

Supplemental Online Content

Li AY, Gaebe K, Zulfiqar A, et al. Association of brain metastases with survival in patients with limited or stable extracranial disease: a systematic review and meta-analysis. *JAMA Netw Open*. 2023;6(2):e230475. doi:10.1001/jamanetworkopen.2023.0475

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eReferences

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods. Supplemental Methods

Search strategy

Grey literature sources searched in this study include Google Scholar (first 150 results), ClinicalTrials.gov, PROSPERO, Scopus, the International Clinical Trials Registry Platform of the World Health Organisation, and the websites of American Society of Clinical Oncology (ASCO), European Society of Medical Oncology (ESMO), and Society for Neuro-oncology (SNO). A sample of the search strategy performed on MEDLINE on June 21, 2021 can be found in Supplementary Table S3.

Data extraction

Four authors (K.G., A.Y.L., A.Z., G.L.) extracted pre-specified study-level data in pairs using predetermined extraction forms, including study characteristics (author, country, design, study design, follow-up), patient characteristics (age, sex, primary cancer type, performance status), and survival (overall survival and progression-free survival as medians and hazard ratios). All data items were pre-specified, collected, and reported; data that are not shown in the manuscript (treatment regimens and associated outcomes) were not reported in the included studies. Only outcomes specific to patients with IMD-SE and IMD-PE were extracted.

Data sharing statement

All study-level data used in this analysis as well as relevant software scripts (R) may be accessed at the following URL: <https://www.dropbox.com/sh/ili4y7jlbxdus6q/AADfadR6rKH6k728-9yg688Za?dl=0>.

eTable 1. Search strategy in MEDLINE (June 21, 2021).

#	Searches	Results
1	exp Central Nervous System Neoplasms/	190498
2	exp Cerebral Cortex/	371952
3	exp Brain/	1242152
4	exp blood-brain barrier/	29084
5	1 or 2 or 3 or 4	1388676
6	exp Neoplasm Metastasis/	210601
7	5 and 6	7199
8	exp Central Nervous System Neoplasms/sc	18431
9	((brain* or intra?cranial or cerebral or cerebrum or crani* or skull* or central nervous system or cns or leptomening* or mening* or posterior fossa or frontal lobe or parietal lobe or temporal lobe or occipital lobe or insula* or cortex or cortic* or encephal* or hippocamp* or gyrus or limbic or dentate or white matter or gr\$y matter) adj3 (metasta* or (secondar* adj3 (malig* or cancer* or disease* or neoplas* or tumo?r* or carcinoma* or spread*))))).mp.	24726
10	(metasta* or (secondar* adj3 (malig* or cancer* or disease* or neoplas* or tumo?r* or carcinoma* or spread*))))).mp.	640987
11	5 and 10	31603
12	7 or 8 or 9 or 11	43949
13	oligo?met*.mp.	2434
14	(secondar* adj3 (malig* or cancer* or disease* or neoplas* or tumo?r* or carcinoma* or spread*) adj5 (limit* or stable or isolat* or restrict* or control* or confin* or constrain* or local* or asymptomatic)).mp.	851
15	13 or 14	3281
16	12 and 15	298

eTable 2. Study definitions of controlled ECD.

Study	Definition of controlled ECD	Notes
Armstrong et al., 2019 ²	information unavailable	Binary yes/no for controlled ECD
Chamberlain et al., 1996 ³	information unavailable	Inclusion criteria of systemic disease controlled or treatable with a life expectancy \geq 6 months in the absence of BrM
Gu et al., 2019 ^{4,*}	information unavailable	Binary yes/no for controlled ECD
Mariya et al., 2010 ¹	information unavailable	Binary yes/no for active extracranial metastatic lesions
McTyre et al., 2016 ⁵	information unavailable	Binary stable/progressive for systemic disease status
Mitin et al., 2011 ⁶	information unavailable	Binary yes/no for no ECD progression
Nogi et al., 2013 ⁷	information unavailable	Inclusion criteria of no extracranial tumour progression within 3 months of treatment
Pessina et al., 2016 ⁸	information unavailable	Inclusion criteria of controlled extracranial metastases
Pessina et al., 2017 ^{9,*}	information unavailable	Inclusion criteria of controlled extracranial disease
Rodrigues et al., 2011 ¹⁰	information unavailable	Inclusion criteria for non-rapidly progressive extracranial disease OR systemic disease absent or controlled on treatment

BrM, brain metastases; CI, confidence interval; ECD, extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable ECD.
^{*}Study reports two separate cohorts of patients, including one cohort of patients with IMD and stable or controlled ECD without further detailing extracranial metastases or prior treatment, as well as one cohort of patient that explicitly met our criteria for IMD-SE.

eTable 3. Characteristics of the 68 included studies.

