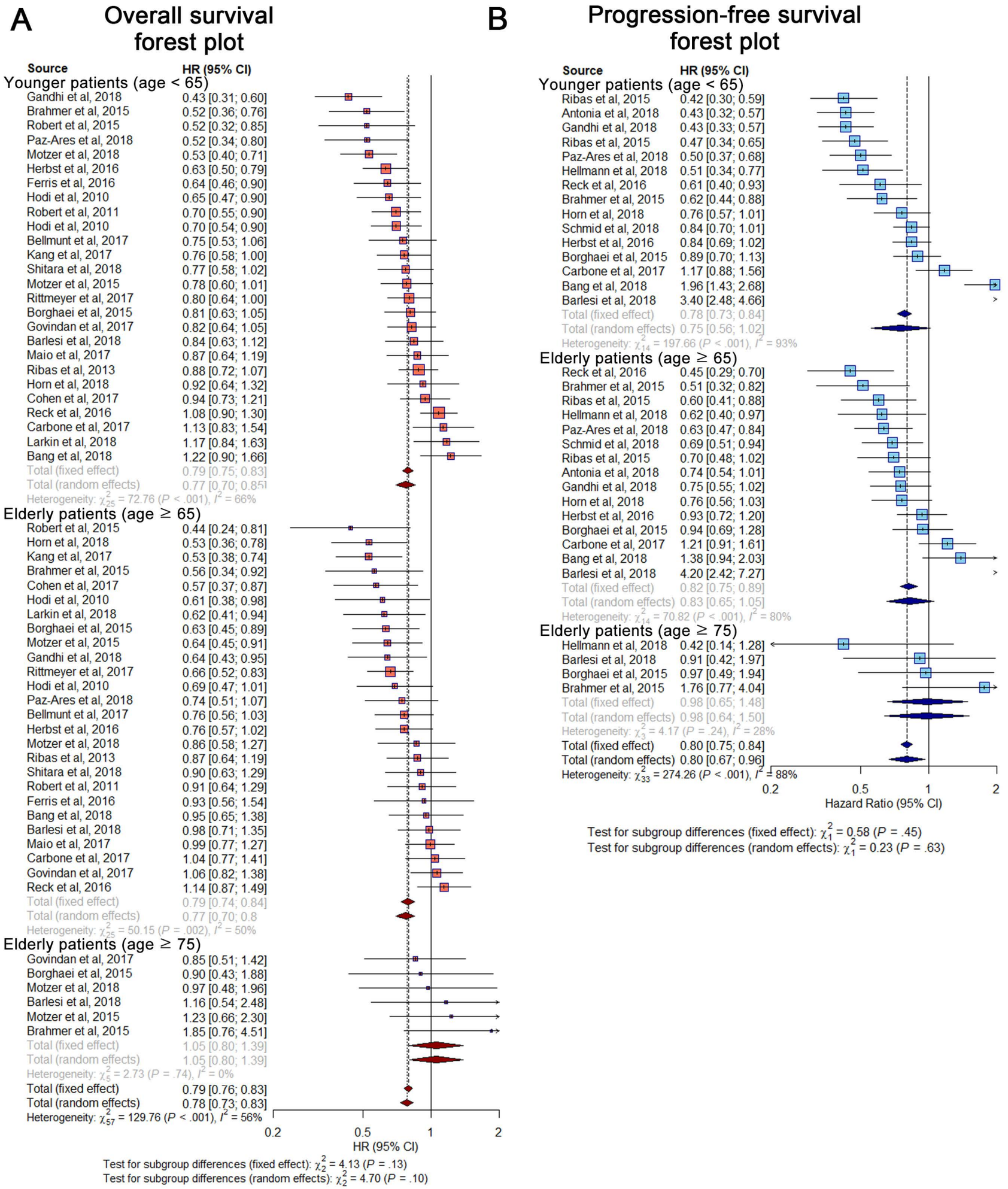
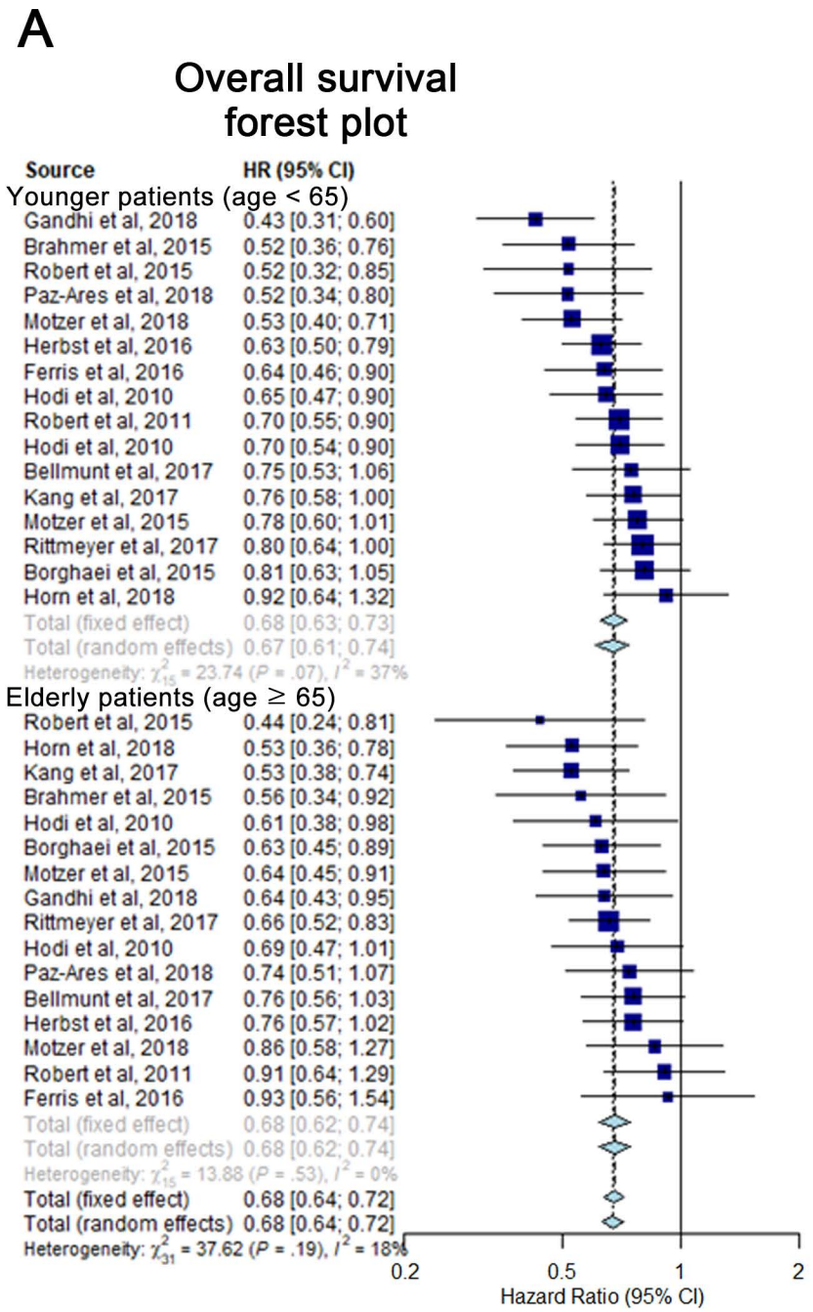
