Economic Burden Of Incident Brain Metastases In Medicare Beneficiaries With ALK+ Metastatic Non-Small Cell Lung Cancer

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Objective

To estimate the cumulative direct total healthcare costs associated with brain metastases (BMs) in Medicare beneficiaries with anaplastic lymphoma kinase positive (ALK+) metastatic non-small cell lung cancer (mNSCLC) treated with any ALK tyrosine kinase inhibitors (TKI) in the first line (1L) setting at 12, 24, 36, and 48 months.

Conclusions

Among Medicare beneficiaries with ALK+ mNSCLC treated with an ALK TKI in the 1L setting, incident BMs occurred in 19.7% of beneficiaries and were associated with substantial additional healthcare costs conditional on survival.

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Background

- BMs are a common and clinically important complication in ALK+ mNSCLC[1,2,3,4]
- Contemporary evidence on the economic burden of BM development in older adults who have ALK+ mNSCLC and are receiving ALK TKIs in the 1L setting in real-world data is limited[5,6,7]
- This study quantified cumulative direct total healthcare costs associated with BMs in US Medicare beneficiaries with ALK+ mNSCLC treated with 1L ALK TKIs

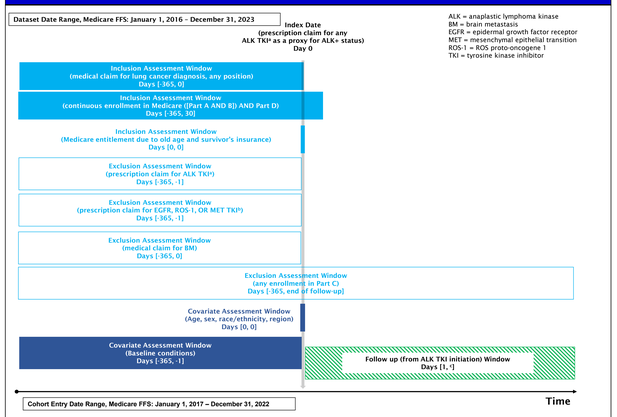
Materials and Methods

- 100% Medicare Parts A, B, and D claims (2016–2023) were used to identify beneficiaries with mNSCLC and no baseline BM who initiated a 1L ALK TKI (**Fig 1**)
- Incident BM was defined as the first claim with ICD-10-CM code C79.31 following ALK TKI initiation. For the cost analysis, follow-up was anchored at BM onset.
- A modified clone-censoring framework assigned follow-up time as follows: BM arm = observed post-BM time; non-BM arm = observed time without BM and pre-BM (clone-censored) time for those who later developed a BM
- Beneficiaries without observed BMs were assigned pseudo-BM dates based on the observed distribution of BM timing
- Total direct spending (inflation-adjusted to 2023 dollars) included all Medicare, beneficiary, and third-party payments on medical and pharmacy claims
- Incremental monthly BM-attributable spending was modeled with a log-gamma GEE with an unstructured correlation matrix adjusted for baseline covariates; incremental spending differences between arms were interpreted as BM-attributable
- Analyses were conducted conditional on survival, and cumulative incremental spending was evaluated through 48 months after incident BM, and reported at 12, 24, 36, and 48 months post-BM

Results

- A total of 985 beneficiaries with ALK+ mNSCLC who initiated an ALK TKI in the 1L setting were included in the cohort (**Fig 2**).

Figure 1. Study Design



a. Alectinib, brigatinib, ceritinib, crizotinib, ensartinib, or lorlatinib
b. Afatinib, amivantamab-vmjw, capmatinib, dacomitinib, entrectinib, erlotinib, gefitinib, mobocertinib, osimertinib, repotrectinib, tepotinib
c. Details on analytic approach specified in Materials and Methods

Figure 2. Patient Attrition

Inclusion Criteria

≥1 ALK TKI claim (proxy for ALK+) during the period from January 1, 2017, through December 31, 2022 in 100% Medicare Part D file (earliest is the index date)[1]
N = 5,936

≥1 fee-for-service claim with a diagnosis code in any position for lung cancer (ICD-10-CM: C34*, C39.9) in the year preceding and including the index date[2]
N = 3,482

Continuous enrollment in Medicare Parts A, B & D for the 12 months prior to the month of the index date and the month of the index date (13 months total)
N = 2,466

Current reason for Medicare entitlement is "old age and survivor's insurance," as recorded in the enrollment file for the calendar year of the index date
N = 2,198

Exclusion Criteria

≥1 prescription drug claim for an ALK TKI in the year preceding the index date[3]
N = 1,864

≥1 prescription drug claim for any EGFR TKI , ROS-1 TKI or MET TKI in the year preceding the index date[3]
N = 1,741

≥1 claim with a diagnosis code in any position for brain metastases (ICD-10-CM: C79.31) in the year preceding and including the index date[2]
N = 1,316

Any enrollment in Medicare Part C or residence outside of the United States in the year preceding the index date, on the index date, or at any point during the follow-up period
N = 1,044

Disenrollment/death during first month of follow-up
N = 985

1. Treatments of interest were identified as the following: alectinib, brigatinib, ceritinib, crizotinib, ensartinib, lorlatinib.
2. Diagnosis codes from inpatient facility, outpatient facility, and carrier fee-for-service claims were used to identify lung cancer and brain metastases.
3. Treatments included were as follows: EGFR TKIs - afatinib, amivantamab-vmjw, dacomitinib, erlotinib, gefitinib, mobocertinib, or osimertinib; ROS-1-TKIs - entrectinib, repotrectinib; MET TKIs - capmatinib, tepotinib.
Abbreviations: ALK = anaplastic lymphoma kinase; EGFR = epidermal growth factor receptor; ICD-10-CM = International Classification of Diseases, Tenth Revision, Clinical Modification; MET - mesenchymal epithelial transition; mNSCLC = metastatic non-small cell lung cancer; ROS-1 = ROS proto-oncogene 1; TKI = tyrosine kinase inhibitor.