Study	Publication Type	Study Design	Primary Cancer	IMD-SE Criteria	Median Follow-up (months)	IMD-SE (n)	IMD-PE (n)
Alhalabi et al., 2021 ¹¹	Full text	RCS	BC	≤ 2 EC sites	–	74	–
Andrews et al., 2004 ¹²	Full text	RCT	Mixed	≤ 2 EC sites	–	291	–
Aoyama et al., 2003 ¹³	Full text	RCS	Mixed	≤ 2 EC sites	6.3	34	53
Armstrong et al., 2019 ²	Full text	RCS	BC	Controlled ECD	10.33	35	16
Bai et al., 2016 ¹⁴	Full text	RCS	NSCLC	≤ 2 EC sites	–	76	–
Balducci et al., 2015 ¹⁵	Full text	RCS	Mixed	≤ 2 EC sites	102	47	–
Bates et al., 2015 ¹⁶	Full text	RCS	Melanoma	≤ 2 EC sites	–	10	63
Bilani et al., 2020 ¹⁷	Full text	RCS	BC	≤ 2 EC sites	–	805	–
Bodor et al., 2019 ¹⁸	Full text	RCS	NSCLC	≤ 2 EC sites	–	23	–
Buglione et al., 2020 ¹⁹	Full text	RCS	NSCLC	≤ 2 EC sites	18	108	–
Chamberlain et al., 1996 ³	Full text	PCS	Mixed	Controlled ECD	–	20	30
Chen et al., 2021 ²⁰	Full text	RCS	NSCLC	≤ 2 EC sites	49	125	127
Cheufou et al., 2014 ²¹	Full text	RCS	NSCLC	≤ 2 EC sites	17.3	37	–
Churilla et al., 2017 ²²	Full text	RCT	Mixed	≤ 2 EC sites	26	329	–
Collaud et al., 2012 ²³	Full text	RCS	NSCLC	≤ 2 EC sites	–	19	–
Congedo et al., 2012 ²⁴	Full text	RCS	NSCLC	≤ 2 EC sites	28	39	–
D'Agostino et al., 2011 ²⁵	Full text	RCS	Mixed	≤ 2 EC sites	95	97	–
Della Seta et al., 2019 ²⁶	Full text	RCS	Mixed	≤ 2 EC sites	–	13	35
Endo et al., 2014 ²⁷	Full text	PCS	NSCLC	≤ 2 EC sites	54.4	17	–
Ferro et al., 2016 ²⁸	Full text	PCS	Mixed	≤ 2 EC sites	76	30	–
Frost et al., 2018 ²⁹	Full text	RCS	Lung	≤ 2 EC sites	Intervention: 32.2 Control: 18.8	80	–
Gauvin et al., 2021 ³⁰	Full text	RCS	NSCLC	≤ 2 EC sites	13	50	–
Gorovets et al., 2014 ^{31,*}	Abstract	RCS	Mixed	≤ 2 EC sites	9.4	–	–
Gorovets et al., 2015 ^{32,*}	Full text	RCS	Mixed	≤ 2 EC sites	–	78	65
Gorovets et al., 2016 ^{33,*}	Full text	RCS	Mixed	≤ 2 EC sites	72.7	255	297
Gray et al., 2014 ³⁴	Full text	RCS	NSCLC	≤ 2 EC sites	31.9	66	–
Griffioen et al., 2013 ³⁵	Full text	RCS	NSCLC	≤ 2 EC sites	26.1	36	–
Gu et al., 2019 ⁴	Full text	RCS	Mixed	≤ 2 EC sites	48.5	70	91
Guo et al., 2014 ³⁶	Abstract	RCS	NSCLC	≤ 2 EC sites	17.2	53	–
Harat et al., 2020 ³⁷	Full text	RCS	Mixed	≤ 2 EC sites	9.5	82	–
Hirschmann et al., 2018 ³⁸	Abstract	RCS	NSCLC	≤ 2 EC sites	79.5	–	–
Inoue et al., 2010 ³⁹	Full text	RCS	Mixed	≤ 2 EC sites	20	24	–
Kaba et al., 2021 ⁴⁰	Full text	RCS	NSCLC	≤ 2 EC sites	mean ± SD (min-max): 25.71 ± 23.47 (4-92)	28	–
Karlovičs et al., 2009 ⁴¹	Full text	RCS	Mixed	≤ 2 EC sites	13	27	25
Kocher et al., 2010 ⁴²	Full text	RCT	Mixed	≤ 2 EC sites	49	359	–
Loi et al., 2019 ⁴³	Full text	RCS	NSCLC	≤ 2 EC sites	–	42	–
Lopez Guerra et al., 2012 ⁴⁴	Full text	RCS	NSCLC	≤ 2 EC sites	–	27	–
Macchia et al., 2015 ⁴⁵	Abstract	PCS	–	≤ 2 EC sites	–	27	–
Mariya et al., 2010 ¹	Full text	RCS	NSCLC	Controlled ECD	8.5	21	63
McTyre et al., 2016 ⁵	Full text	RCS	Mixed	Controlled ECD	53.9	399	264
Mitchell et al., 2020 ⁴⁶	Full text	RCS	NSCLC	≤ 2 EC sites	52.3	86	–
Mitin et al., 2011 ^{6,*}	Abstract	RCS	–	Controlled ECD	–	–	–
Mitin et al., 2013 ^{47,*}	Full text	RCS	Mixed	≤ 2 EC sites	16.2	46	123
Naqash et al., 2019 ⁴⁸	Abstract	RCS	NSCLC	≤ 2 EC sites	–	42	–
Navarria et al., 2019 ⁴⁹	Abstract	PCS	Mixed	≤ 2 EC sites	25	135	–
Nieder et al., 2020 ^{50,*}	Full text	RCS	Mixed	≤ 2 EC sites	15	89	–
Nieder et al., 2020 ^{51,*}	Full text	RCS	Mixed	≤ 2 EC sites	25	198	–
Niibe et al., 2016 ⁵²	Full text	RCS	NSCLC	≤ 2 EC sites	–	61	–
Nikitas et al., 2020 ⁵³	Full text	RCS	NSCLC	≤ 2 EC sites	9	6	–
Nogi et al., 2013 ⁷	Full text	RCS	Mixed	Controlled ECD	–	59	159
Pessina et al., 2016 ^{8,*}	Full text	RCS	Mixed	Controlled ECD	24	69	–
Pessina et al., 2017 ^{9,*}	Full text	RCS	NSCLC	≤ 2 EC sites	14.8	101	55
Pikin et al., 2011 ^{54,*}	Abstract	RCS	NSCLC	≤ 2 EC sites	–	32	–
Pikin et al., 2017 ^{55,*}	Abstract	RCS	NSCLC	≤ 2 EC sites	52	82	–
Raez et al., 2019 ⁵⁶	Abstract	RCS	NSCLC	≤ 2 EC sites	–	45	–
Rodrigues et al., 2011 ¹⁰	Full text	RCS	Mixed	Controlled ECD	4.7	–	–
Rogers et al., 2006 ⁵⁷	Full text	PCS	Mixed	≤ 2 EC sites	–	31	–

