

Insights on Treatment Experience from Patients with ALK+ NSCLC Treated with 1st-line Brigatinib, Lorlatinib and Alectinib

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Background and Research Question



Background

NSCLC



NSCLC accounts for 80-90% of lung cancers, with 3-13% of patients harboring ALK gene rearrangements that make them candidates for targeted ALK inhibitor therapy rather than traditional chemotherapy.^{1, 2}

ALK Inhibitors



Next-generation ALK inhibitors (alectinib, brigatinib, lorlatinib) have demonstrated superior efficacy compared to first-generation crizotinib in clinical trials, leading to FDA/EC approvals as first-line treatments for ALK+ NSCLC.^{3, 4, 5}

Limited Real-World Data



Although pivotal clinical trials have established efficacy endpoints, comprehensive data on patient-reported outcomes, symptom profiles, and health-related quality of life measures across different ALK inhibitors in real-world clinical practice remain limited.

References:

1. Janssens R AR, Schoefs E et al. . Key Determinants of Health-Related Quality of Life Among Advanced Lung Cancer Patients: A Qualitative Study in Belgium and Italy. *Frontiers in Pharmacology*. 2021;12.
2. Campelo MRG LH, Zhu Y et al. . Health-related quality of life in randomized phase III trial of brigatinib vs crizotinib in advanced ALK-inhibitor-naive ALK +non-small cell lung cancer (ALTA-1L). *Lung Cancer*. 2021;155:68-77.
3. Araghi M MR, Maleki AH et al. Recent advances in non-small cell lung cancer targeted therapies: an update review. *Cancer Cell International*. 2023;162.
4. Maione P GC, Troiani T, Ciardiello F. Combining Target Therapies and Drugs with Multiple Targets in the Treatment of NSCLC. *The Oncologist*. 2006;11:274-284.
5. Society AC. Signs and Symptoms of Lung Cancer. Published 2024. Accessed 26 February 2024.

Research Question & Study Aim



Research Question

How do patients with ALK-positive advanced NSCLC experience treatment with first-line ALK inhibitors (alectinib, brigatinib, or lorlatinib) in terms of symptom management, functional status, and health-related quality of life?



Study Aim

To characterize the real-world treatment experiences and patient-reported outcomes among individuals with ALK-positive advanced NSCLC receiving alectinib, brigatinib, or lorlatinib as their initial targeted therapy.

Methodology



Overview of Study Design

A non-interventional, cross-sectional qualitative study was conducted among US adults with ALK-positive advanced NSCLC who received first-line targeted TKI therapy for ≥ 4 weeks within the past 12 months.

Study Preparation



- ✓ Developed a study protocol, screening and enrollment forms, and interview guide
- ✓ Ethics/IRB Review (deemed exempt)
- ✓ Partnered with ALK Positive, Inc- a patient-founded and patient-driven nonprofit organization committed to transforming the future for everyone affected by ALK-positive cancer.

Recruitment



- ✓ Utilized a purposive sampling approach to enroll three patient cohorts (i.e., alectinib, brigatinib, or lorlatinib) with the goal of $n \sim 15$ per cohort.
- ✓ ALK Positive utilized multiple recruitment channels (e.g., direct-to-patient, virtual support groups/discussion forums) to ensure representative sampling

Qualitative Interviews



- ✓ Qualitative interviews (~60 minutes) were conducted virtually via Microsoft Teams
- ✓ Experienced qualitative researchers used a semi-structured interview guide, with audio recording and verbatim transcription.

Coding and Analysis



- ✓ Participant responses from the interview discussion were coded in Atlas.ti
- ✓ The analysis process characterized patients' experiences and organized responses within groupings related to the interview guide.

