Asian patients. IPI, ipilimumab; NIVO, nivolumab; CT, chemotherapy; SE, standard error; df, degrees of freedom; CI, confidence interval.

Study or subgroup	Log [hazard ratio] SE	Weight	Hazard ratio IV, Fixed, 95% C	Hazard ratio IV, Fixed, 95% CI
1.2.1 Asian OS CHECKMATE-648 (NIVO + CT) 2022 CHECKMATE-648 (NIVO + IPI) 2022 CHECKMATE-649 2021 KEYNOTE-590 2021 ORIENT-15 2022	-0.301 0.119 -0.186 0.116 -0.315 0.125 -0.446 0.118 -0.462 0.108	5 10.5% 5 9.0% 8 10.1%	0.83 [0.66, 1.04] 0.73 [0.57, 0.93] 0.64 [0.51, 0.81]	
Subtotal (95% Cl) Heterogeneity: Chi ² = 3.98, df = 4 (P = 0.4 Test for overall effect: Z = 6.63 (P < 0.0000 1.2.2 Non-Asian OS	1); I² = 0%		0.71 [0.64, 0.78]	•
CHECKMATE-648 (NIVO + CT) 2022 CHECKMATE-648 (NIVO + CT) 2022 CHECKMATE-649 2021 KEYNOTE-590 2021 Subtotal (95% CI) Heterogeneity: Chi ² = 0.96, df = 3 (P = 0.8° Test for overall effect: $Z = 4.58$ (P < 0.0000		5.1% 27.9%	0.69 [0.50, 0.96] 0.79 [0.69, 0.91] 0.83 [0.66, 1.05]	 * *
Total (95% CI) Heterogeneity: Chi ² = 6.69, df = 8 (P = 0.5 Test for overall effect: Z = 7.95 (P < 0.0000 Test for subgroup differences: Chi ² = 1.75)1)		0.74 [0.69, 0.80]	0.01 0.1 1 10 100 Favours [experimental] Favours [control]

Figure S8. A leave-one-out sensitivity of the incidence of grade 3 and above adverse events in the two groups. IPI, ipilimumab; NIVO, nivolumab; CT, chemotherapy; SE, standard error; df, degrees of freedom; CI, confidence interval; M-H, Mantel-Haenszel.

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
ATTRACTION-4 2022	71	359	57	358	4.7%	1.24 [0.91, 1.70]	
CHECKMATE-648 2022 NIVO+CT	147	310	108	304	8.2%	1.33 [1.10, 1.62]	-
CHECKMATE-648 2022 NIVO+IPI	102	322	108	304	7.2%	0.89 [0.72, 1.11]	-
CHECKMATE-649 2021	466	782	341	767	12.1%	1.34 [1.22, 1.48]	•
ESCORT-1st 2021	189	298	201	297	11.3%	0.94 [0.83, 1.05]	-
JUPITER-06 2022	188	257	180	257	11.6%	1.04 [0.94, 1.16]	+
KEYNOTE-062 2022 (PEMBRO+CT)	183	250	169	244	11.5%	1.06 [0.94, 1.18]	+
KEYNOTE-590 2021	318	370	308	370	13.5%	1.03 [0.97, 1.10]	•
KEYNOTE-811 2021	124	217	124	216	9.3%	1.00 [0.85, 1.17]	+
ORIENT-15 2022	196	327	181	332	10.6%	1.10 [0.96, 1.25]	+
Total (95% CI)		3492		3449	100.0%	1.08 [1.00, 1.18]	•
Total events	1984		1777				
Heterogeneity: Tau ² = 0.01; Chi ² = 38.4	2, df = 9 (F	< 0.00	01); I ² = 7	7%			
Test for overall effect: Z = 1.86 (P = 0.0							0.01 0.1 1 10 100 Favours [experimental] Favours [control]