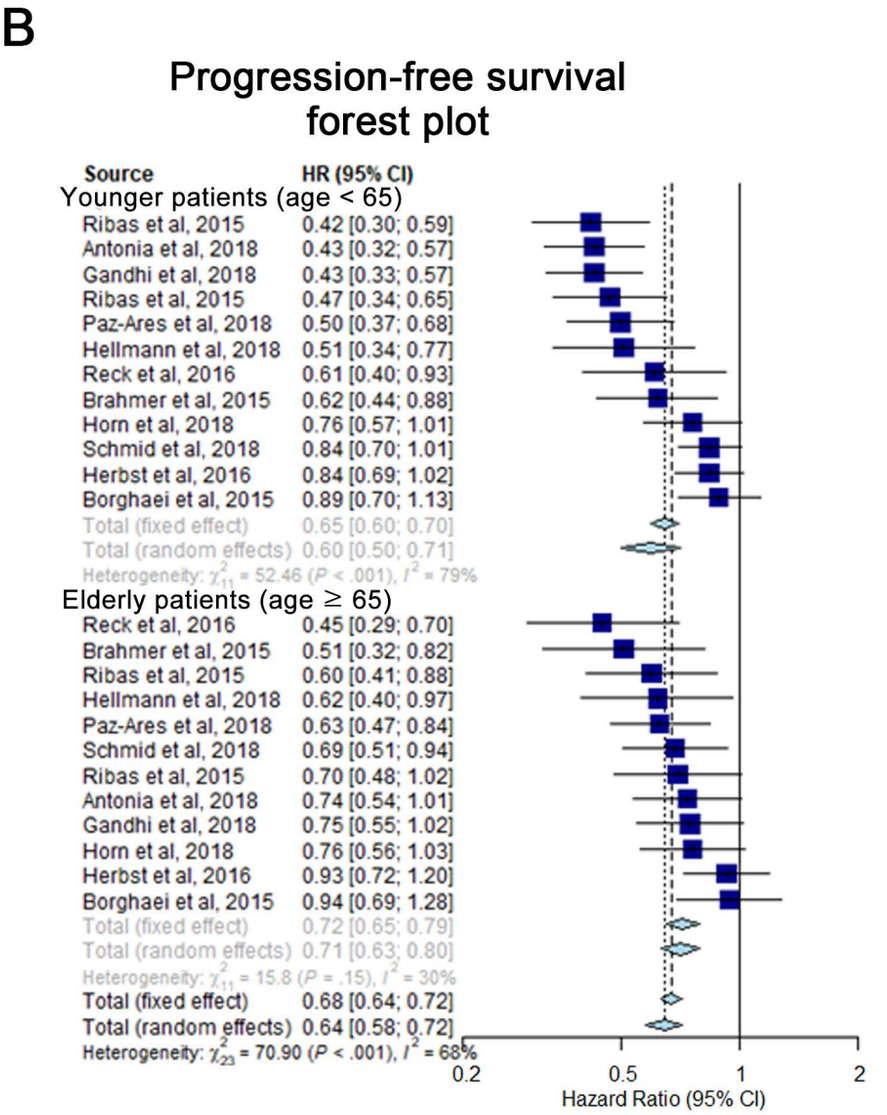
Supplementary Figure 1