Study	Publication Type	Study Design	Primary Cancer	IMD-SE Criteria	Median Follow-up (months)	IMD-SE (n)	IMD-PE (n)
Salvador Coloma et al., 2018 ⁵⁸	Abstract	RCS	NSCLC	≤ 2 EC sites	–	67	–
Sato et al., 2018 ⁵⁹	Full text	RCS	NSCLC	≤ 2 EC sites	16	19	–
Shibata et al., 2019 ⁶⁰	Full text	RCS	SCLC	≤ 2 EC sites	–	11	–
Shirasawa et al., 2019 ⁶¹	Full text	RCS	SCLC	≤ 2 EC sites	–	6	–
Song et al., 2020 ⁶²	Full text	RCS	NSCLC	≤ 2 EC sites	11	5	–
Suzuki et al., 2021 ⁶³	Full text	PCS	NSCLC	≤ 2 EC sites	63	18	–
Wang et al., 2018 ⁶⁴	Full text	RCS	NSCLC	≤ 2 EC sites	Range: 12-72	74	–
Xu et al., 2018 ⁶⁵	Abstract	RCS	NSCLC	≤ 2 EC sites	–	41	–
Yamaguchi et al., 2017 ⁶⁶	Full text	RCS	NSCLC	≤ 2 EC sites	37.8	13	–
Yegya-Raman et al., 2019 ⁶⁷	Full text	RCS	NSCLC	≤ 2 EC sites	54.9	18	–
Zhang et al., 2019 ⁶⁸	Full text	RCS	NSCLC	≤ 2 EC sites	20.87	18	–

BC, breast cancer; EC, extracranial; ECD, extracranial disease; IMD-PE, intracranial metastatic disease in the setting of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease; NSCLC, non-small cell lung cancer; PCS, prospective cohort study; RCS, retrospective cohort study; RCT, randomized controlled trial; SCLC, small cell lung cancer; SD, standard deviation; –, information unavailable.

* Several studies were published by the same primary author across different years. All articles were screened to ensure minimal-to-overlap between study cohorts. Gorovets et al., 2014³¹ and 2015³² were not included in our analysis as they did not report on our pre-specified primary/secondary outcomes. Mitin et al., 2011⁶ and 2014⁴⁷ reported on different outcome measures that were incorporated into our meta-analysis and pooled survival analysis. Nieder et al., 2020⁵⁰ and 2020⁵¹ reported on two different cohorts of patients. Pessina et al., 2016⁸ and 2017⁹ reported on two different cohorts of patients. Pikin et al. 2011⁵⁴ and 2017⁵⁵ report on cohorts of patients with different baseline characteristics.

eTable 4. Median OS as reported by studies and derived based on digitized Kaplan-Meier curves in patients with IMD-SE versus IMD-PE. All studies listed were included in the primary meta-analysis comparing OS of IMD-SE with IMD-PE except Mitin et al., 2013⁴⁷ and Hirschmann et al., 2018³⁸ due to insufficient data.

Study	IMD-SE					IMD-PE					HR			
	No. patients	Median OS Reported		Median OS Derived		No. patients	Median OS Reported		Median OS Derived		HR Reported		HR Derived	
		Months	95% CI	Months	95% CI		Months	95% CI	Months	95% CI	HR	95% CI	HR	95% CI
Gu et al., 2019 ⁴	70	24	–	–	–	91	13	–	–	–	0.61	0.4-0.9	–	–
Armstrong et al., 2019 ²	35	21.9	12.6-31.1	21	12-42	16	7.3	4-10.6	7.1	5.1-	–	–	0.33	0.1-0.7
Bates et al., 2015 ^{16,*}	10	15.2	–	–	–	63	2.4	–	–	–	0.34	0.2-0.7	–	–
Chen et al., 2021 ²⁰	125	–	–	–	–	127	–	–	–	–	0.66	0.5-0.9	–	–
Mitin et al., 2013 ⁴⁷	46	21.7	–	–	–	123	10.3	–	–	–	–	–	–	–
Mariya et al., 2010 ¹	21	32	–	32.4	14.9-	63	7	–	7.5	5.6-9.5	–	–	0.18	0.1-0.3
Mitin et al., 2011 ^{6,*}	–	–	–	–	–	–	–	–	–	–	0.64	0.4-1.0	–	–
Hirschmann et al., 2018 ³⁸	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Karlovičs et al., 2009 ⁴¹	27	22	–	22.3	16.3-	25	13	–	12.8	8.3-17.3	–	–	0.42	0.2-0.8
Della Seta et al., 2019 ^{26,*}	13	–	–	–	–	35	–	–	–	–	0.56	0.3-1.2	–	–
Pessina et al., 2017 ⁹	101	18.6	13.6-23.6	–	–	55	12.1	9.7-14.5	–	–	0.91	0.5-2.3	–	–
Rodrigues et al., 2011 ¹⁰	–	–	–	–	–	–	–	–	–	–	0.81	0.5-1.3	–	–

In studies where a univariable HR was not reported, published Kaplan-Meier curves were digitized, from which median OS and HR were derived using the method by Guyot et al.⁶⁹; CI, confidence interval; HR, hazard ratio; IMD-PE, intracranial metastatic disease in the setting of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease; OS, overall survival; –, information unavailable.