- From ALK TKI initiation through end of available follow-up, 194 beneficiaries (19.7%) had an incident BM following ALK-TKI initiation and 791 (80.3%) did not (**Table 1**).
- Baseline characteristics were broadly similar between those who had an incident BM and those who did not; the incident BM group had a higher proportion in the youngest age category (65-74 years) (**Table 1**).

Table 1. Baseline Characteristics of Beneficiaries (N = 985)

	Beneficiary had an incident BM during follow-up	Beneficiary did not have an incident BM during follow-up	Total
N (%)	194 (19.7)	791 (80.3)	985 (100.0)
Age category, n (%)			
65-74	104 (53.6)	345 (43.6)	449 (45.6)
75-84	68 (35.1)	350 (44.2)	418 (42.4)
85+	22 (11.3)	96 (12.1)	118 (12.0)
Female, n (%)			
Yes	109 (56.2)	466 (58.9)	575 (58.4)
Race and ethnicity, n (%)			
White non-Hispanic	142 (73.2)	605 (76.5)	747 (75.8)
Other	52 (26.8)	186 (23.5)	238 (24.2)
Census region, n (%)			
Northeast	44 (22.7)	193 (24.4)	237 (24.1)
South	54 (27.8)	252 (31.9)	306 (31.1)
Midwest	39 (20.1)	164 (20.7)	203 (20.6)
West	57 (29.4)	182 (23.0)	239 (24.3)
ALK TKI initiation year, n (%)			
2017	52 (26.8)	155 (19.6)	207 (21.0)
2018	41 (21.1)	116 (14.7)	157 (15.9)
2019	44 (22.7)	176 (22.3)	220 (22.3)
2020	22 (11.3)	121 (15.3)	143 (14.5)
2021	19 (9.8)	91 (11.5)	110 (11.2)
2022	16 (8.2)	132 (16.7)	148 (15.0)
Medicaid dual-eligible, n (%)			
Yes	40 (20.6)	187 (23.6)	227 (23.0)
No	154 (79.4)	604 (76.4)	758 (77.0)
Systemic treatment[a], n (%)			
Yes	30 (15.5)	104 (13.1)	134 (13.6)
No	164 (84.5)	687 (86.9)	851 (86.4)
Baseline medication count[b], n (%)			
0-4	15 (7.7)	61 (7.7)	76 (7.7)
5-9	53 (27.3)	235 (29.7)	288 (29.2)
10-14	62 (32.0)	244 (30.8)	306 (31.1)
15-19	41 (21.1)	151 (19.1)	192 (19.5)
20+	23 (11.9)	100 (12.6)	123 (12.5)

[a]Defined as a binary measure of any lung cancer chemotherapy or immunotherapy drugs per: Choi YC, Zhang D, Tyczynski JE. Comparison between health insurance claims and electronic health records (EHRs) for metastatic non-small-cell lung cancer (NSCLC) patient characteristics and treatment patterns: a retrospective cohort study. Drugs Real World Outcomes 2021;8:577–587.
[b]Defined as a count of the total number of unique outpatient prescription medications per beneficiary.

- Mean adjusted cumulative incremental spending (including medical and pharmacy spending) following incident BM, at 12, 24, 36, and 48 months after the incident BM, is presented in **Fig 3**, and as follows:
  - 12 months: $26,618 (95% confidence interval [CI]: $8,389, $44,847)
  - 24 months: $47,343 (95% CI: $7,793, $86,892)
  - 36 months: $59,978 (95% CI: −$2,457, $122,413)
  - 48 months: $76,590 (95% CI: −$4,880, $158,060)

Figure 3. Cumulative Incremental Spending Following Incident Brain Metastases at 12, 24, 36, and 48 Months[a]

[a]Beneficiaries were censored at the earliest of death, FFS Medicare disenrollment, or December 31, 2023. Total healthcare costs are inflation-adjusted to 2023 dollars using the Personal Consumption Expenditure price index for Health (PCE-Health). Incremental costs are adjusted differences (BM arm vs. non-BM arm); negative values are possible and indicate lower spending in the BM arm at that time point. Precision decreases at later time points due to attrition in the number of beneficiaries with an incident BM (N=194 at month 1; N=70 at month 12; N=41 at month 24; N=20 at month 36; N=14 at month 48), resulting in wider confidence intervals over time.

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Disclosures: DA is employed by and has stock in Pfizer. **ZM, AE,** and **MD** are employed by Medicus Economics, LLC which received funding for this research. **RM** is employed by YourCareChoice which received funding for this research. **LS** is employed by and has stock in Pfizer. **PR** is employed by and has stock in Pfizer. **BL** is employed by and has stock in Pfizer. **KR** is employed by and has stock in Pfizer. **LB** served in a consulting or advisory role for Genentech/Roche, Regeneron, Merck, Neuvogen, Bayer, Sanofi, Novocure, AbbVie, InterVenn Biosciences, Elevation Oncology, Janssen Oncology, Gilead Sciences, Anheart Therapeutics, BioAtla, Pfizer, Teligene, Boehringer Ingelheim, Summit Pharmaceuticals, BMS, AstraZeneca, and Daichi.

Acknowledgments: This presentation is the intellectual property of Pfizer, Inc. Contact the author at devin.abrahami@pfizer.com for permission to reprint and / or distribute. Study sponsored by Pfizer.

ISPOR 2026 • May 17–20, 2026 • Philadelphia, PA