Supplementary Figure 2





Test for subgroup differences (fixed effect): χ^2_2 = 4.13 (P = .13)
Test for subgroup differences (random effects): χ^2_2 = 4.70 (P = .10)

Supplementary Table 1. PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 3-4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 4 and Figure 1
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 4-5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5 and Table 1-2
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 5 and Table 1-2
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6 and Supplementary table 2
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 5-6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Not applicable
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 6 and Figure 2
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6-7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 6 and

Section and Topic	Item #	Checklist item	Location where item is reported
			Table 3-4-5
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not applicable
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not applicable
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 7-8 and Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Page 7-8 and Table 1-2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 8 and Supplementary table 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 8-9 and Table 1-2 and Figure 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 8-11
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 8-11 and Table 3-4-5
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 6
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not applicable
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 9-10 and Table 1-5
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 11-12
	23b	Discuss any limitations of the evidence included in the review.	Page 12-13
	23c	Discuss any limitations of the review processes used.	Page 12-13
	23d	Discuss implications of the results for practice, policy, and future research.	Page 13
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 4

Section and Topic	Item #	Checklist item	Location where item is reported
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 14
Competing interests	26	Declare any competing interests of review authors.	Page 14
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 4

Supplementary Table 2. Baseline characteristics of 26 randomized controlled studies for overall survival.

