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Patient and oncologist preferences for TKIs in first-line treatment of ALK+ advanced NSCLC: commonalities and disconnects

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Objectives

This qualitative study aimed to understand the preference of oncologists and patients for key attributes associated with ALK-targeted TKIs in the first-line setting and their willingness to trade-off between benefits and risks.

Conclusions

- This multi-method interview study demonstrates that both patients and oncologists considered efficacy as the primary driver in treatment decision-making and that patients were willing to tolerate AEs for improvements in efficacy.
- By understanding the trade-offs that inform patient treatment choices, oncologists and patients can select the most suitable ALK inhibitor for the personalized treatment of ALK+ advanced NSCLC.
- Findings from this study informed development of a quantitative preference elicitation survey with 150 patients and 150 oncologists to assess treatment choices in the first-line setting of ALK+ advanced NSCLC.

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Background

- Tyrosine kinase inhibitors (TKIs) targeting anaplastic lymphoma kinase (ALK) have transformed treatment of ALK-positive advanced non-small-cell-lung-cancer (NSCLC) in the first-line setting.
- Newer generation ALK inhibitors were designed to penetrate the blood brain barrier (BBB) to control the development of brain metastases and have demonstrated superiority over the first-generation ALK inhibitor - crizotinib.
- Current guidelines now recommend second generation (alectinib, brigatinib) and third generation (lorlatinib) ALK inhibitors as first-line treatments for ALK+ advanced NSCLC.
- While head-to-head clinical trials comparing alectinib, brigatinib, and lorlatinib are lacking, available clinical trial data indicate that these treatments differ in their systemic and intracranial efficacy and safety profile.[1, 2]
- By evaluating the risk-benefit trade-offs for newer ALK inhibitors, oncologists can optimize treatment plans to effectively meet patient medical needs and respect individual preferences.

Methods

- Thirty one-on-one, in-depth qualitative interviews using a semi-structured interview guide were conducted via web-assisted telephone with US oncologists and patients with a self-reported diagnosis of ALK+ advanced NSCLC.
- The interview guide was developed based on insights from a targeted literature review of patients' preferences for NSCLC treatment and advice from steering committee members, including an expert oncologist and patient representative.
- Patients were recruited from independent panels, databases, and patient advisory groups between April and May 2023. Patients had to have ALK+ advanced NSCLC and be receiving treatment with an ALK inhibitor.
- Oncologists were recruited from physician panel. Oncologists had to be oncology certified and treating at least 1 new ALK+ NSCLC patient per year.
- Participants were asked open-ended questions followed by specific questions about their treatment experiences and expectations.
- A coding framework was developed using an interview guide and iteratively refined during initial interviews to incorporate emerging concepts.
- Descriptive sociodemographic and clinical data were collected by using an online questionnaire.
- Qualitative data were analyzed using an inductive thematic approach to identify key themes that described important concepts raised by participants.
- The study protocol was approved by an external institutional review board (Salus: 23056) and written informed consent was obtained from all participants.

Results

Participant characteristics

- Most patients were female (60%) and White (80%), with a mean age of 52 years (range 38-69) (**Table 1**).
- Most patients reported being on their current treatment line for over one year (75%), having metastases (85%), and a restricted in functional activity (65%).
- Most oncologists practiced in community settings (90%) and had experience with all available ALK inhibitors.

Table 1. Patient and Oncologist Characteristics

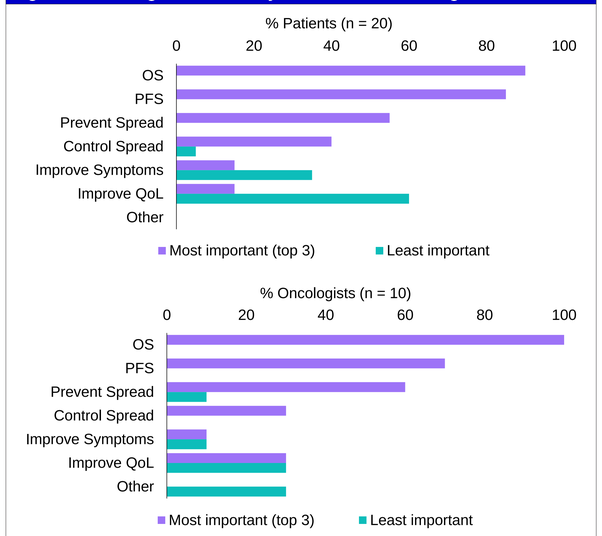
Patient Characteristics	Overall (N=20)	Oncologist Characteristics	Overall (N=10)
Age, mean years (range)	52 (38-69)	**Female sex**	2 (20%)
Female sex	12 (60%)	**Race**	
Race		White or Caucasian	6 (60%)
White or Caucasian	16 (80%)	Asian/Asian American	4 (40%)
Black/African American	2 (10%)	**Practice Setting (population)**	
Asian/Asian American	1 (5%)	Major city, > 500,000	4 (40%)
American Indian/Alaska Native	1 (5%)	Suburb, > 100,000	4 (40%)
Years since diagnosis		Small city, 30,000-100,000	1 (10%)
1-2 years	3 (15%)	Rural/small town, < 30,000	1 (10%)
3-5 years	8 (40%)	**Practice US Region**	
6 years or more	9 (45%)	Northeast	3 (30%)
Disease Status		Midwest	0 (0%)
Stable	17 (85%)	South	5 (50%)
In remission	3 (15%)	West	2 (20%)
Current Progression		**# ALK+ aNSCLC prescriptions in past 12 months**	
Local progression	3 (15%)	1 per month	2 (20%)
Metastatic	17 (85%)	2-5 per month	5 (50%)
Time on Current Treatment Line		≥5 per month	3 (30%)
0-3 months	1 (5%)	**Number of new ALK patients/month**	
4-6 months	1 (5%)	≥1 new patient in last 12 months	2 (20%)
7-12 months	3 (15%)	1 new patient	2 (20%)
1 year or more	15 (75%)	2-5 new patients	5 (50%)
Current Functioning Level*		≥5 new patients	1 (10%)
Fully active	7 (35%)		
Restricted activity	13 (65%)		

