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**Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences**

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# Disparities in Health Outcomes and Care Among ALK-Positive Non-Small Cell Lung Cancer Patients: Real-World Evidence of Social Determinants of Health

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## BACKGROUND

- Anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) is a rare subtype primarily affecting non-smokers[1]

- Clinical trials show promising efficacy for ALK tyrosine kinase inhibitors (TKIs) such as alectinib, brigatinib, and lorlatinib[2-4]

- Lack of head-to-head comparisons and scarce real-world evidence (RWE) create significant treatment outcome uncertainty

- As an orphan disease with limited available data, disparities and distributional analyses have been understudied[5-6]

## OBJECTIVE

To examine disparities in clinical outcomes and healthcare costs among patients with advanced ALK+ NSCLC receiving first-line (1L) ALK tyrosine kinase inhibitors (TKIs), with a focus on social determinants of care and health outcomes.

## METHODS

**Study Design:** Retrospective observational cohort study

**Data Source:** Optum Clinformatics® Data Mart (CDM) administrative claims data from 2016 to 2021, covering a large national sample of commercially insured and Medicare Advantage patients in the US

**Study Population:** Advanced ALK-positive NSCLC patients initiating first-line treatment with an ALK tyrosine kinase inhibitor (TKI)

**Inclusion Criteria (must satisfy both):**
1) Lung cancer diagnosis, based on International Classification of Diseases, Tenth Revision [ICD-10] code: C34x
2) Receipt of any of the following ALK TKIs: alectinib, brigatinib, ceritinib, crizotinib, ensartinib, or lorlatinib

**Exclusion Criteria:**
1) Age < 18 years at index date (first ALK TKI fill)
2) <6 months of continuous enrollment on health plan prior to index date

**Outcomes:**
Healthcare Utilization and Costs:
- Utilization and costs were captured per-patient-per-month (PPPM) across pharmacy, inpatient, outpatient, professional, and ancillary services
- Costs were adjusted to 2024 USD using the Consumer Price Index (CPI)

Clinical Outcomes:
- Inpatient admissions
- Time-to-treatment discontinuation (TTD)
- Overall survival (OS)

**Statistical Analysis:**
Descriptive Statistics
- Baseline demographics, utilization, and cost summaries by treatment group

Generalized Linear Model (GLM)
- Examined factors affecting PPPM costs, using gamma distribution with a log link

Survival Analysis
- Kaplan-Meier Estimates: TTD and OS with Log-Rank test comparisons
- Cox Proportional Hazards Model: Assessed treatment association with TTD and OS, controlling for observable confounders