Source	Phase	Tumor type	Line	N	Treatment	Control	Median age (years)	Median follow-up (months)	N (%)		OS, HR (95% CI)		
									<65 y	≥65 y	All	<65 y	≥65 y
Gandhi, 2018[24]	3	NSCLC	1	616	Pembrolizumab + Platinum	Placebo, Platinum	Int: 65 (34–84); cont: 64(34-84)	10.5 (0.2-20.4)	312 (51)	304 (49)	0.49 (0.38–0.64)	0.43 (0.31–0.61)	0.64 (0.43–0.95)
Barlesi, 2018[25]	3	NSCLC	>1	264	Avelumab	Docetaxel	Int: 64 (58–59); cont: 63 (57-69)	18.3 (IQR, 13.2–22.7)	134 (51)	130 (49)	0.90 (0.72–1.12)	0.84 (0.63–1.13)	0.98 (0.71–1.34)
Paz-Ares, 2018[26]	3	NSCLC	1	559	Pembrolizumab + ICC	Placebo + ICC	Int: 65 (29–87); cont: 65 (36-88)	7.8 (0.1–19.1)	254 (45)	305 (55)	0.64 (0.49–0.85)	0.52 (0.34–0.80)	0.74 (0.51–1.07)
Horn, 2018[29]	3	SCLC	1	403	Atezolizumab + carboplatin + etoposide	Placebo + carboplatin + etoposide	Int: 64 (28–90); cont: 64 (26–87)	13.9 (NR)	217 (54)	186 (46)	0.70 (0.54–0.91)	0.92 (0.64–1.32)	0.53 (0.36–0.77)
Larkin, 2018[30]	3	Melanoma	>1	405	Nivolumab	Placebo	61 (23–88)	24 (NR)	257 (63)	148 (37)	0.92 (0.71–1.18)	1.17 (0.84–1.63)	0.62 (0.41–0.94)
Shitara, 2018[32]	3	Gastric or GE junction carcinoma	2	395	Pembrolizumab	Paclitaxel	62.5 (54–70)	7.9 (IQR, 3.4–14.6)	232 (59)	163 (41)	0.82 (0.66–1.03)	0.77 (0.58–1.02)	0.90 (0.63–1.29)
Bang, 2018[33]	3	Gastric or GE junction carcinoma	3	371	Avelumab	CTx	59 (29–86)	8.0 weeks* (2–66)	230 (62)	141 (38)	1.1 (0.9–1.4)	1.22 (0.89–1.65)	0.95 (0.65–1.38)
Motzer, 2018[34]	3	ccRCC	1	847	Nivolumab + ipilimumab	Sunitinib	Int: 62 (26–85); cont: 51 (21–85)	25.2 (NR)	524 (62)	323 (38)	0.66 (0.53–0.82)	0.53 (0.40–0.71)	0.86 (0.58–1.27)
Govindan, 2017[62]	3	NSCLC	1	749	Ipilimumab + docetaxel + carboplatin	Placebo + docetaxel + carboplatin	64 (28–85)	Int: 12.5(NR); Cont: 11.8(NR)	380 (51)	369 (49)	0.91 (0.77–1.07)	0.82 (0.64–1.04)	1.06 (0.81–1.37)
Carbone, 2017[36]	3	NSCLC	1	541	Nivolumab	ICC	64 (29–89)	13.5 (NR)	281 (52)	260 (48)	1.08 (0.87–1.34)	1.13 (0.83–1.54)	1.04 (0.77–1.41)
Rittmeyer, 2017[37]	3	NSCLC	1	850	Atezolizumab	Docetaxel	64 (33–85)	21 (NR)	453 (53)	397 (47)	0.73 (0.62-0.87)	0.80 (06.4-1.00)	0.66 (0.52-0.83)
Cohen, 2017[38]	3	HNSCC	2	495	Pembrolizumab	ICC	60 (19–85)	7.3	332 (67)	163 (33)	0.80 (0.65–0.98)	0.94 (0.73–1.20)	0.57 (0.37–0.87)
Bellmunt, 2017[39]	3	Urothelial carcinoma	>1	542	Pembrolizumab	ICC	66 (26–88)	14.1 (9.9–22.1)	230 (52)	312 (48)	0.73 (0.59–0.91)	0.75 (0.53–1.05)	0.76 (0.56–1.02)
Kang, 2017[40]	3	Gastric or GE junction carcinoma	>1	493	Nivolumab	Placebo	62 (IQR, 53–69)	Int: 8.87 (IQR, 6.57–12.37); cont: 8.59 (IQR, 5.65–11.37)	284 (58)	209 (42)	0.65 (0.53–0.80)	0.76 (0.58–1.00)	0.53 (0.38–0.74)
Maio, 2017[41]	3	Mesothelioma	>1	571	Tremelimumab	Placebo	67 (IQR, 60–73)	NR	237 (42)	334 (58)	0.92 (0.76–1.12)	0.87 (0.64–1.20)	0.99 (0.77–1.26)
Ferris, 2016[42]	3	HNSCC	>1	361	Nivolumab	ICC	60 (28–83)	5.1 (0–16.8)	248 (69)	113 (31)	0.69 (0.53–0.91)	0.64 (0.45–0.89)	0.93 (0.56–1.54)

