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Real-World Treatment Sequencing and Outcomes in ALK-Positive Advanced Non-Small Cell Lung Cancer

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Objectives

- To examine real-world treatment sequencing and clinical outcomes of patients with ALK positive advanced NSCLC treated with 1L ALK TKIs.
- To quantify real-world overall survival and progression-free survival in patients treated with 1L ALK TKIs in a cohort of patients similar to patients from the CROWN trial using propensity score matching.

Conclusion

- Most patients (95%) in this study received 2G TKIs at 1L, primarily alectinib, with few patients receiving other ALK-TKIs for upfront treatment recommended during the study period, i.e. brigatinib.
- The cohort entry period for this analysis is primarily prior to US FDA approval of 1L brigatinib (May 2020) and 1L lorlatinib (March 2021), potentially explaining high levels of 1L alectinib use.
- Adjusted median rwOS with 1L alectinib was 54.0 months and rwPFS with 1L alectinib was 26.8 months.
- The data may not be generalizable to settings outside of the US or practices outside the Flatiron Health network.
- Some eligibility criteria from the CROWN study could not be applied due to a lack of data fields in the Flatiron Health EHR database to derive the criteria.
- Future research will be able to capture treatments such as 1L lorlatinib that were not represented in the current study period and provide additional evidence rwPFS estimates compared to ALK TKI trials.

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References:

1. Arbour KC, et al. Hematol Oncol Clin North Am. Feb 2017;31(1):101-111.
2. National Comprehensive Cancer Network. Non-small cell lung cancer, version 11.2024.
3. Hendriks LE, et al. Ann Oncol. Apr 2023;34(4):358-376.
4. Peters S, et al. N Engl J Med 2017, 377, 829-838.
5. Mok T, et al. Ann Oncol. Aug 2020;31(8):1056-1064.
6. Camidge DR, et al. N Engl J Med 2018, 379, 2027-2039.
7. Camidge DR, et al. J Thorac Oncol 2021, 16, 2091-2108.
8. Shaw AT, et al. N Engl J Med. Nov 19 2020;383(21):2018-2029.
9. Solomon BJ, et al. J Clin Oncol 2024, 42, 3400-3409.
10. Birnbaum B, et al. arXiv preprint arXiv:200109765. 2020.
11. Ma X, et al. medRxiv.org2020.

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Background

- Approximately 3-5% of non-small cell lung cancer (NSCLC) cases are anaplastic lymphoma kinase (ALK)-positive.[1]
- For these patients, first line (1L) treatment with ALK tyrosine kinase inhibitors (TKIs) is recommended.[2,3]
- Newer generation TKIs including alectinib and brigatinib (second generation [2G]), and lorlatinib (3rd generation [3G]), are preferred over crizotinib (1st generation [1G]), based on superior outcomes in their respective clinical trials (ALEX [alectinib],[4,5] ALTA-1L [brigatinib],[6,7] and CROWN [lorlatinib][8,9]).
- For patients with disease progression on a 2G ALK TKI, lorlatinib or cytotoxic chemotherapy is recommended,[2] however there remains a need to understand the real-world treatment patterns and clinical outcomes in these patients.

Methods

Study design and data source

- This was a retrospective cohort study of patients with ALK-positive aNSCLC treated with ALK TKIs (alectinib, brigatinib, ceritinib, crizotinib, or lorlatinib) as 1L therapy between 01 November 2017 through 30 November 2023 in the real-world setting in the United States (US) (**Figure 1**).
- This study used the Advanced Non-Small Cell Lung Cancer ALK & BRAF Solution, a dataset from the nationwide (US) Flatiron Health electronic health record (EHR)-derived de-identified database.[10,11]

Study population

- Adult patients (≥18 years old) with ALK+ aNSCLC treated with a 1L ALK TKI 01 November 2017 and 30 November 2021, without prior treatment for advanced disease (**Figure 1**).
- Where data in the Flatiron database allowed, similar exclusion criteria to the CROWN study were applied (**Figure 2**).[8]

Statistical analyses

- Baseline characteristics of patients receiving 1L alectinib were adjusted using aggregate baseline characteristic data from the CROWN trial (NCT03052608)[8] using propensity score weighting for age, sex, race/ethnicity, ECOG PS, histology, and brain metastases.
- Characteristics were summarized before and after weighting to evaluate balance, and weight distribution was assessed for extreme values.
- Missing covariate data for weighting variables were imputed using multiple imputation methods.
- Kaplan-Meier analyses estimated unadjusted and adjusted real-world overall survival (rwOS) and progression-free survival (rwPFS), reported as median months with 95% CIs.