**Additional Information:**
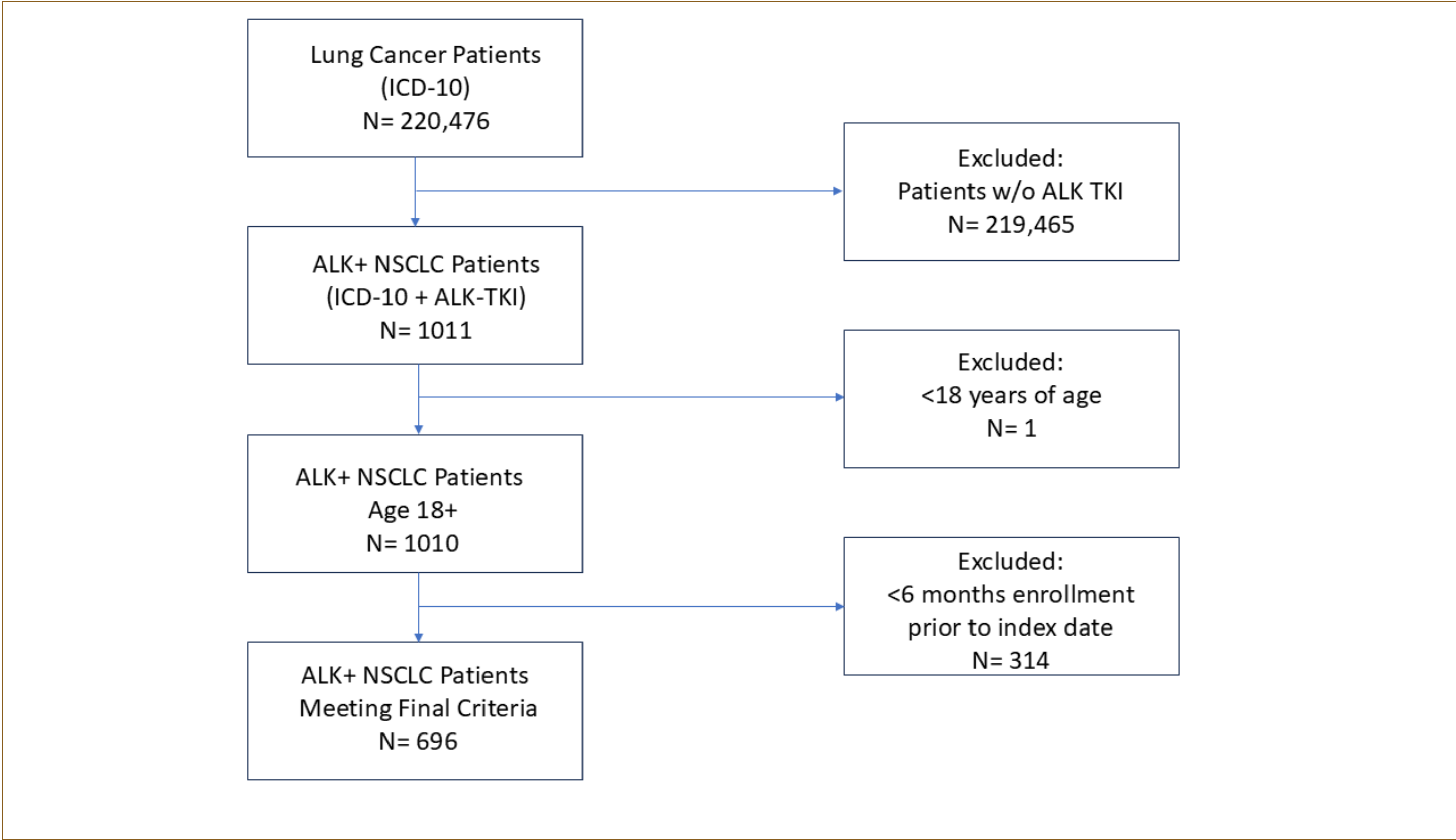- Analyses were conducted using SAS software, version 9.4 and STATA software, version 18.0

## RESULTS


Figure 1. Study population selection.

Lung Cancer Patients (ICD-10) N= 220,476 → Excluded: Patients w/o ALK TKI N= 219,465
ALK+ NSCLC Patients (ICD-10 + ALK-TKI) N= 1011 → Excluded: <18 years of age N= 1
ALK+ NSCLC Patients Age 18+ N= 1010 → Excluded: <6 months enrollment prior to index date N= 314
ALK+ NSCLC Patients Meeting Final Criteria N= 696