*Median follow-up information was not reported in these studies.

eTable 5. Median OS as reported by studies and derived based on digitized Kaplan-Meier curves of patients with BrM and controlled versus uncontrolled ECD.

Study	Controlled Extracranial Disease (IMD-SE)					Uncontrolled Extracranial Disease (IMD-PE)					HR			
	No. patients	Median OS Reported		Median OS Derived		No. patients	Median OS Reported		Median OS Derived		HR Reported		HR Derived	
		mo	95% CI	mo	95% CI		mo	95% CI	mo	95% CI	HR	95% CI	HR	95% CI
Gu et al., 2019 ^{4,*}	–	24	–	–	–	–	13.5	–	–	–	0.60	0.4-0.9	–	–
Armstrong et al., 2019 ²	35	21.9	12.6-31.1	21	12-42	16	7.3	4-10.6	7.1	5.1-	–	–	0.33	0.1-0.7
Mariya et al., 2010 ¹	21	32	–	32.4	14.9-	63	7	–	7.52	5.6-9.5	–	–	0.18	0.1-0.3
Mitin et al., 2011 ^{6,**}	–	–	–	–	–	–	–	–	–	–	0.62	0.4-1.0	–	–
Rodrigues et al., 2011 ¹⁰	–	–	–	–	–	–	–	–	–	–	0.81	0.5-1.3	–	–

In studies where a univariable hazard ratio (HR) was not reported, published Kaplan-Meier curves were digitized, from which median overall survival (OS) and HR were derived using the method by Guyot et al.⁶⁹

BrM, brain metastases; CI, confidence interval; ECD, extracranial disease; HR, hazard ratio; IMD-PE, intracranial metastatic disease in the setting of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease; mo, months; OS, overall survival; –, information unavailable.

* Median OS and HRs from the subgroup of patients with BrM and controlled versus uncontrolled ECD were derived for meta-analysis.

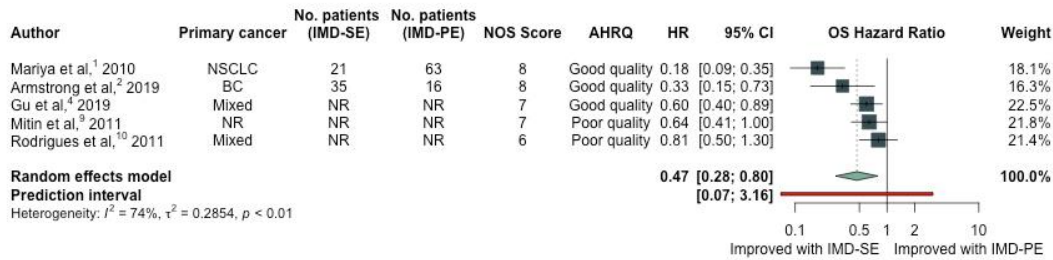
** Median follow-up information was not reported in this study.

eTable 6. Reported iPFS of patients with IMD-SE versus IMD-PE.

Study	IMD-SE			IMD-PE			HR		P-value
	No. patients	Median iPFS		No. patients	Median iPFS		HR	95% CI	
		mo	95% CI		mo	95% CI			
Della Seta et al., 2019 ^{26,*}	13	–	–	35	–	–	0.78	0.3-2.2	0.64
Rodrigues et al., 2011 ¹⁰	–	–	–	–	–	–	0.74	0.3-2.0	0.55
Gorovets et al., 2016 ³³	255	13.6	10.2-15	297	5.5	4.9-6.6	0.64	0.5-0.8	< 0.001
Bates et al., 2015 ^{16,*}	10	5	–	63	1.9	–	0.41	0.2-0.9	0.021

CI, confidence interval; HR, hazard ratio; IMD-PE, intracranial metastatic disease in the setting of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease; iPFS, intracranial progression-free survival; mo, months; –, information unavailable.

*Median follow-up information was not reported in these studies.



eFigure 1. Random-effects meta-analysis of the primary outcome of OS in patients with IMD-SE versus IMD-PE in studies that do not detail extracranial metastases or prior treatment. AHRQ, Agency for Healthcare Research and Quality; BC, breast cancer; IMD-PE, intracranial metastatic disease in the setting of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease; NOS, Newcastle-Ottawa Scale; NR, not reported; NSCLC, non-small cell lung cancer; OS, overall survival. The number of patients with IMD-SE and IMD-PE were not reported in three studies and were not included in the total number of patients.^{4,6,10}

