

References

- 97 Kawamura T, Murakami H, Kobayashi H, et al. Leptomeningeal recurrence after long-term alectinib therapy for non-small cell lung cancer harboring an EML4-ALK fusion protein. *Invest New Drugs* 2019;37:184-7.

Table S1 Search terms used

MeSH Terms	“leptomeningeal metastases” “meningeal metastases” “LM” “Non-small cell lung cancer” “NSCLC” “mechanisms” “diagnosis” “Treatment” “therapy”
Free text search terms	“The blood-brain barrier ” “circulating tumor DNA” “circulating tumor cells” “extracellular vesicles ” , etc.
Filters	The following filters are applied in the PubMed database: select ‘Review’ and ‘Clinical Trial’ for document type; set the publication time to ‘2017 - 2024’; and select ‘English’ for language. In other databases, similar criteria were used to obtain literature that met the requirements

Table S2 Case reports that assessed ALK TKIs and other inhibitors in patients with leptomeningeal metastasis from non-small cell lung cancer in the last six years

Researcher (year)	Administration method	Research type	Mutation type	LM (n)	ORR	DCR	mPFS	mOS	Improve the situation
Metro G (84) <i>et al.</i> (2023)	Reprotrectinib 160 mg	Case 1	G2032R ROS1+	1					Symptom relief
Li, Z.(81) <i>et al.</i> (2020)	Alectinib 600 mg Alectinib 900 mg Lorlatinib 100 mg (in turn)	Case 1	LOC388942-ALK LINC00211-ALK	1					PD 7.6 PD 2.1 PD 8.7
Gaye, Elisabeth(75) <i>et al.</i> (2019)	Brigatinib	Case 1	ALK+	1					PR>14
Kawamura, T.(97) <i>et al.</i> (2019)	alectinib	Case 1	ALK+	1					Symptom relief
Yamamoto, K.(83) <i>et al.</i> (2021)	Sequential therapy (5 types)	Case 1	ALK+	1					Symptom relief
Nakashima, K.(78) <i>et al.</i> (2021)	Lorlatinib	Case 1	drug resistance (alectinib brigatinib)	1					PFS>8
Sasaki, K.(79) <i>et al.</i> (2021)	Lorlatinib (nasogastric tube administration)	Case 1	PD after treatment (alectinib)	1					OS 16
Facchinetti, F.(77) <i>et al.</i> (2021)	Lorlatinib	Case 1	EZR-ROS1+	1					PR>9
Sun, S.(74) <i>et al.</i> (2022)	Lorlatinib	stagel/II	4ALK+ 1ROS1+	5	80% (4/5)	100% (5/5)			
Guaitoli, G.(76) <i>et al.</i> (2024)	Lorlatinib	Case 1	ALK+ Previous Medications (crizotinib Lorlatinib)	1					PR>36

ALK=anaplastic lymphoma kinase, ROS1=c-ros oncogene 1. PD=progressive disease