| Table 1. Patient Characteristics | |
|---|---|
| **Variable** | n = 696 |
| **Age, years** | |
| Mean (SD) | 64.2 (13.7) |
| **Sex, n (%)** | |
| Male | 317 (45.6) |
| Female | 379 (54.4) |
| **Race, n (%)** | |
| White | 438 (68.5) |
| Black | 82 (12.8) |
| Hispanic | 64 (10.0) |
| Asian | 55 (8.6) |
| **Insurance Type, n (%)** | |
| Commercial | 352 (50.6) |
| Medicare | 344 (49.4) |
| **Charlson Comorbidity Index (CCI) Score** | |
| Mean (SD) | 5.0 (2.2) |
| **1st-line ALK TKI Type, n (%)** | |
| Alectinib | 267 (38.4) |
| Brigatinib | 22 (3.2) |
| Ceritinib | 25 (3.6) |
| Crizotinib | 366 (52.6) |
| Lorlatinib | 16 (2.3) |
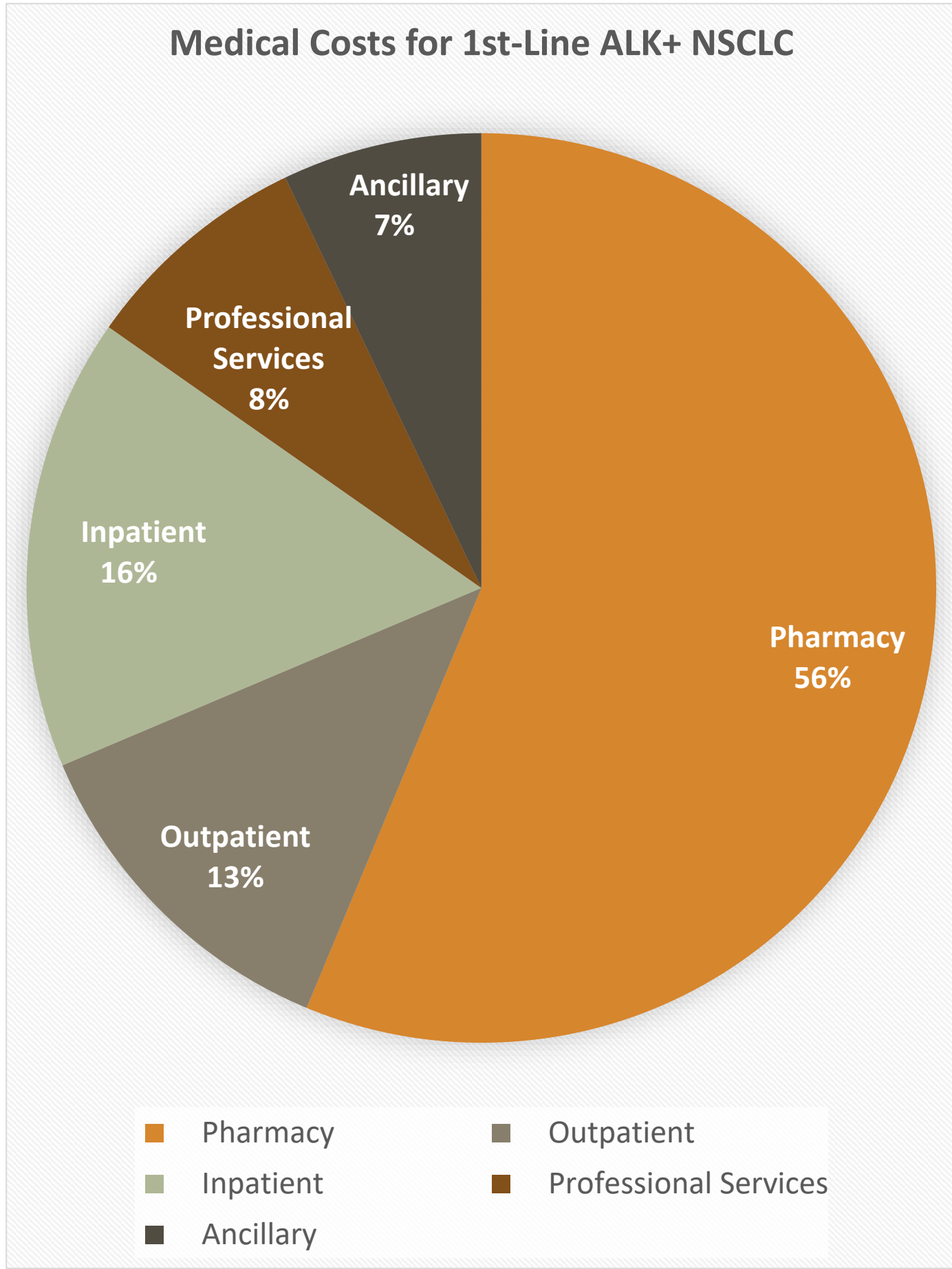

Figure 2. Monthly medical costs by service category.