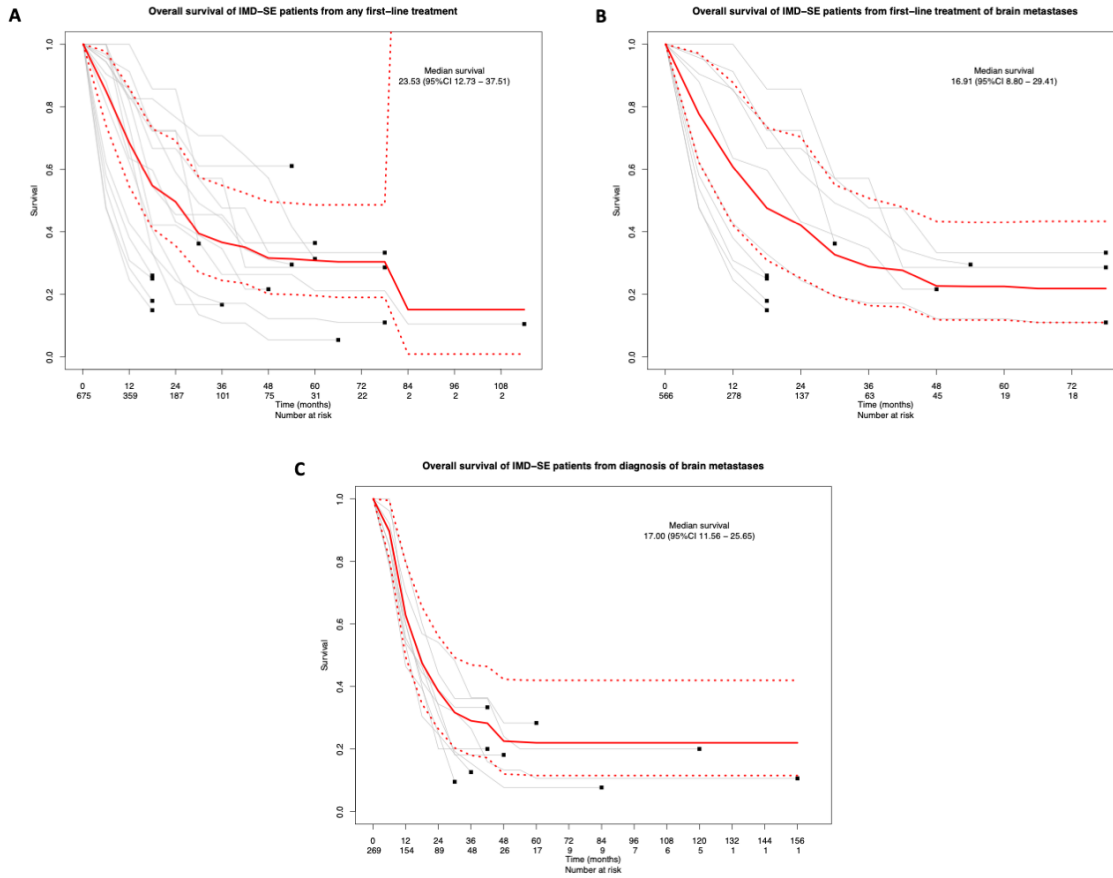






















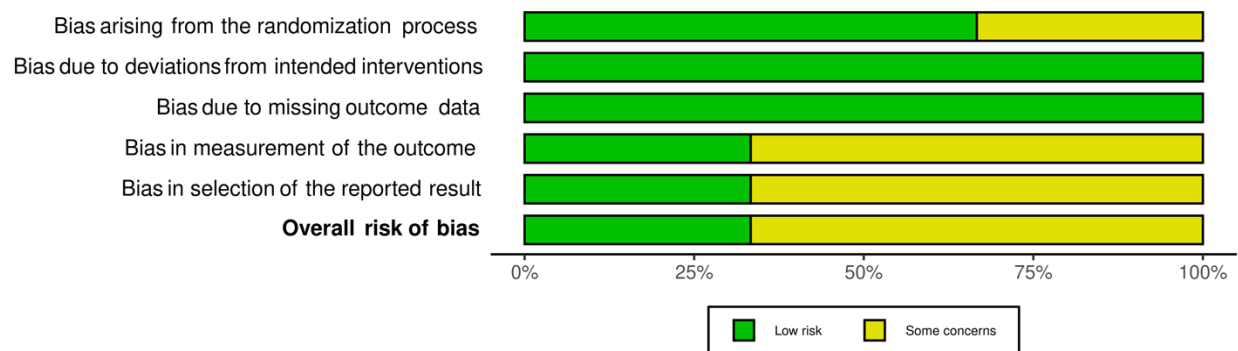
Figure 2. Summary OS curves of patients with IMD-SE. Overall survival (OS) from (A) any first-line treatment, including from treatment of primary cancer and/or brain metastases, (B) treatment of brain metastases only, and (C) diagnosis of brain metastases. Grey lines represent OS curves for individual studies. The red solid lines represent the summary survival curves, and the red dashed lines represent the 95% confidence interval. IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease.

		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Kocher et al., 2010						
	Churilla et al., 2017						
	Andrews et al., 2004						

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
 Some concerns
 Low

eFigure 3. Traffic light plot for risk of bias in RCTs.



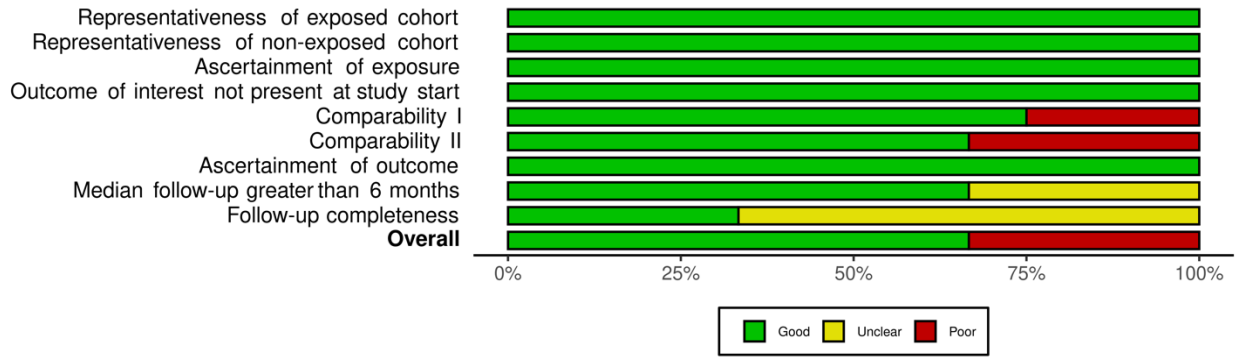
eFigure 4. Risk of bias summary plot for RCTs.