Herbst, 2016[44]	2,3	NSCLC	>1	1033	Pembrolizumab	Docetaxel	63 (IQR, 54–70)	13.1 (IQR, 8.6–17.7)	604 (58)	429 (42)	0.67 (0.56–0.80)	0.63 (0.50–0.79)	0.76 (0.57–1.02)
Reck, 2016[43]	3	SCLC	1	954	Ipilimumab + etoposide + platinum	Placebo + etoposide + platinum	63 (35–85)	Int: 10.5 (NR); cont: 10.2 (NR)	576 (60)	378 (40)	0.94 (0.81–1.09)	1.08 (0.9–1.31)	1.14 (0.87–1.49)
Brahmer, 2015[46]	3	NSCLC	>1	272	Nivolumab	Docetaxel	63 (39–85)	11.0 (NR)	152 (56)	120 (44)	0.59 (0.44–0.78)	0.52 (0.35–0.75)	0.56 (0.34–0.91)
Borghaei, 2015[47]	3	NSCLC	>1	582	Nivolumab	Docetaxel	62 (21–88)	13.2 (NR)	339 (58)	243 (42)	0.75 (0.62–0.91)	0.81 (0.62–1.04)	0.63 (0.45–0.89)
Robert, 2015[48]	3	Melanoma	1	418	Nivolumab	Dacarbazine	65 (18–87)	Int:8.9 (NR); cont:6.8 (NR)	200 (48)	218 (52)	0.42 (0.30–0.59)	0.52 (0.32–0.85)	0.44 (0.24–0.81)
Motzer, 2015[49]	3	ccRCC	>1	821	Nivolumab	Everolimus	62 (23–88)	NR	497 (61)	324 (39)	0.76 (0.62–0.92)	0.78 (0.60–1.01)	0.64 (0.45–0.91)
Ribas, 2013[63]	3	Melanoma	1	655	Tremelimumab	ICC	57 (22–90)	NR	455 (69)	200 (31)	0.88 (0.75–1.04)	0.88 (0.72–1.07)	0.87 (0.64–1.19)
Robert, 2011[53]	3	Melanoma	1	502	Ipilimumab + Dacarbazine	Placebo + Dacarbazine	56.9 (NR)	54 (NR)	342 (68)	160 (32)	0.72 (0.59–0.87)	0.70 (0.55–0.90)	0.91 (0.64–1.28)
Hodi, 2010[52]	3	Melanoma	>1	273	Ipilimumab	gp100	56.8 (NR)	21.0 (ipilimumab + gp100),	189 (69)	84 (31)	0.64 (0.49–0.84)	0.65 (0.47–0.90)	0.61 (0.38–0.99)
Hodi, 2010[52]	3	Melanoma	>1	539	Ipilimumab + gp100	gp100	56.2 (NA)	27.8 (ipilimumab), 17.2 (gp100)	385 (71)	154 (29)	0.69 (0.56–0.85)	0.70 (0.54–0.90)	0.69 (0.47–1.01)

#subgroup of patients with PD-L1+

Abbreviations: NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; HNSCC, head and neck squamous cell carcinoma; RT, radiotherapy; CTx, chemotherapy; GE, gastroesophageal; ccRCC, clear cell renal cell carcinoma; Cont, control group, PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; ICC, investigator's choice of chemotherapy; int, intervention; group; IQR, interquartile range; NR, not reported; N, number; CI, confidence interval

Supplementary Table 3. Baseline characteristics of 15 randomized controlled studies for progression-free survival.