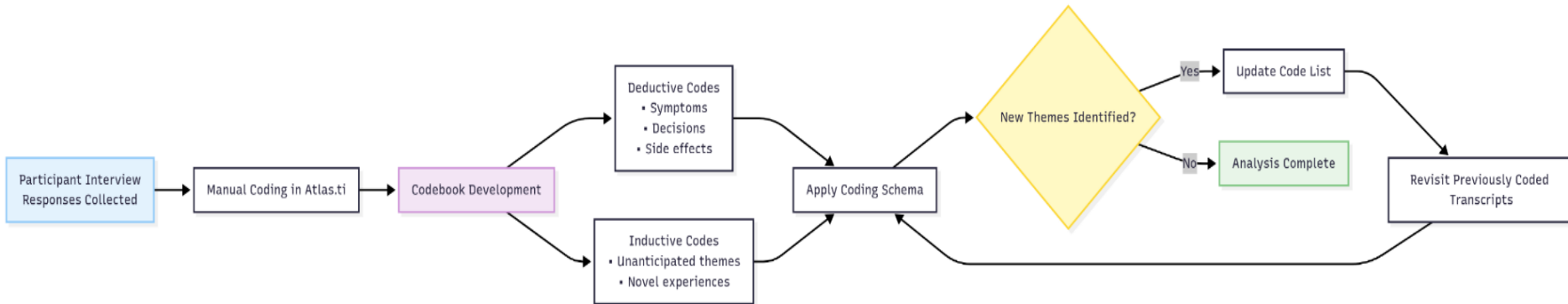
Inclusion Criteria

- Adults currently living in the US diagnosed with ALK + NSCLC
- Treated (i.e., has received at least 4 weeks of treatment) within the past 12 months with brigatinib, alectinib, or lorlatinib as their first targeted TKI therapy
 - Patients who initiated TKI therapy but did not tolerate the first drug and switched to a second drug (among alectinib, brigatinib, or lorlatinib) within 4 weeks, were enrolled in the cohort of the second drug providing receipt of the second drug for at least 4 weeks within the past 12 months



Coding and analysis of qualitative data

- Transcripts were coded to systematically identify and classify emerging concepts and themes observed during individual interviews with participants.
- A codebook was developed to ensure transparent, consistent classification of participant narratives, which combined:
 - **Deductive Codes:** Predefined categories reflecting known NSCLC symptoms, treatment decision factors, and new symptoms or side effects addressed in the interview guide.
 - **Inductive Codes:** Emergent labels added to capture novel experiences and themes reported by participants.
- When new themes arose, the code list was updated accordingly, and previously coded transcripts were revisited, as necessary.



Assessment of Concept Saturation



Saturation Method

Concept saturation was assessed using the established methodology by Guest et al⁶. (2020).

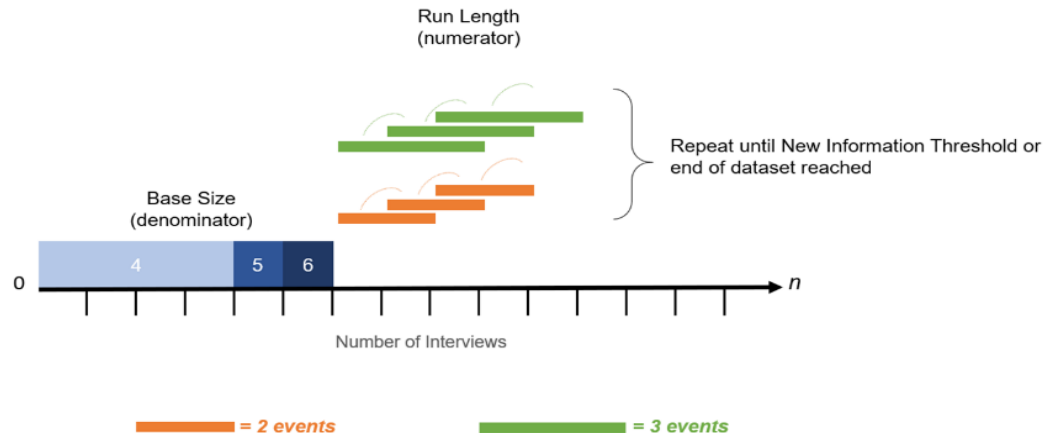


Saturation Definition

Saturation was operationally defined when two consecutive transcripts yielded <5% new information, suggesting thematic stability and further data collection was unlikely to produce substantially new insights.