Study	Risk of bias									Overall
	D1	D2	D3	D4	D5	D6	D7	D8	D9	
Gu et al., 2019	+	+	+	+	+	X	+	+	-	+
Armstrong et al., 2019	+	+	+	+	X	+	+	+	+	+
Bates et al., 2015	+	+	+	+	+	X	+	-	-	X
Chen et al., 2021	+	+	+	+	+	+	+	+	+	+
Mitin et al., 2013	+	+	+	+	+	+	+	+	+	+
Mariya et al., 2010	+	+	+	+	+	+	+	+	-	+
Mitin et al., 2011	+	+	+	+	+	+	+	-	-	X
Hirschmann et al., 2018	+	+	+	+	X	+	+	+	-	+
Karlovits et al., 2009	+	+	+	+	+	X	+	+	-	+
Della Seta et al., 2019	+	+	+	+	X	+	+	-	-	X
Pessina et al., 2017	+	+	+	+	+	X	+	+	+	+
Rodrigues et al., 2011	+	+	+	+	+	+	+	-	-	X

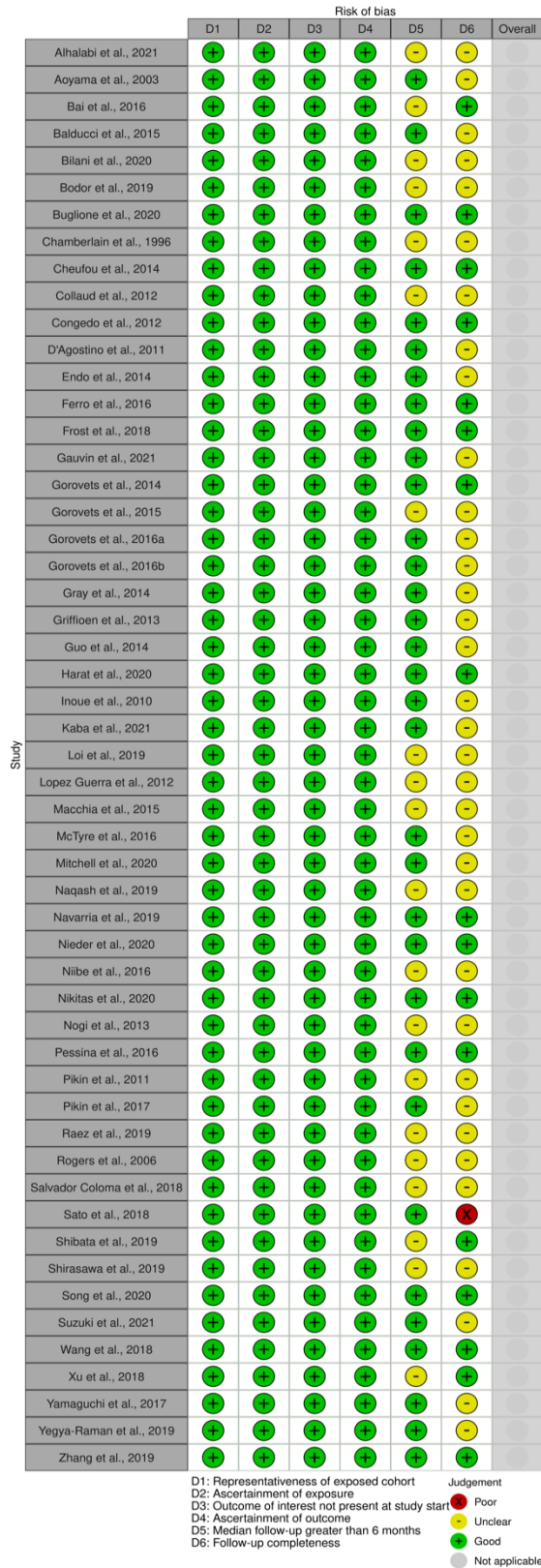
D1: Representativeness of exposed cohort
 D2: Representativeness of non-exposed cohort
 D3: Ascertainment of exposure
 D4: Outcome of interest not present at study start
 D5: Comparability I
 D6: Comparability II
 D7: Ascertainment of outcome
 D8: Median follow-up greater than 6 months
 D9: Follow-up completeness