Source	Phase	Tumor type	Line	N	Treatment	Control	Median age (years)	Median follow-up (months)	N (%)		PFS, HR (95% CI)		
									<65 y	≥65 y	All	<65 y	≥65 y
Gandhi, 2018[24]	3	NSCLC	1	616	Pembrolizumab + Platinum	Placebo, Platinum	Int: 65 (34–84); cont: 64 (34-84)	10.5 (0.2-20.4)	312 (51)	304 (49)	0.52 (0.43–0.64)	0.43 (0.32–0.56)	0.75 (0.55–1.02)
Barlesi, 2018[25]	3	NSCLC	>1	264	Avelumab	Docetaxel	Int: 64 (58–59); cont: 63 (57-69)	18.3 (IQR, 13.2-22.7)	134 (51)	130 (49)	3.4 (2.7–4.9)	3.4 (2.5-4.7)[#]	4.2 (2.1-6.3)[#]
Paz-Ares, 2018[26]	3	NSCLC	1	559	Pembrolizumab + ICC	Placebo + ICC	Int: 65 (29–87); cont: 65 (36-88)	7.8 (0.1–19.1)	254 (45)	305 (55)	0.56 (0.45–0.70)	0.50 (0.37-0.69)	0.63 (0.47-0.84)
Antonia, 2018[27]	3	NSCLC	>1	713	Durvalumab	Placebo	64 (23–90)	25.2 (0.2–43.1)	391 (55)	322 (45)	0.55 (0.45–0.68)	0.43 (0.32-0.57)	0.74 (0.54-1.01)
Hellmann, 2018[28]	3	NSCLC	1	326	Nivolumab + ipilimumab	CTx	64 (41–87)	NR	156 (48)	170 (52)	0.58 (0.43–0.77)	0.51 (0.34-0.77)	0.62 (0.40-0.97)
Horn, 2018[29]	3	SCLC	1	403	Atezolizumab + carboplatin + etoposide	Placebo + carboplatin + etoposide	Int: 64 (28–90); cont: 64 (26–87)	13.9 (NR)	217 (54)	186 (46)	0.77 (0.62–0.96)	0.76 (0.57–1.01)	0.76 (0.56–1.03)
Schmid, 2018[31]	3	Breast cancer	1	902	Atezolizumab + nab-paclitaxel	Placebo + nab-paclitaxel	55 (20–82)	12.9	68 3 (76)	219 (24)	0.81 (0.70–0.93)	18–40yr: 0.79 (0.53–1.16), 41-64yr: 0.84 (0.70–1.01)	0.69 (0.51–0.94)
Bang, 2018[33]	3	Gastric or GE junction carcinoma	3	371	Avelumab	CTx	59 (29–86)	8.0 weeks* (2–66)	230 (62)	141 (38)	1.73 (1.4–2.2)	1.96 (1.43–2.67)	1.38 (0.94–2.04)
Carbone, 2017[36]	3	NSCLC	1	541	Nivolumab	ICC	64 (29–89)	13.5 (NR)	281 (52)	260 (48)	1.19 (0.97–1.46)	1.17 (0.88–1.56)	1.21 (0.91–1.62)
Reck, 2016[43]	3	NSCLC	1	305	Pembrolizumab	ICC	65 (33–90)	11.2 (6.3–19.7)	141 (46)	164 (54)	0.50 (0.37–0.68)	0.61 (0.40–0.92)	0.45 (0.29–0.70)
Herbst, 2016[44]	2,3	NSCLC	>1	103 3	Pembrolizumab	Docetaxel	63 (IQR, 54–70)	13.1 (IQR, 8.6–17.7)	604 (58)	429 (42)	0.85 (0.73–0.98)	0.84 (0.69–1.02)	0.93 (0.72–1.19)
Brahmer, 2015[46]	3	NSCLC	>1	272	Nivolumab	Docetaxel	63 (39–85)	11.0 (NR)	152 (56)	120 (44)	0.63 (0.48–0.82)	0.62 (0.44–0.89)	0.51 (0.32–0.82)
Borghaei, 2015[47]	3	NSCLC	>1	582	Nivolumab	Docetaxel	62 (21–88)	13.2 (NR)	339 (58)	243 (42)	0.91 (0.76–1.09)	0.89 (0.70–1.13)	0.94 (0.69–1.27)
Ribas, 2015[50]	2	Melanoma	>1	359	Pembrolizumab 2mg/kg	CTx	62 (15–87)	NR	200 (56)	159 (44)	0.57 (0.45–0.73)	0.47 (0.34–0.66)	0.70 (0.48–1.01)
Ribas, 2015[50]	2	Melanoma	>1	360	Pembrolizumab 10mg/kg	CTx	60 (27–89)	NR	204 (57)	156 (43)	0.50 (0.37–0.64)	0.42 (0.30–0.59)	0.60 (0.41–0.88)