Study measures

- Demographic and clinical characteristics at baseline were reported for the full cohort and stratified by 1L ALK TKI.
- Only 1L alectinib was considered as a stratification; other 1L ALK TKIs subgroups had low patient counts (n<50) and were not further described in this analysis.
- Treatment sequencing from 1L to second line (2L), rwOS, and rwPFS were summarized for patients who received 1L alectinib.
  - rwOS defined as time from index date until death
  - rwPFS defined as time from index date until first real-world progression event date or death date, whichever occurred first.
  - Censoring for both outcomes occurred at last confirmed activity date (latest occurrence of clinic visit, medication administration, or non-canceled order)

Results

Patient attrition

- After applying the study eligibility criteria, a total of 272 patients were included (**Figure 2**).
- Most patients received 2G TKIs (n=258, 95%), primarily alectinib (n=240, 88%), with few patients receiving brigatinib (n=15, 6%) or ceritinib (n<5). Use of crizotinib (n=14, 5%) was also limited.
- Due to low patient counts for other ALK TKI, only patients treated with 1L alectinib were included in further analyses.

Baseline characteristics before and after weighting

- Compared to the CROWN trial, patients in this study were older, a greater proportion were White, and more patients had an ECOG score of 2 (**Table 1**).
- After weighting, characteristics were well-balanced between those in the 1L alectinib cohort (ESS = 165.2) compared to the CROWN study (total study population) (**Table 1**).

Treatment patterns following 1L alectinib

- Median follow-up time was 41.7 months (95% CI: 37.7, 48.3).
- Among the 240 patients that received 1L alectinib, 100 (42%) subsequently received 2L treatment (**Table 2**).
  - Most of these patients (84%) received a TKI.
  - Among 2L TKI use, lorlatinib was predominant (76%), followed by brigatinib (19%).
- Only a subset of patients had recorded progression events during 1L treatment (N=117).
- Of patients with a progression event, 84 (72%) received 2L treatment (**Table 2**).
  - 87% received a TKI.
  - Lorlatinib was the most prevalent TKI (84%), followed by brigatinib (14%) at 2L.

Clinical Outcomes

- The unadjusted median rwOS was 56.5 months (95% CI: 48.7-not estimable [NE]) for patients treated with 1L alectinib (**Figure 3a**).
- After weighting, median rwOS was 54.0 months (95% CI: 37.9-NE) (**Figure 3a**).
- The unadjusted median rwPFS was 28.5 months (95% CI: 24.5-36.4) for patients treated with 1L alectinib (**Figure 3b**).
- After weighting, rwPFS was 26.8 months (95% CI: 19.6-35.8) (**Figure 3b**).

Table 1. Baseline Characteristics

Characteristic	Unweighted Cohort Overall (n = 272)	Unweighted Cohort 1L Alectinib (n = 240)	Weighted Cohort 1L Alectinib (ESS = 165.2)	CROWN Study Overall (n = 296)
Age at Index Date, years				
Mean (SD)	61.2 (13.5)	60.9 (13.4)	57.4 (13.8)	57.4 (13.4)
Sex, N (%)				
Male	110 (40.4)	99 (41.3)	40.9%	121 (40.9)
Female	162 (59.6)	141 (58.8)	59.1%	175 (59.1)
Race/Ethnicity, N (%)				
White	163 (70.6)	147 (71.7)	52.4%	144 (48.6)
Other	68 (29.4)	58 (28.3)	47.6%	131 (44.3)
Missing	-	-	-	21 (7.1)
Smoking History, N (%)				
History	108 (39.7)	100 (41.7)	40.2%	120 (40.5)
No history	164 (60.3)	140 (58.3)	59.8%	175 (59.1)
Stage of Disease at Initial Diagnosis, N (%)				
I	20 (7.4)	19 (7.9)	8.8%	7 (2.4)
II	13 (4.8)	9 (3.8)	3.0%	10 (3.4)
III	31 (11.4)	23 (9.6)	7.4%	36 (12.2)
IV	207 (76.4)	188 (78.7)	80.8%	241 (81.4)
Other	-	-	-	1 (0.3)
Unknown	-	-	-	1 (0.3)
Histology, N (%)				
Non-squamous cell carcinoma	258 (94.9)	230 (95.8)	94.6%	280 (94.6)
Other	14 (5.1)	10 (4.2)	5.4%	16 (5.4)
ECOG PS, N (%)				
0	77 (46.7)	65 (44.2)	41.9%	124 (41.9)
1	67 (40.6)	63 (42.9)	54.1%	160 (54.1)
2	21 (12.7)	19 (12.9)	4.1%	12 (4.0)
Presence/History of Brain Metastases, N (%)				
Yes	73 (26.8)	65 (27.1)	26.4%	78 (26.4)
No	199 (73.2)	175 (72.9)	73.6%	218 (73.6)
Previous Anticancer Drug Therapy, N (%)				
Yes	31 (11.4)	20 (8.3)	8.0%	21 (7.1)
No	241 (88.6)	220 (91.7)	92.0%	275 (92.9)

