Acceptance code: EE231

Cost of managing brain metastases in patients with *ALK*+ aNSCLC receiving first-line tyrosine kinase inhibitors (TKIs) in Sweden

Fredrik Nilsson,[1] Hannah Le,[2] Daniel Ladino Montero,[3] Marianne Wittrup Larsen[1]

[1]Pfizer, Stockholm, Sweden; [2]Pfizer, New York, NY, USA; [3]Lumanity, Dublin, Ireland

Conclusions

- Our study demonstrates the direct relationship between a lower cumulative incidence of progression of brain metastases (BM) and lower cost burden in patients with anaplastic lymphoma kinase (*ALK*)-positive advanced non-small cell lung cancer (aNSCLC) receiving first-line (1L) ALK tyrosine kinase inhibitors (TKIs) in Sweden
- The longitudinal cost data demonstrate that 1L lorlatinib leads to lower management costs of BM in patients with *ALK*-positive aNSCLC compared with other 1L ALK TKIs, like crizotinib, brigatinib, and alectinib
  - These results are consistent with data from the phase 3 CROWN study, where the cumulative incidence of progression of BM with 1L lorlatinib was low
- Cost savings increased significantly over time and were greatest in patients without baseline BM, reflecting the prevention of BM with 1L lorlatinib
  - From year 1 to year 4, cost savings with lorlatinib vs crizotinib increased by 5 times in the intention-to-treat (ITT) population and by 8 times in patients without baseline BM

Background

- Approximately 24% of patients with *ALK*-positive aNSCLC have BM at diagnosis, and more than 50% develop BM over the course of their disease[1]
- Previous studies demonstrated a high economic and humanistic burden in patients with *ALK*-positive aNSCLC with BM compared with those without BM[2,3]
- Several phase 3 studies with second- and third-generation ALK TKIs have shown superior brain penetration effect compared with crizotinib.[4-6] In the CROWN study, the cumulative incidence of progression of BM was lower with lorlatinib than with crizotinib in patients with and without baseline BM (**Table 1**)[7]
- This study estimates the annual costs of managing BM in patients with *ALK*-positive aNSCLC receiving 1L lorlatinib, alectinib, brigatinib, and crizotinib in Sweden

Table 1: Cumulative incidence of progression of BM from 12 to 48 months[a]

		CROWN trial[b]		ALEX trial[b]		ALESIA trial[b,c]	
		Lorlatinib	Crizotinib	Alectinib	Crizotinib	Alectinib	Crizotinib
12 months	ITT population, %[d]	2.8[6]	33.2[6]	9.4[4]	41.4[4]	4.7[8]	23.6[8]
	Without baseline BM, %	1.0[7]	17.8[7]	4.6[9]	31.5[9]	3.9[8]	13.0[8]
	With baseline BM, %	7.4[7]	72.3[7]	16.0[9]	58.3[9]	6.5[8]	45.1[8]
24 months	ITT population, %	5[10]	45[10]	NR	NR	8.9[8]	32.2[8]
	Without baseline BM, %	1.1[10]	28.8[10]	7.2[11]	45.3[11]	6.5[8]	18.0[8]
	With baseline BM, %	18[10]	91[10]	NR	NR	13.6[8]	55.7[8]
36 months	ITT population	8[12]	73[12]	–	–	11.6[8]	34.0[8]
	Without baseline BM, %	5[12]	64[12]	–	–	9.1[8]	23.1[8]
	With baseline BM, %	NA[12,e]	NA[12,e]	–	–	16.2[8]	55.7[8]
48 months	ITT population, %	8[12]	73[12]	–	–	13.4[8]	34.0[8]
	Without baseline BM, %	5[12]	64[12]	–	–	9.1[8]	23.1[8]
	With baseline BM, %	NA[12,e]	NA[12,e]	–	–	20.7[8]	55.7[8]

BM, brain metastases; CNS, central nervous system; ITT, intention-to-treat; NA, not available; NR, not reported.
[a] Baseline characteristics were not adjusted between trials; therefore, comparisons between trials should be made with caution. [b] Decimal places reported as published in the original studies. [c] ALEX does not provide CNS data in ITT patients and patients with baseline BM beyond 12 months; therefore, ALESIA data was used from 36 months onward. [d] The cumulative incidence of progression of BM in the ITT population of the ALTA-1L trial at 12 months was 12.0% with brigatinib and 22.6% with crizotinib. [e] There is no update to provide, as the cumulative incidence stopped at the last event, which was at approximately 24 months in this subgroup in the CROWN study.