References:

6. Guest G, Namey E, Chen M. A simple method to assess and report thematic saturation in qualitative research. PLoS One. 2020 May 5;15(5):e0232076. doi: 10.1371/journal.pone.0232076. PMID: 32369511; PMCID: PMC7200005.



Results

Concept Saturation Findings

- All three cohorts **independently achieved concept saturation**, confirming the adequacy and comprehensiveness of the collected data across subgroups.
- Within each cohort, evidence of saturation was observed at,
 - Alectinib: 13th of 15 interviews
 - Brigatinib: 10th of 15 interviews
 - Lorlatinib: 8th of 16 interviews

Participant Demographic and Clinical Characteristics*

Characteristics	Alectinib Cohort (n=15)	Brigatinib Cohort (n=15)	Lorlatinib Cohort (n=16)	Total (n=46)
Age				
Mean (SD)	46.07 (9.27)	54.13 (10.06)	47.69 (9.48)	49.26 (10.02)
Min, Max	33-68	39-76	29-67	29-76
Sex				
Female	11 (73.3%)	9 (60.0%)	12 (75.0%)	32 (69.6%)
Insurance†				
Employer	10 (66.7%)	8 (53.3%)	11 (68.8%)	29 (63.0%)
Medicare/Medicaid	1 (6.7%)	2 (13.3%)	1 (6.3%)	4 (8.7%)
Uninsured	0 (0.0%)	1 (6.7%)	4 (25.0%)	5 (10.9%)
Disability	2 (13.3%)	2 (13.3%)	0 (0.0%)	4 (8.7%)
Other‡	2 (13.3%)	2 (13.3%)	0 (0.0%)	4 (8.7%)
Employment				
Full-time	9 (60.0%)	6 (40.0%)	8 (50.0%)	23 (50.0%)
Part-time	2 (13.3%)	2 (13.3%)	2 (12.5%)	6 (13.0%)
Homemaker	0 (0.0%)	1 (6.7%)	0 (0.0%)	1 (2.2%)
Retired	1 (6.7%)	2 (13.3%)	5 (31.3%)	8 (17.4%)
Unemployed	0 (0.0%)	1 (6.7%)	0 (0.0%)	1 (2.2%)
Disability/Medical Leave	3 (20.0%)	2 (13.3%)	1 (6.3%)	6 (13.0%)
Other	0 (0.0%)	3 (20.0%)	1 (6.3%)	4 (8.7%)

Characteristics	Alectinib Cohort (n=15)	Brigatinib Cohort (n=15)	Lorlatinib Cohort (n=16)	Total (n=46)
Brain Metastasis prior to first use of a TKI, n (%)				
Yes	5 (33.3%)	4 (26.7%)	4 (25.0%)	13 (28.3%)
Drug transitioned to after first use of TKI n (%)				
None, still on first TKI	12 (80.0%)	15 (100.0%) [§]	14 (87.5%)	41 (89.1%)
Brigatinib	3 (20.0%)	0 (0.0%)	0 (0.0%)	3 (6.5%)
Alectinib	0 (0.0%)	0 (0.0%)	1 (6.3%)	1 (2.2%)
Chemotherapy +/- Immunotherapy	0 (0.0%)	0 (0.0%)	1 (6.3%)	1 (2.2%)
Problems with speech or memory n (%)				
Yes	5 (33.3%)	0 (0.0%)	6 (37.5%)	11 (24.4%)

* Participant demographic and clinical characteristics were self-reported by the participants.

† For insurance, participants can select multiple options.

‡ Other includes the Veterans Affairs insurance program

§ 2 participants in the Brigatinib cohort were first on Alectinib for a brief period (<4 weeks) but transitioned to Brigatinib due to side effects. Based on the participant definition in this study, Brigatinib is considered their first TKI therapy due to the short duration use of Alectinib

Patients' Experiences of Fatigue (Before and During Treatment)

Before Treatment

ALECTINIB

"I was a little bit fatigued, but it's hard to separate that out when you're a mom of two active kids. So I didn't feel abnormally tired." (47-year-old, female)

