

Figure S1. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

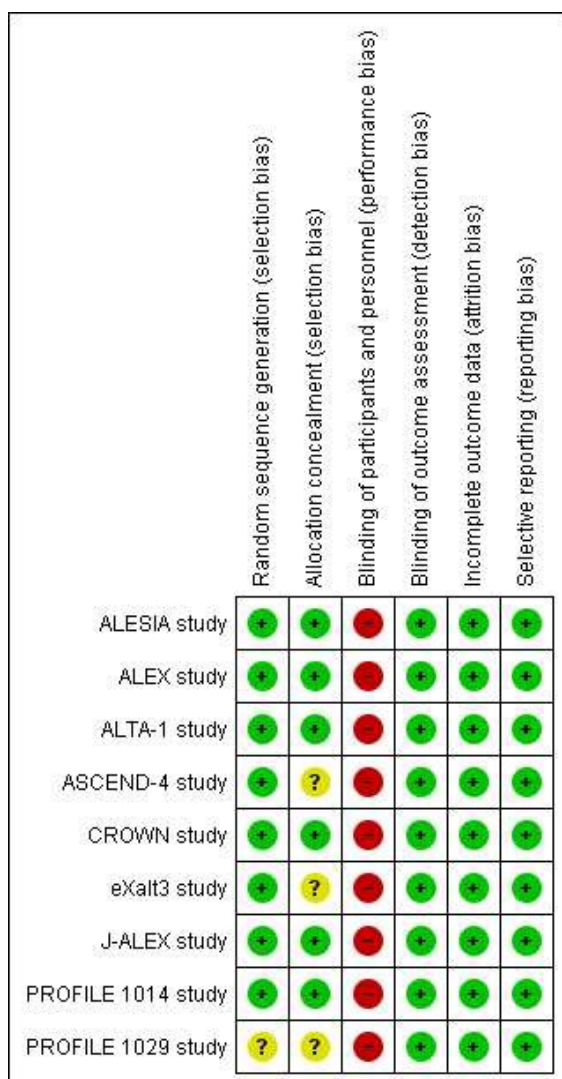


Figure S2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study. Green legend: low risk of bias; yellow legend: unclear risk of bias, red legend: high risk of bias

Table S1. Summary of the included studies

Study	Year	Updated results	Primary endpoint	Number of patients (treatment)	Number of patients (control)	Treatment	Control
Study	2014	2019	BICR-PFS	172	171	Crizotinib 250 mg BID	Cisplatin 75 mg/m ² or carboplatin AUC 5–6 plus pemetrexed 500 mg/m ² q21
PROFILE 1014 [6, A]	2017	NA	BICR-PFS	189	187	Ceritinib 750 mg	Cisplatin 75 mg/m ² or carboplatin AUC 5–6 plus pemetrexed 500 mg/m ² q21
ASCEND-4 [11]	2017	2020	BICR-PFS	103	104	Alectinib 300 mg BID	Crizotinib 250 mg BID
J-ALEX [9, B]	2017	2020	Investigator-assessed PFS	152	151	Alectinib 600 mg BID	Crizotinib 250 mg BID
ALEX [12, 22]	2018	NA	BICR-PFS	77	89	Crizotinib 250 mg BID	Cisplatin 75 mg/m ² or carboplatin AUC 5–6 plus pemetrexed 500 mg/m ² q21
PROFILE 1029 [C]	2020	2022	BICR-PFS	149	147	Lorlatinib 100 mg	Crizotinib 250 mg BID
CROWN [10, D]	2019	NA	Investigator-assessed PFS	125	62	Alectinib 600 mg BID	Crizotinib 250 mg BID
ALESIA [8]	2018	2021	BICR-PFS	137	138	Brigatinib 180 mg	Crizotinib 250 mg BID
ALTA-1 [E, F]	2021	NA	BICR-PFS	143	147	Ensartinib 225 mg	Crizotinib 250 mg BID