References:

1. Rangachari et al. *Lung Cancer*. 2015; 88(1):108-111. **2.** Isla et al. *Lung Cancer Manag*. 2020; 9(1):LMT28. **3.** Guérin et al. *J Med Econ*. 2016; 19(5):526-536. **4.** Peters et al. *N Engl J Med*. 2017; 377(9):829-38. **5.** Camidge et al. *N Engl J Med*. 2018; 379:2027-2039. **6.** Shaw et al. *N Engl J Med*. 2020; 383(21):2018-29. **7.** Solomon et al. *J Clin Oncol*. 2022; 40(31):3593-602. **8.** Zhou et al. *JTO Clin Res Rep*. 2024:5(9):100700. **9.** Gadgeel et al. *Ann Oncol*. 2018; 29(11):2214-22. **10.** Solomon et al. *Lancet Respir Med*. 2023; 11(4):354-366. **11.** Burudpakdee et al. *Lung Cancer*. 2018; 119:103-11. **12.** Solomon et al. *J Clin Oncol*. 2024:JCO2400581. **13.** Le et al. Poster P2.10-05. Presented at: World Conference on Lung Cancer (WCLC); September 2023; Singapore. Published in: *J Thorac Oncol*. 2023;18(11S):S353-S354. **14.** Regional prices and reimbursements for the Southern Healthcare Region 2023. Southern Healthcare Region. Accessed October 24, 2024. https://sodrasjukvardsregionen.se/download/regionala-priser-och-ersattningar-for-sodra-sjukvardsregionen-2023/

Acknowledgments:

This study was sponsored by Pfizer AB. Editorial and medical writing support was provided by Arrianna Carey, PhD, of Nucleus Global, and funded by Pfizer.

Disclosures:

F Nilsson and **M W Larsen** are employed by Pfizer AB, Sweden. **H Le** is employed by Pfizer Inc., USA. **D Ladino** is employed by Lumanity, UK.

Presented at the ISPOR EU Congress 2024 | November 17-20, 2024 | Barcelona, Spain

Correspondence: Fredrik Nilsson; Fredrik.Nilsson@pfizer.com

Methods

- This study used results from another study performed in the UK where resource use frequencies of managing patients with *ALK*-positive aNSCLC with and without BM were estimated[13]
- The resource use frequencies were combined with Swedish cost data to estimate the costs of managing patients in Sweden
- Healthcare resources included medical visits, hospitalizations, laboratory tests, imaging, and surgical procedures. Diagnostic tests and treatment costs were excluded from the analysis. Adverse event (AE) costs were considered in a scenario analysis. Unit costs were sourced from the Swedish Southern Healthcare Region 2023 price list[14]
- Resource consumption is based on the UK's National Health Service and was validated through interviews with 3 UK thoracic oncologists specializing in lung cancer. The validation interviews differentiated the resource utilization for patients with and without BM during the first and subsequent years of treatment
- The estimation of the annual cost of managing patients with *ALK*-positive aNSCLC with or without the development of BM was made by multiplying resource consumption by the corresponding unit cost
- The total annual cost with each TKI was estimated for the ITT population by weighting the annual cost of managing patients with and without BM using 12-, 24-, 36-, and 48-month cumulative incidence of progression of BM from the CROWN, ALEX, ALESIA, and ALTA-1L trials
- The cumulative incidence results for 12, 24, 36, and 48 months represent the management costs for treatment years 1, 2, 3, and 4, respectively
- An alternative analysis was modeled considering the management costs of treatment-emergent grade 3-5 AEs reported in ≥5% of patients in the ITT population
- AE management costs were included as a one-off cost