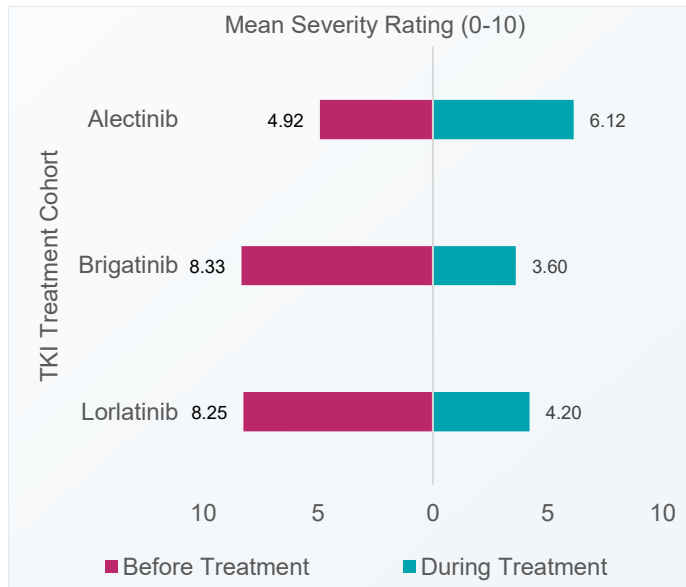
BRIGATINIB

"I just recall being tired all the time, sleeping a lot. My fatigue was severe." (54-year-old, female)

LORLATINIB

"...I didn't have the energy to do anything. I couldn't grocery shop. I couldn't go to the store. I couldn't drive." (67-year-old, female)

Symptom Severity*



During Treatment

ALECTINIB

"I would say my fatigue is actually a little bit worse on Alectinib. I have to constantly kind of fight being tired, even though I'm getting a full night's sleep." (47-year-old, female)

BRIGATINIB

"I do experience fatigue. It's very on and off." (54-year-old, female)

LORLATINIB

"I felt like I was getting my energy back and doing some things. So I guess I started noticing fatigue, probably only in the last couple weeks." (67-year-old, female)

*Participants rated symptom severity on a 0–10 numeric scale, where 0 = none and 10 = extremely severe. Ratings were collected for each symptom twice: Before treatment initiation (retrospective baseline) and During treatment (treatment experience).

Mean ratings based on number of participants reporting and rating fatigue at each time point: Alectinib before (n=6), after (n=13); Brigatinib before (n=3), after (n=5); and Lorlatinib before (n=2), after (n=5).

Patients' Experiences of Shortness of Breath (Before and During Treatment)

Before Treatment

ALECTINIB

"So at that point [right before diagnosis], I had really shortness of breath that wouldn't go away. I definitely felt like I was getting winded." (51-year-old, female)

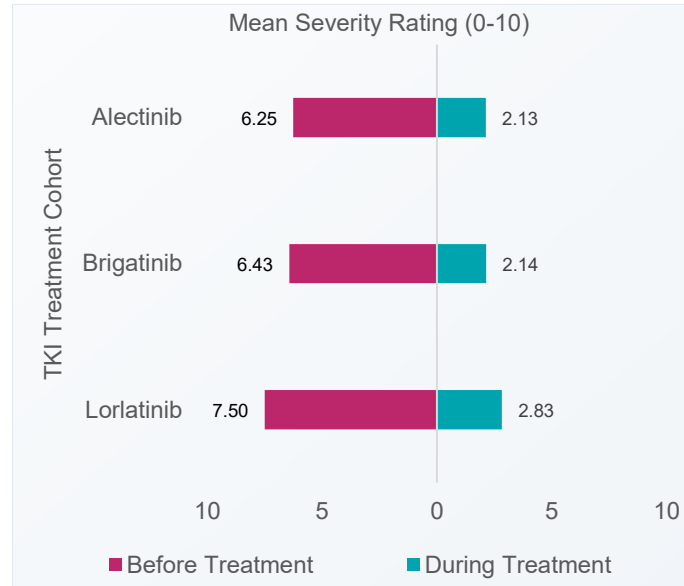
BRIGATINIB

"Even coming up the stairs, sometimes I'd be like, "Oh, my gosh." I'd get winded." (56-year-old, female)