Medical Costs for 1st-Line ALK+ NSCLC
- Pharmacy 56%
- Outpatient 13%
- Inpatient 16%
- Professional Services 8%
- Ancillary 7%

| Table 2. Associations Between Social Determinants, Clinical Characteristics, and Costs Per Month | | | | | | |
|---|---|---|---|---|---|
| Dependent Variable: Total Costs Per Month (USD) | Coefficient | Std. Err. | t | P>\|t\| | Lower Bound | Upper Bound |
| **Treatment (ref: Alectinib)** | | | | | | |
| Brigatinib | -1624.87 | 6266.27 | -0.26 | 0.80 | -13930.60 | 10680.86 |
| Ceritinib | -4056.71 | 6355.98 | -0.64 | 0.52 | -16538.61 | 8425.19 |
| Crizotinib | 809.10 | 2563.21 | 0.32 | 0.75 | -4224.55 | 5842.74 |
| Lorlatinib | 9007.80 | 7435.69 | 1.21 | 0.23 | -5594.44 | 23610.04 |
| **Insurance (ref: Commercial)** | | | | | | |
| Medicare | -8621.05 | 3299.49 | -2.61 | 0.01 | -15100.59 | -2141.51 |
| Age | 30.95 | 590.73 | 0.05 | 0.96 | -1129.14 | 1191.04 |
| Age^2 | -0.78 | 4.74 | -0.16 | 0.87 | -10.10 | 8.54 |
| **Sex (ref: Male)** | | | | | | |
| Female | -1618.04 | 2124.10 | -0.76 | 0.45 | -5789.35 | 2553.28 |
| **Index Year (ref: 2016)** | | | | | | |
| 2017 | 8298.84 | 3377.31 | 2.46 | 0.01 | 1666.47 | 14931.21 |
| 2018 | 9265.76 | 3665.52 | 2.53 | 0.01 | 2067.40 | 16464.11 |
| 2019 | 4707.90 | 3569.35 | 1.32 | 0.19 | -2301.60 | 11717.41 |
| 2020 | 5684.27 | 3807.99 | 1.49 | 0.14 | -1793.87 | 13162.41 |
| 2021 | 1595.00 | 4107.31 | 0.39 | 0.70 | -6470.94 | 9660.95 |
| Months of Continuous Enrollment Prior to Index Date | -50.19 | 26.49 | -1.89 | 0.06 | -102.21 | 1.83 |
| Charlson Comorbidity Inex (CCI) | 1440.56 | 532.07 | 2.71 | 0.01 | 395.68 | 2485.43 |
| Baseline Brain Metastases | 6673.57 | 2292.99 | 2.91 | 0.00 | 2170.59 | 11176.55 |
| **Race (ref: Non-Hispanic White)** | | | | | | |
| Black | -3187.01 | 3297.18 | -0.97 | 0.33 | -9662.02 | 3288.01 |
| Hispanic | 7117.11 | 3562.65 | 2.00 | 0.05 | 120.77 | 14113.45 |
| Asian | 3135.02 | 3818.84 | 0.82 | 0.41 | -4364.43 | 10634.47 |
| Constant | 22003.26 | 18627.10 | 1.18 | 0.24 | -14576.71 | 58583.23 |



Overall Survival (OS) by 1st-Line Treatment
- Alectinib
- Brigatinib
- Ceritinib
- Crizotinib
- Lorlatinib