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group Performance Status

Table 2. 2L Treatment Patterns Post 1L Alectinib

2L Treatment Regimen	1L Alectinib (n = 240) N	1L Alectinib (n = 240) % (95% CI)	1L Alectinib with Progression Event (n = 117) N	1L Alectinib with Progression Event (n = 117) % (95% CI)
Did not receive 2L treatment	140	58.3% (51.8%, 64.6%)	33	28.2% (20.3%, 37.3%)
Received 2L treatment	100	41.7% (35.4%, 48.2%)	84	71.8% (62.7%, 79.7%)
Any TKI	84	84.0% (75.3%, 90.6%)	73	86.9% (77.8%, 93.3%)
1st generation TKI	<5	-	<5	-
Crizotinib	<5	-	<5	-
2nd generation TKI	18	18.0% (11.0%, 26.9%)	10	11.9% (5.86%, 20.8%)
Brigatinib	16	19.0% (11.3%, 29.1%)	10	13.7% (6.77%, 23.8%)
Alectinib	<5	-	<5	-
Ceritinib	<5	-	<5	-
Ensartinib	<5	-	<5	-
3rd generation TKI	64	64.0% (53.8%, 73.4%)	61	72.6% (61.8%, 81.8%)
Lorlatinib	64	76.2% (65.7%, 84.8%)	61	83.6% (73.0%, 91.2%)
Other treatments				
Chemotherapy	8	8.0% (3.52%, 15.2%)	5	6.0% (1.96%, 13.3%)
Immunotherapy	<5	-	<5	-
Chemotherapy + Immunotherapy	<5	-	<5	-
Other TKI	<5	-	<5	-

Abbreviations: 1L, first line; 2L, second line; CI, confidence interval; TKI, tyrosine kinase inhibitors

Figure 1. Study Design

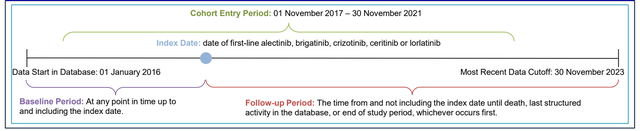
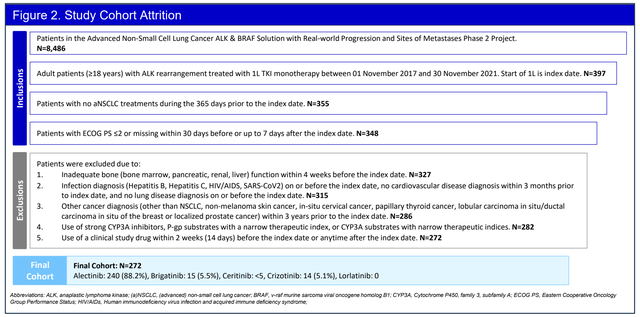
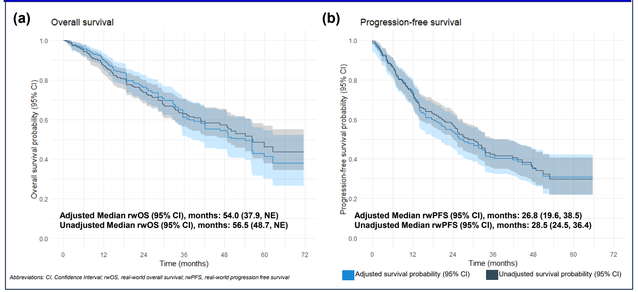


Figure 2. Study Cohort Attrition



Abbreviations: ALK, anaplastic lymphoma kinase; (a)NSCLC, (advanced) non-small cell lung cancer; BRAF, v-raf murine sarcoma viral oncogene homolog B1; CYP3A, Cytochrome P450, family 3, subfamily A; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HIV/AIDs, Human immunodeficiency virus infection and acquired immune deficiency syndrome.

Figure 3. Unadjusted and Adjusted (a) Real-World Overall Survival (rwOS) and (b) Progression-Free Survival (rwPFS) in Months



Abbreviations: CI, Confidence Interval; rwOS, real-world overall survival; rwPFS, real-world progression free survival