LORLATINIB

"It was really, really difficult to breathe. My shortness of breath was extreme at that particular moment [walking up the hill]. I thought I was going to pass out.." (40-year-old, male)

Symptom Severity*



During Treatment

ALECTINIB

"I'd say within the first month, I noticed it. Fairly early on, I noticed an improvement in that [shortness of breath]." (51-year-old, female)

BRIGATINIB

"I don't feel short of breath at all." (56-year-old, female)

LORLATINIB

"Oh, yeah. I mean, my shortness of breath, I really don't have it anymore where I worked outside-- all year round, I worked outside and walking up and down hills and very athletic. I work out all the time" (40-year-old, male)

*Participants rated symptom severity on a 0–10 numeric scale, where 0 = none and 10 = extremely severe. Ratings were collected for each symptom twice: Before treatment initiation (retrospective baseline) and During treatment (treatment experience)

Mean ratings based on number of participants reporting and rating shortness of breath at each time point: Alectinib before (n=8), after (n=8); Brigatinib before (n=7), after (n=7); Lorlatinib before (n=6) and after (n=6).

Patients' Experiences of Cough (Before and During-Treatment)

Before Treatment

ALECTINIB

"You couldn't stop coughing. You'd take a breath in, and you would cough, and you couldn't stop."
(68-year-old, female)

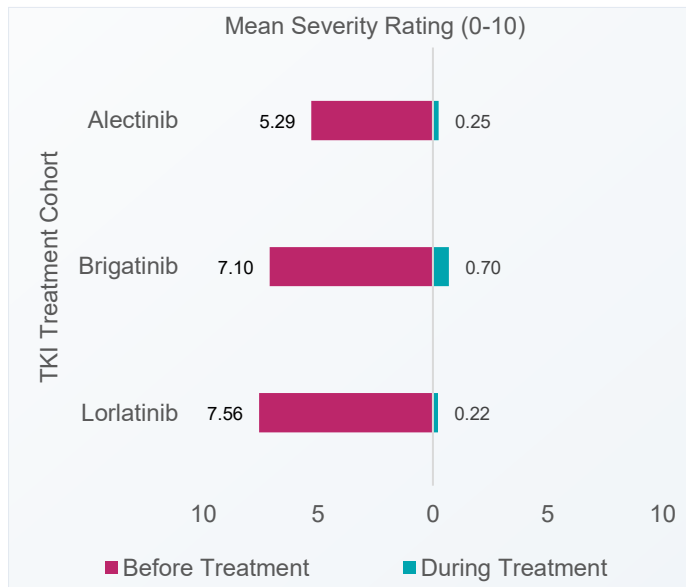
BRIGATINIB

"And my cough actually became consistent and a little more persistent and violent."
(44-year-old, male)

LORLATINIB

"The cough was rather difficult because I would just get-- I'd have these coughing spells that were just kind of difficult to manage throughout the day."
(46-year-old, female)

Symptom Severity*



During Treatment

ALECTINIB

"Pretty soon after starting treatment, I can't remember if I had it [cough] anymore, so [went away] very quickly."
(68-year-old, female)

BRIGATINIB

"Probably within a week or two of starting the medication, the severity of the cough started going down. I think within a month, it [cough] was gone."
(44-year-old, male)

LORLATINIB

"It was fairly quickly. Probably within a week, I noticed my cough was not as persistent.."
(46-year-old, female)

*Participants rated symptom severity on a 0–10 numeric scale, where 0 = none and 10= extremely severe. Ratings were collected for each symptom twice: Before treatment initiation (retrospective baseline) and During treatment (treatment experience)

Mean ratings based on number of participants reporting and rating cough at each time point: Alectinib before (n=12), after (n=12); Brigatinib before (n=10), after(n=10); Lorlatinib before (n=9) and after (n=9).