Results

- Management costs were Swedish krona (SEK) 62,456 per patient-year (PPY) for patients without BM and SEK 167,121 PPY for patients with BM in the first year, resulting in cost savings of SEK 104,665 in the first year when BM are avoided (**Table 2**)

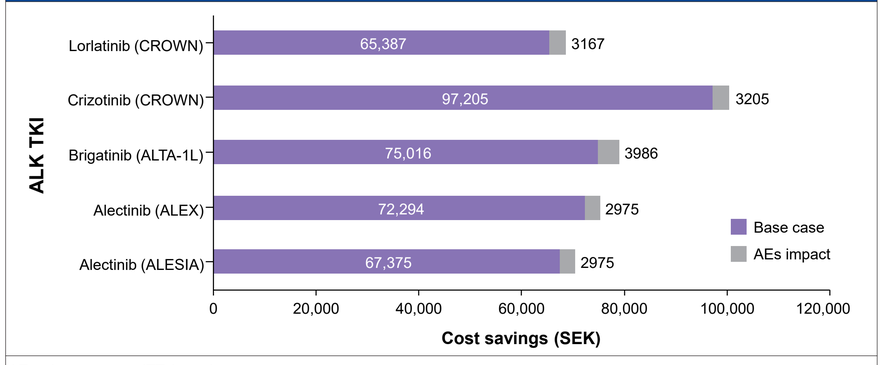
Table 2: Consumption of resources associated with the management of patients with vs without BM, unit costs, and management costs[a,b]

	Patients without BM (first and subsequent years)		Patients with BM (first year)		Patients with BM (subsequent years)		Unit cost	Cost difference between patients with and without baseline BM in the first year	Cost difference between patients with and without baseline BM in subsequent years
	Patients, %	Resources/year, n	Patients, %	Resources/year, n	Patients, %	Resources/year, n	SEK, 2023	SEK	SEK
Specific procedures for the treatment of metastases[c]								49,826	20,284
Holocranial brain RT	0	0	4	5	0	0	13,337	2667	0
Radiosurgery or stereotactic RT	0	0	43.3	3	21.6	3	28,487	37,005	18,502
Surgical resection	0	0	5.7	1	1	1	178,141	10,154	1781
Hospitalizations								8183	15,605
General admission (acute complications related to BM)	8.3	1	16.7	1	33.4	1	40,959	3441	10,281
Radiation oncology	0	0	1.3	2	6.5	2	40,959	1065	5325
Elective surgery	0	0	5.3	1	0	0	69,383	3677	0
Imaging techniques								8289	8289
Bone scan	3	1	3	1	3	1	3273	0	0
Cerebral MRI	50	1.7	94.3	4	94.3	4	3029	8901	8901
Thorax/abdomen computed tomography	100	4	100	4	100	4	2087	0	0
Brain computed tomography	30	1.3	4	2.7	4	2.7	2087	-612	-612
Medical visits								38,367	38,367
Medical oncology	70	13	70	13	70	13			
Medical oncology (first visit)							5214	0	0
Medical oncology (successive visits)							2677	0	0
Emergencies	70	1	70	2	70	2	4445	3112[d]	3112[d]
Radiation oncology	30	12	100	16	100	16			
Radiation oncology (first visit)							5214	3650	3650
Radiation oncology (successive visits)							2677	31,321	31,321
Surgery	0	0	10	2	10	2	2846	285	285
Laboratory tests								0	0
Blood count	100	12	100	12	100	12	278	0	0
Biochemistry	100	12	100	12	100	12	278	0	0
Thoracentesis	10	1	10	1	10	1	9328	0	0
Total management costs								104,665	82,545

BM, brain metastases; MRI, magnetic resonance imaging; RT, radiotherapy; SEK, Swedish krona.
[a] The type and frequency of resources used are similar between the UK and Sweden. [b] This table was derived from the resource table reported in Isla et al., 2020[2] and updated after validation interviews with medical oncologists in the UK. [c] No specific procedures for the treatment of metastases were given in 47% of patients with BM (first year) and in 77.4% of patients with BM (subsequent years). [d] Cost difference is for *successive* emergency visits; *first* emergency visits had no cost difference.