#subgroups of patients with PD-L1-positive
Abbreviations: NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; HNSCC, head and neck squamous cell carcinoma; RT, radiotherapy; CTx, chemotherapy; GE, gastroesophageal; ccRCC, clear cell renal cell carcinoma; Cont, control group, PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; ICC, investigator's choice of chemotherapy; int, intervention; group; IQR, interquartile range; NR, not reported; N, number; CI, confidence interval

Supplementary Table 4. Summary of Jadad score by randomization, blinding, and account. A score of 0–2 is considered low, and a score of 3–5 is defined as high quality.

Study (Year)	Randomization	Blinding	Account	Jadad Score
Barlesi et al, 2018	2	0	1	3
Bellmunt et al, 2017	2	0	1	3
Borghaei et al, 2015	2	0	1	3
Brahmer et al, 2015	2	0	1	3
Carbone et al, 2017	2	0	1	3
Ferris et al, 2016	2	0	1	3
Herbst et al, 2016	2	0	1	3
Larkin et al, 2018	2	0	1	3
Motzer et al, 2015	2	0	1	3
Motzer et al, 2018	2	0	1	3
Reck et al, 2016	2	0	1	5
Ribas et al, 2013	2	0	1	3
Rittmeyer et al, 2017	2	0	1	5
Robert et al, 2015	2	0	1	3
Coehn et al, 2017	2	0	1	3
Bang et al, 2018	2	0	1	3
Ribas et al, 2015	2	0	1	3
Shitara et al, 2018	2	0	1	3
Hellmann et al, 2018	2	0	1	3
Schmid et al, 2018	2	0	1	3
Antonia et al, 2018	2	2	1	5
Gandhi et al, 2018	2	2	1	5
Govindan et al, 2017	2	2	1	5
Horn et al, 2018	2	2	1	5
Kang et al, 2017	2	2	1	5
Maio et al, 2017	2	2	1	5
Paz-Arez et al, 2018	2	2	1	5
Reck et al, 2016	2	2	1	5
Robert et al, 2011	2	2	1	5
Hodi et al, 2010	2	2	1	5

Supplementary Table 5. Subgroup analysis of immunotherapy efficacy in terms of overall survival (OS) between younger age (<65 years old) and older age (≥65 years old) in clinical trials with positive outcomes.

Variables	Number of studies	Number of participants			Pooled HR (95% CI)			Test for Difference
		all	<65	≥65	all	<65	≥65	*P* value
All	16	9,111	5,230	3,881	0.67 (0.64, 0.71)	0.67 (0.61, 0.74)	0.68 (0.62, 0.74)	0.85
Primary disease site								
NSCLC	7	4,454	2,344	2,110	0.67 (0.60, 0.74)	0.64 (0.53, 0.77)	0.69 (0.61, 0.78)	0.50
melanoma	4	1,732	1,116	616	0.62 (0.51, 0.77)	0.67 (0.58 0.78)	0.69 (0.52, 0.90)	0.89
Other tumors	5	2,925	1,770	1,155	0.69 (0.63, 0.77)	0.71 (0.59, 0.85)	0.66 (0.53, 0.81)	0.59
Type of immunotherapy								
anti-PD-1/PD-L1 antibody	12	6,950	3,790	3,160	0.66 (0.61, 0.72)	0.68 (0.60, 0.77)	0.66 (0.59, 0.72)	0.69
Anti-CTLA-4 antibody	3	1,314	916	398	0.69 (0.61, 0.78)	0.69 (0.59, 0.80)	0.75 (0.59, 0.96)	0.54
Combination treatment	1	847	524	323	-	-	-	-
Line of treatment								
0	9	4,916	2,928	1,988	0.69 (0.64, 0.74)	0.70 (0.64, 0.77)	0.67 (0.60, 0.76)	0.61
1	7	4,195	2,302	1,893	0.63 (0.55, 0.72)	0.62 (0.51, 0.77)	0.69 (0.59, 0.80)	0.44

Abbreviations: NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval

Supplementary Table 6. Subgroup analysis of immunotherapy efficacy in terms of progression-free survival (PFS) between younger age (<65 years old) and older age (≥65 years old) in clinical trials with positive outcomes.