NA: not applicable

Table S2. Results of studies included

Study	Follow up	Year	Median Follow Up	Progression free survival	Overall survival
PROFILE 1014 [6, A]	First publication	2014	16.7 months and 17.4 months, respectively	7 vs 10.9, HR 0.45 [95% CI, 0.35 to 0.4]; $P < 0.001$	NR vs NR HR 0.82 [95% CI, 0.54 to 1.26]; $P < 0.36$
	Updated results	2018	45.5 months and 45.7 months, respectively	NA	47.5 vs NR HR 0.760 [95% CI, 0.548 to 1.053]; $P < 0.0978$
ASCEND-4 [11]	First publication	2017	19.7 months in both arms	8.1 vs 16.6, HR 0.55 [95% CI, 0.42 to 0.73]; $P < 0.001$	26.2 vs NR HR 0.73 [95% CI, 0.5 to 1.08]; $P < 0.056$
	Updated results	NA	NA	NA	NA
J-ALEX [9, B]	First publication	2017	12.2 months and 12 months, respectively	10.2 vs NR, HR 0.34 [95% CI, 0.17 to 0.71]; $P < 0.0001$	NA
	Updated results	2020	42.2 months and 42.4 months, respectively	10.2 vs 34.1, HR 0.37 [95% CI, 0.26 to 0.52];	43.7 vs NR HR 0.8 [95% CI, 0.35 to 1.82];
ALEX [12, 22]	First publication	2017	17.6 months and 18.36 months, respectively	11.1 vs NR, HR 0.47 [95% CI, 0.34 to 0.65]; $P < 0.001$	NR vs NR HR 0.76 [95% CI, 0.48 to 1.2]; $P < 0.24$
	Updated results	2020	46 months in both arms	10.9 vs 34.8, HR 0.43 [95% CI, 0.32 to 0.58]; $P < 0.0001$	57.4 vs NR HR 0.67 [95% CI, 0.46 to 0.98]; $P < 0.0376$
PROFILE 1029 [C]	First publication	2018	21.6 months and 22.5 months, respectively	6.8 vs 11.1, HR 0.402 [95% CI, 0.286 to 0.565]; $P < 0.0001$	27.7 vs 28.5 HR 0.879 [95% CI, 0.556 to 1.445]; $P < 0.327$
	Updated	NA	NA	NA	NA

	results				
CROWN [10, D]	First publication	2020	14.8 months and 18.3 months, respectively	9.3 vs NR, HR 0.28 [95% CI, 0.19 to 0.41]; <i>P</i> < 0.001	NR vs NR HR 0.72 [95% CI, 0.41 to 1.25]; <i>P</i> n.s.
	Updated results	2022	29.3 months and 36.7 months, respectively	9.3 vs NR, HR 0.27 [95% CI, 0.18 to 0.39];	NA
ALESIA [8]	First publication	2019	15 months and 16.2 months, respectively	11.1 vs NR, HR 0.22 [95% CI, 0.13 to 0.38]; <i>P</i> < 0.0001	NR vs NR HR 0.28 [95% CI, 0.12 to 0.68];
	Updated results	NA	NA	NA	NA
ALTA-1 [E, F]	First publication	2018	9.3 months and 11 months, respectively	9.8 vs NR, HR 0.49 [95% CI, 0.33 to 0.74]; <i>P</i> < 0.001	NR vs NR HR 0.98 [95% CI, 0.5 to 1.93];
	Updated results	2021	15.2 months and 40.4 months, respectively	11.1 vs 40.4, HR 0.48 [95% CI, 0.35 to 0.66]; <i>P</i> < 0.0001	NR vs NR HR 0.81 [95% CI, 0.53 to 1.22];
eXalt3 [13]	First publication	2021	20.2 months and 23.8 months, respectively	12.7 vs 25.8, HR 0.51 [95% CI, 0.35 to 0.72]; <i>P</i> < 0.0001	NR vs NR HR 0.91 [95% CI, 0.54 to 1.54]; <i>P</i> = 0.73
	Updated results	NA	NA	NA	NA

NA: not applicable

References of supplementary materials

A. Solomon BJ, Kim DW, Wu YL, Nakagawa K, Mekhail T, Felip E, et al. Final overall survival analysis from a study comparing first-line crizotinib *versus* chemotherapy in ALK-mutation-positive non-small-cell lung cancer. *J Clin Oncol.* 2018;36:2251–8.

B. Nakagawa K, Hida T, Nokihara H, Morise M, Azuma K, Kim YH, et al. Final progression-free survival results from the J-ALEX study of alectinib *versus* crizotinib in *ALK*-positive non-small-cell lung cancer. *Lung Cancer*. 2020;139:195–9.

C. Wu YL, Lu S, Lu Y, Zhou J, Shi YK, Sriuranpong V, et al. Results of PROFILE 1029, a phase III comparison of first-line crizotinib *versus* chemotherapy in East Asian patients with *ALK*-positive advanced non-small cell lung cancer. *J Thorac Oncol*. 2018;13:1539–48.

D. Qing Z, Kim HR, Soo RA, Chiu CH, Hayashi H, Kim SW, et al. 992P Updated analyses from the CROWN study of first-line lorlatinib *vs* crizotinib in Asian patients with *ALK*-positive non-small cell lung cancer (NSCLC). *Ann Oncol*. 2022;33:S1007.

E. Camidge DR, Kim HR, Ahn MJ, Yang JCH, Han JY, Hochmair MJ, et al. Brigatinib *versus* crizotinib in *ALK* inhibitor-naïve advanced *ALK*-positive NSCLC: final results of phase 3 ALTA-1L trial. *J Thorac Oncol*. 2021;16:2091–108. Erratum in: *J Thorac Oncol*. 2022;[Epub ahead of print].

F. Camidge DR, Kim HR, Ahn MJ, Yang JC, Han JY, Lee JS, et al. Brigatinib *versus* crizotinib in *ALK*-positive non-small-cell lung cancer. *N Engl J Med*. 2018;379:2027–39.