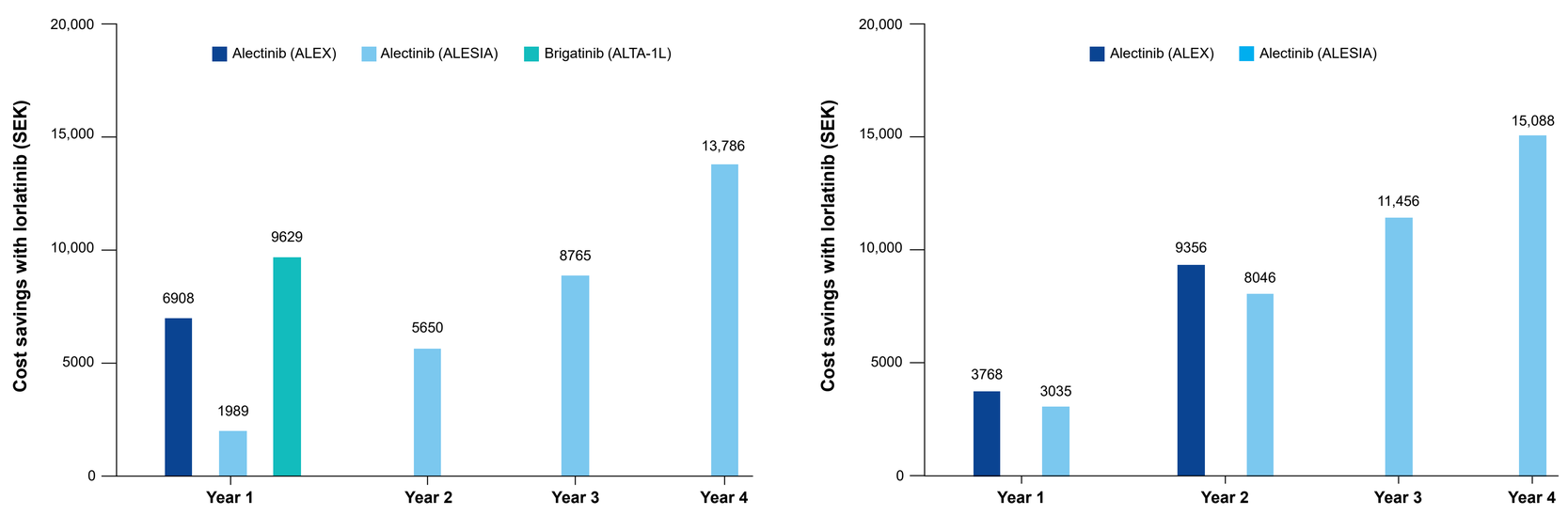
- The annual cost savings of lorlatinib per patient in year 1 vs crizotinib, alectinib, and brigatinib was SEK 31,818, SEK 6908, and SEK 9629 in the ITT population
- In the ITT population, the total management annual costs per patient in year 1 were:
  - SEK 65,387 for lorlatinib (per CROWN)
  - SEK 72,294 for alectinib (per ALEX)
  - SEK 75,016 for brigatinib (per ALTA-1L)
  - SEK 86,110 for crizotinib (per ALTA-1L)
  - SEK 97,205 for crizotinib (per CROWN)
  - SEK 105,787 for crizotinib (per ALEX)
- Cumulative cost savings with lorlatinib increased from year 1 to year 4 (**Figure 1**)
  - With lorlatinib vs crizotinib, the increase was 5 times in the ITT population, and the increase was 8 times in patients without baseline BM
- Lorlatinib has a unique AE profile, so it is expected that including AE management costs would reduce lorlatinib's cost savings compared with the base case model. However, the impact of AEs on cumulative cost savings with lorlatinib was minimal (**Figure 2**)

Figure 2: First year cumulative cost in the ITT population by base case and impact of AEs



AE, adverse event; ITT, intention-to-treat.

Figure 1: Cost savings with lorlatinib vs other ALK TKIs



BM, brain metastases; ITT, intention-to-treat.
[a] Cost savings with lorlatinib vs crizotinib are not shown here because savings vs crizotinib far surpassed savings vs other ALK TKIs.