Variables	Number of studies	Number of participants			Pooled HR (95% CI)			Test for Difference
		all	<65	≥65	all	<65	≥65	*P* value
All	12	6,430	3,653	2,777	0.64 (0.56, 0.73)	0.60 (0.50, 0.71)	0.71 (0.63, 0.80)	0.11
Primary disease site								
NSCLC	8	4,406	2,349	2,057	0.63 (0.53, 0.75)	0.59 (0.48, 0.73)	0.71 (0.59, 0.84)	0.20
melanoma	2	719	404	315	0.53 (0.45, 0.64)	0.44 (0.35, 0.56)	0.65 (0.50, 0.85)	0.04*
Other tumors	2	1,305	900	405	0.80 (0.71, 0.90)	0.82 (0.70, 0.95)	0.72 (0.58, 0.90)	0.38
Type of immunotherapy								
anti-PD-1/PD-L1 antibody	11	6,104	3,497	2,607	0.65 (0.56, 0.74)	0.60 (0.50, 0.73)	0.71 (0.63, 0.81)	0.14
Anti-CTLA-4 antibody	0	-	-	-	-	-	-	-
Combination treatment	1	326	156	170	-	-	-	-
Line of treatment								
0	6	3,319	1,890	1,429	0.66 (0.54, 0.81)	0.59 (0.45, 0.78)	0.75 (0.63, 0.90)	0.15
1	6	3,111	1,763	1,348	0.62 (0.52. 0.74)	0.60 (0.48, 0.76)	0.67 (0.58, 0.76)	0.45

Abbreviations: NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval

*$P<0.05$

Supplementary Table 7. Meta-regression analysis to evaluate the impact of covariates on the overall survival and progression-free survival in clinical trials with positive outcomes.

Covariates	Overall survival		Progression-free survival	
	Log HR estimate (CI bound)	*P* value	Log HR estimate (CI bound)	*P* value
Age group	0.013 (-0.128 ~ 0.155)	0.852	0.153 (-0.030 ~ 0.335)	0.101
Line of therapy	-0.045 (-0.191 ~ 0.102)	0.550	-0.294 (-0.534 ~ -0.053)	0.017*
Tumor type (NSCLC)	-0.001 (-0.224 ~ 0.221)	0.990	0.332 (0.051 ~ 0.612)	0.021*
Tumor type (Other tumors)	0.018 (-0.188 ~ 0.223)	0.864	0.668 (0.273 ~ 1.063)	0.001**
Type of immunotherapy	0.017 (-0.136 ~ 0.170)	0.827	0.007 (-0.201 ~ 0.216)	0.946

Abbreviations: NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval

*P<0.05; **P<0.01;

Supplementary Table 8. Meta-regression analysis to evaluate the impact of covariates on the overall survival and progression-free survival, including different age cut-offs.

Covariates	Overall survival		Progression-free survival	
	Log HR estimate (CI bound)	*P* value	Log HR estimate (CI bound)	*P* value
Age group (age≥65)	-0.004 (-0.142 ~ 0.134)	0.958	0.099 (-0.247 ~ 0.447)	0.573
Age group (age≥75)	0.310 (-0.029 ~ 0.649)	0.073	0.116 (-0.581 ~ 0.814)	0.744
Line of therapy	< 0.001 (-0.154 ~ 0.155)	0.999	-0.467 (-0.861 ~ -0.073)	0.020*
Tumor type (NSCLC)	0.042 (-0.164~ 0.247)	0.691	0.648 (0.093 ~ 1.204)	0.022*
Tumor type (Other tumors)	0.110 (-0.078 ~ 0.299)	0.252	0.917 (0.251 ~ 1.589)	0.007**
Type of immunotherapy	0.049 (-0.097 ~ 0.196)	0.509	-0.101 (-0.423 ~ 0.222)	0.541

Abbreviations: NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval

*P<0.05; **P<0.01;