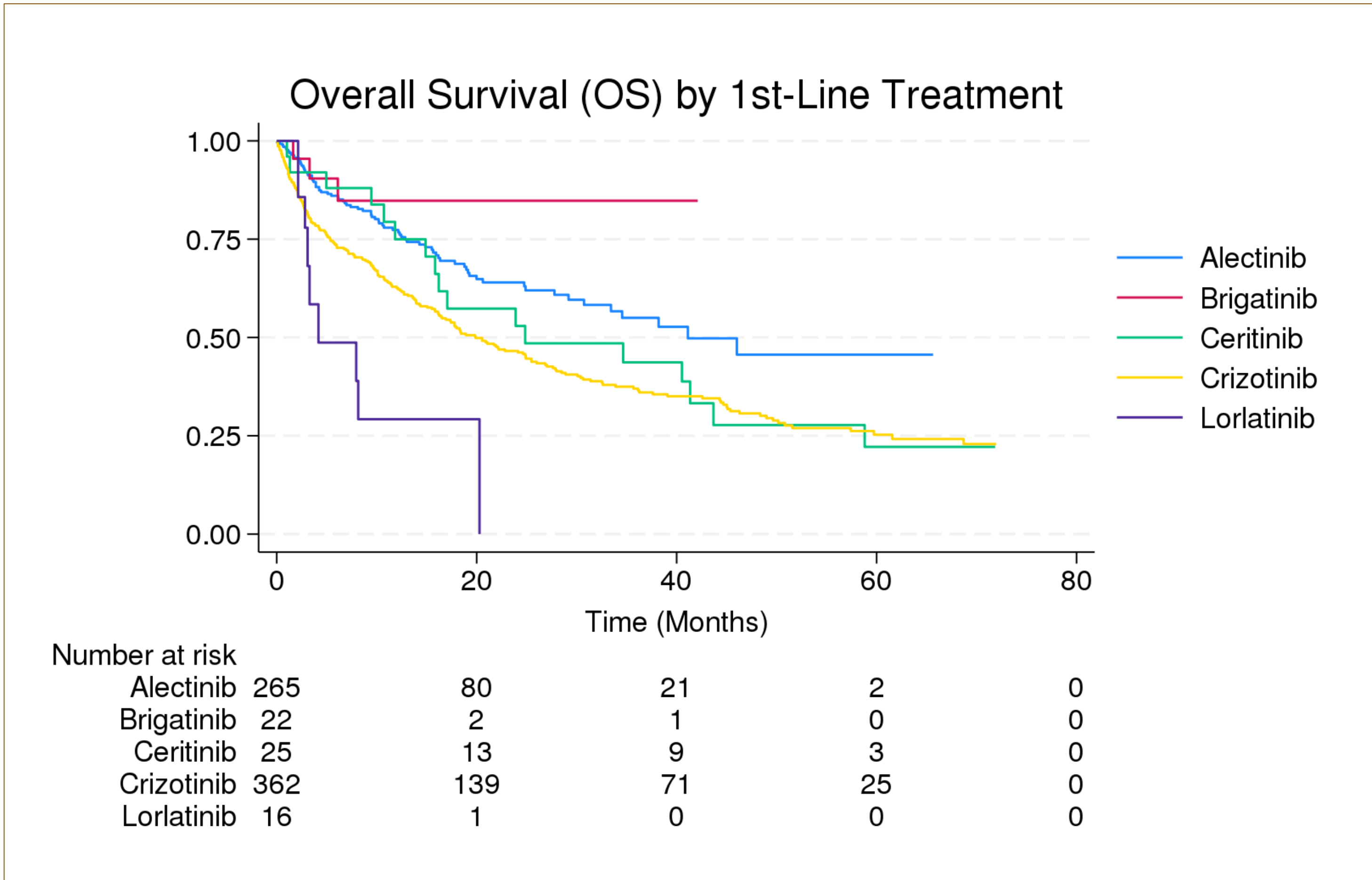| Number at risk | | | | | |
|---|---|---|---|---|---|
| Alectinib | 265 | 80 | 21 | 2 | 0 |
| Brigatinib | 22 | 2 | 1 | 0 | 0 |
| Ceritinib | 25 | 13 | 9 | 3 | 0 |
| Crizotinib | 362 | 139 | 71 | 25 | 0 |
| Lorlatinib | 16 | 1 | 0 | 0 | 0 |

Figure 3. Kaplan-Meier estimates of overall survival by 1st-line treatment.

## RESULTS

Median OS and TTD were 25.5 months (95% CI: 21.1-32.5) and 8.0 months (95% CI: 6.4-9.6), respectively, with mean total monthly costs of $28,216 (95% CI: $26,056-$30,375).

While OS and TTD did not significantly differ by race or ethnicity, Hispanic patients incurred higher total monthly healthcare costs (+$7,117; 95% CI: $121-$14,113) compared to non-Hispanic white patients.

This disparity was driven primarily by professional service costs (+$2,636/month; 95% CI: $849-$4,422), including physician visits, imaging, and lab tests.

## LIMITATIONS

**Data Limitations:**
- Patients could be misclassified as 1st-line users if prior ALK TKI prescriptions are unrecorded

**Nonrandomized Design:**
- Potential selection bias exists due to unobserved factors (e.g., tumor growth rate, TKI resistance), limiting causal inference regarding treatment effectiveness

## CONCLUSION

Despite similar clinical outcomes, Hispanic patients with ALK+ NSCLC experienced higher healthcare costs, particularly in professional services.

These findings highlight the need to better understand how social determinants impact real-world care delivery and equity in oncology.

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