Judgement
 X Poor
 - Unclear
 + Good

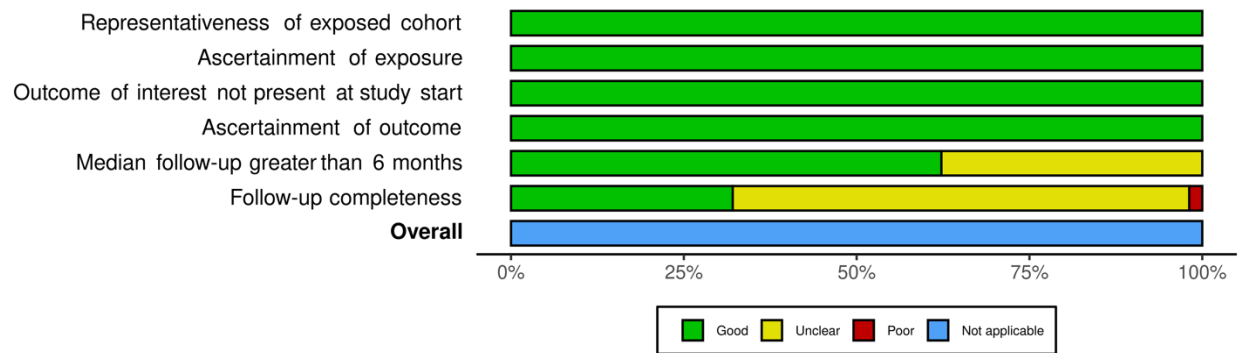
eFigure 5. Traffic light plot for risk of bias in observational studies comparing OS between IMD-SE and IMD-PE. IMD-PE, intracranial metastatic disease in the setting of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease; OS, overall survival.



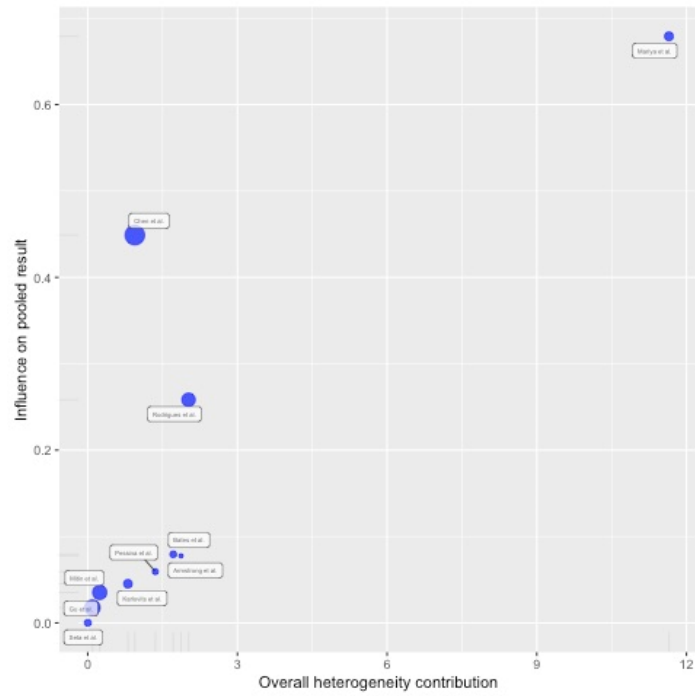
eFigure 6. Risk of bias summary plot for observational studies comparing IMD-SE and IMD-PE. IMD-PE, intracranial metastatic disease in the setting of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease.



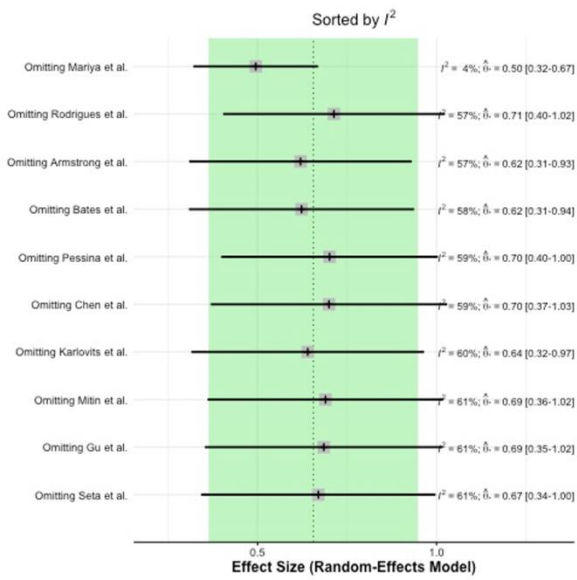
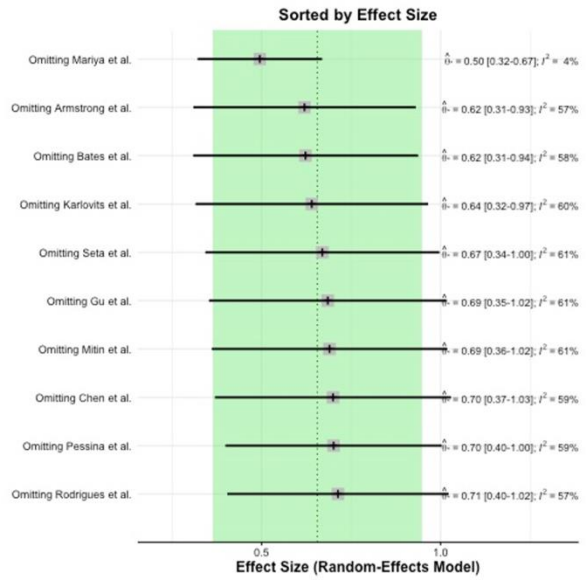
eFigure 7. Traffic light plot for risk of bias in single-arm observational studies.