Patients' Experiences of Chest Pain (Before and During Treatment)

Before Treatment

ALECTINIB

"So no, I didn't have a whole lot of pain. The chest pain was not very much."
(48-year-old, female)

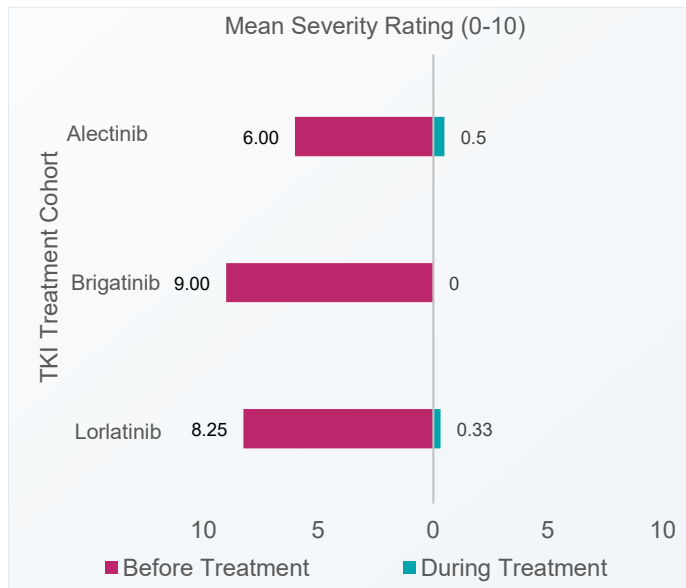
BRIGATINIB

"I noticed that I had a pain in my inner chest...But now that I recall where I had that pain initially, it's exactly where the tumor was located." (52-year-old, female)

LORLATINIB

"It [chest pain] felt like if you were to shoot me with a bullet, it would be in the same spot, in the front and the back."
(44-year-old, female)

Symptom Severity*



During Treatment

ALECTINIB

"I would take it down to 1. It wasn't really there."
(48-year-old, female)

BRIGATINIB

"Chest pain never came back."
(52-year-old, female)

LORLATINIB

"And I haven't been feeling that chest pain that I was feeling. I have new chest pains related to lorlatinib." (44-year-old, female)

*Participants rated symptom severity on a 0–10 numeric scale, where 0 = none and 10 = extremely severe. Ratings were collected for each symptom twice: Before treatment initiation (retrospective baseline) and During treatment (treatment experience).

Mean ratings based on number of participants reporting and rating chest pain at each time point: Alectinib before (n=2), after (n=2); Brigatinib before (n=1), after (n=1); Lorlatinib before (n=6), after (n=6).

Troublesome taking the tablet/s everyday

Participants were asked, “How troublesome did you find taking your tablet(s) every day on a scale of 0–10, where 0 is not at all and 10 is extremely troublesome?”*

Alectinib Cohort

“I mean, you have to swallow four pills at one time, which isn't a party, but. [laughter] It's not [comfortable?], but it's not the worst.”
(47-year-old, female)

Brigatinib Cohort

“I'm so used to it. It's a 0. But for the most part, I don't find it difficult.”
(68-year-old, male)

Lorlatinib Cohort

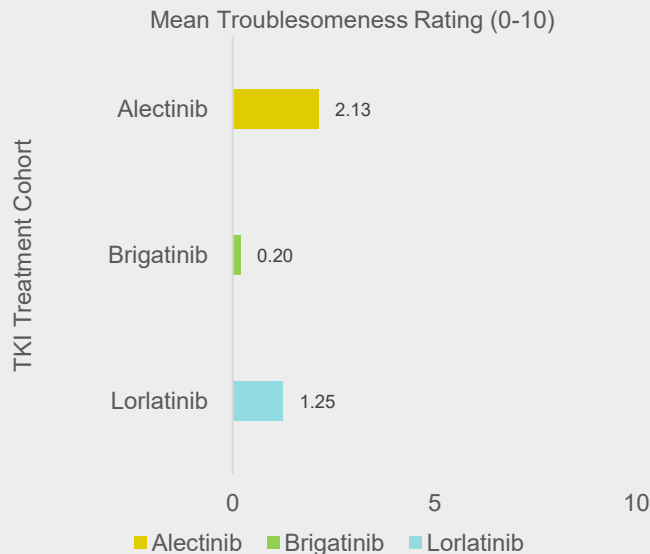
“I just have to remember to take it, which I've gotten into a routine of doing. So that's not as big a deal. I just kind of have it on my person all the time, especially when I'm traveling.”
(40-year-old, male)