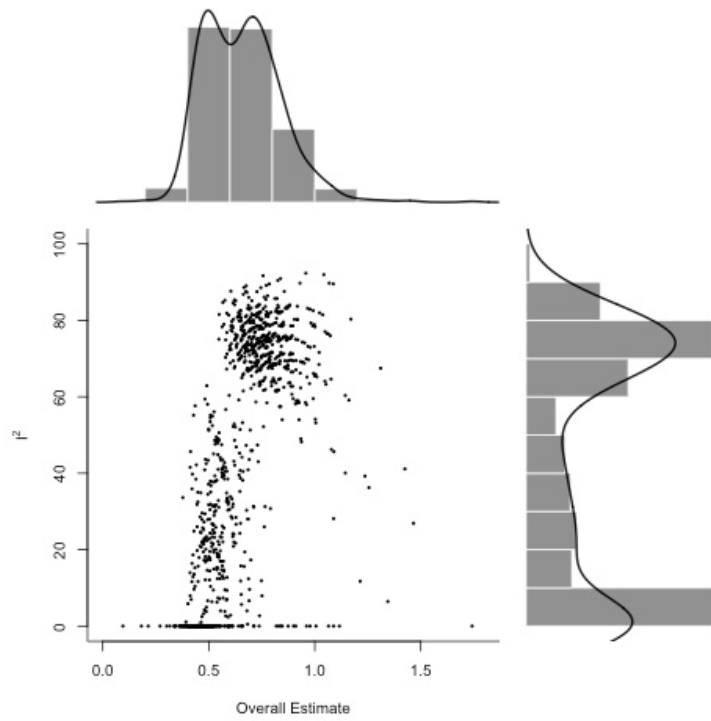
eFigure 8. Risk of bias summary plot for single-arm observational studies.



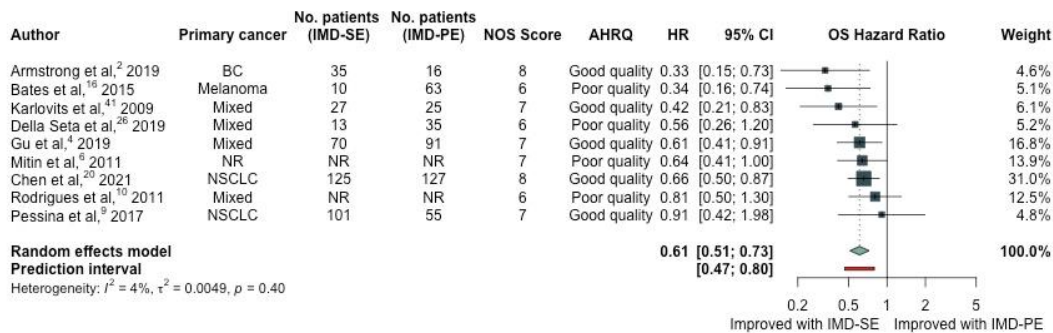
eFigure 9. Baujat plot for the meta-analysis on OS of IMD-SE versus IMD-PE. IMD-PE, intracranial metastatic disease in the setting of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease; OS, overall survival.

A**B**

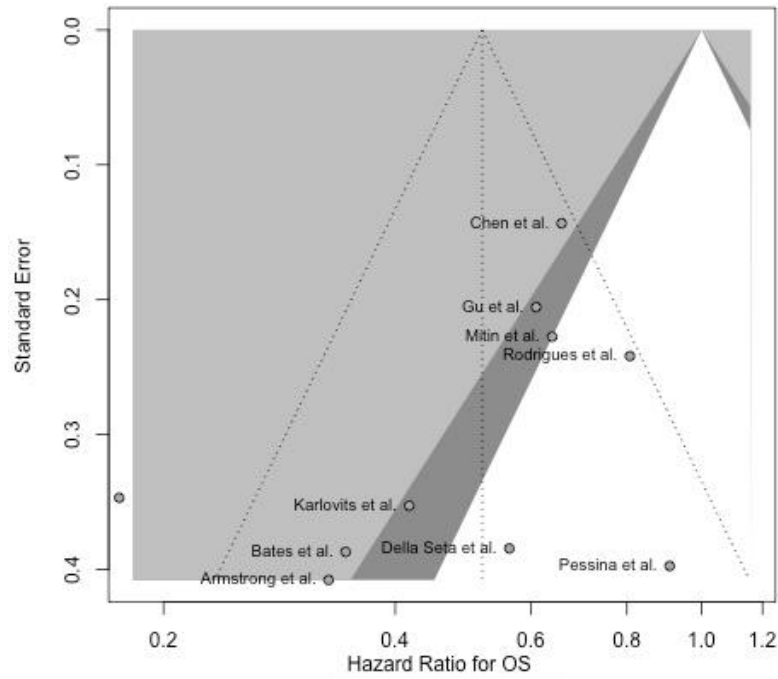
eFigure 10. Forest plots sorted by (A) I^2 heterogeneity and (B) effect size using leave-one-out meta-analysis.



eFigure 11. GOSH plot for the meta-analysis on OS of IMD-SE versus IMD-PE. GOSH, graphic display of heterogeneity; IMD-PE, intracranial metastatic disease in the setting of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease; OS, overall survival.



eFigure 12. Random effects meta-analysis of the primary outcome of OS in patients with IMD-SE compared to IMD-PE, excluding cohorts reported in Mariya et al.¹ AHRQ, Agency for Healthcare Research and Quality; BC, breast cancer; CI, confidence interval; HR, hazard ratio; IMD-PE, intracranial metastatic disease in the context of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the context of stable extracranial disease; NOS, Newcastle-Ottawa Scale; NR, not reported; NSCLC, non-small cell lung cancer; OS, overall survival. The number of patients with IMD-SE and IMD-PE were not reported in two studies and were not included in the total number of patients.^{6,10}



eFigure 13. Funnel plot for the meta-analysis on OS of IMD-SE versus IMD-PE. IMD-PE, intracranial metastatic disease in the setting of progressive extracranial disease; IMD-SE, intracranial metastatic disease in the setting of stable extracranial disease; OS, overall survival.

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