“I hate taking it with food. And they also say that **the food has to be like a high-fat meal. And so I know a lot of people gain weight on the drug..**”
(45-year-old, female)

“0, not at all. **I'm very good in taking them.**”
(52-year-old, female)

“I take pills three times a day, and you just get to a point where **you're just frustrated because you are constantly having to take pills.**”
(46-year-old, female)

Troublesomeness Rating



*Participants were asked: “How troublesome did you find taking your tablet(s) every day on a scale of 0–10, where 0 is not at all and 10 is extremely troublesome?” This question aimed to capture the perceived burden of adherence, accounting for factors such as dosing frequency, pill burden, side effects, and lifestyle disruption. Mean ratings based on number of participants reporting and rating troublesomeness: Alectinib (n=15), Brigatinib (n=15), Lorlatinib (n=16)

Treatment Satisfaction

Participants were asked, “On a scale of 0–10, where 0 is extremely dissatisfied and 10 is extremely satisfied, how satisfied are you with [first TKI therapy]?”*

Alectinib Cohort

“It seems to be working very well. Knock on wood, I don’t have the side effects that make others stop—and I haven’t had progression in five years. No complaints.”
(68-year-old, female)

“I’m very satisfied for the most part—I’d say probably an 8. There are GI issues and weight gain, but overall it’s working effectively for me right now.”
(47-year-old, female)

Brigatinib Cohort

“It’s basically the reason I’m still alive. It’s the combination of being able to do what I do daily versus where I was—dying in the hospital slowly. I can’t say anything bad about it—kept me progression-free for three years.” (44-year-old, male)

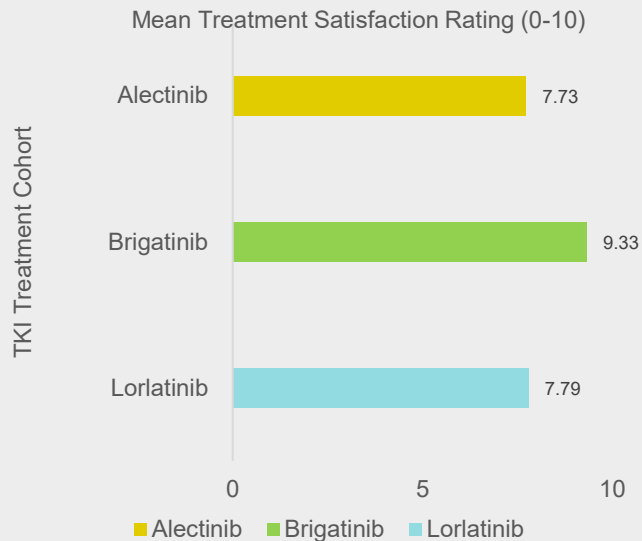
“It’s one pill a day, and I don’t feel like I’m a cancer patient or that it has any negative impact on me...I couldn’t ask for anything differently.”
(44-year-old, male)

Lorlatinib Cohort

“I mean, the weight gain is terrible if you’re not careful. And that’s the thing is food has always been something I’ve liked.”
(40-year-old, male)

“I’m very happy it’s working well with my body. It could always be worse—I only knock it down for the few side effects I have.”
(46-year-old, female)

Satisfaction Rating



*Participants also rated their satisfaction with their first TKI therapy using the following question: “On a scale of 0–10, where 0 is extremely dissatisfied and 10 is extremely satisfied, how satisfied are you with [first TKI therapy]?” This measure provided a global evaluation of treatment acceptability, encompassing efficacy, tolerability, and quality-of-life impact. Mean ratings based on number of participants reporting and rating troublesomeness: Alectinib (n=15), Brigatinib (n=15), Lorlatinib (n=16)

Conclusion

Conclusion

- Unique experiences were reported by patients with ALK+ NSCLC treated with different first-line ALK-TKIs.
- These data illustrate the multifaceted impact of ALK-TKI treatment on daily life, highlighting the importance of addressing both physical and psychosocial dimensions of patient care.
- These findings emphasize the importance of patient experience considerations in treatment decisions for ALK+ NSCLC.