*Based on Eastern Cooperative Oncology Group (ECOG) Performance Status Scale.

Treatment benefits

- Treatment attributes related to benefits were identified in qualitative interviews (**Figure 1**).
- Many patients (40%) commented that their symptoms were mild or "didn't stop [them] from functioning" (P006), hence the unimportance of improving symptoms
- Quality of life improvements were primarily described as coming from cancer control.
- Most oncologists (60%) also spontaneously reported intracranial PFS as an important efficacy endpoint. Similarly, many patients spontaneously reported preventing brain metastases spread and/or control existing brain metastases as important treatment outcomes (35% and 20%).
- Patients and oncologists were then asked to rank treatment benefits from a list of six benefits. The top treatment benefits desired by patients and oncologists were improving overall survival (90% and 100%), progression-free survival (85% and 70%), and preventing metastases (65% and 60%) (**Figure 2**).
- Many patients (40%) commented that their symptoms were mild or "didn't stop [them] from functioning" [P006], hence the unimportance of improving symptoms

Figure 2. Ranking of Benefits By Patients and Oncologists

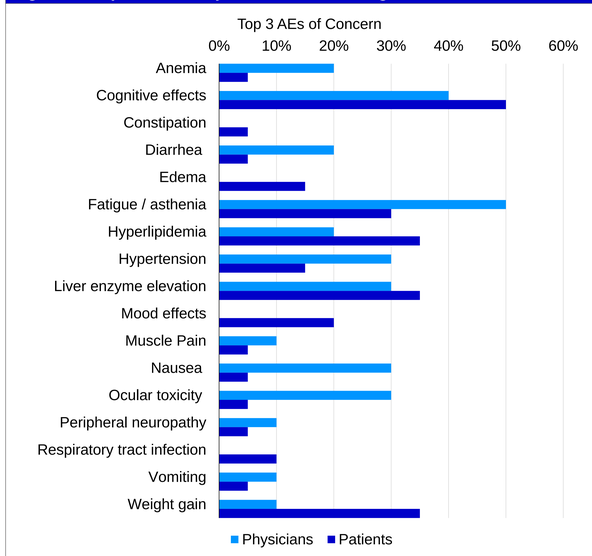


Abbreviations: OS, overall survival; PFS, progression-free survival; QoL, quality of life.
*Other includes the following response options: all of the above, cost, and overall response rate

Treatment risks

- Treatment attributes related to risks were also identified in qualitative interviews (**Figure 3**).
- Patients spontaneously reported AEs as being burdensome (70%) and had the most experience with fatigue (85%), weight gain (65%), and muscle pain (65%).
- Oncologists reported that cognitive effects (30%), fatigue (40%), and gastrointestinal toxicities (50%) were particularly burdensome and that their patients mostly experienced fatigue (80%), nausea (60%), and cognitive effects (50%).
- Both patients and oncologists were most concerned about fatigue (30% and 50%) and cognitive effects (50% and 40%) (**Figure 4**).
- Patients were more concerned than oncologists about weight gain (35% vs 10%) and hyperlipidemia (35% vs 20%), whereas oncologists were more concerned than patients about fatigue (50% vs 30%) nausea (30% vs 5%), and ocular toxicity (30% vs 5%).
- Although patients had considered dose reduction or discontinuation due to treatment-related AEs (70%), many indicate they were willing to tolerate AEs in exchange for efficacy.

Figure 4: Top 3 AEs that patients and oncologists want to avoid



Abbreviations: AEs, adverse events.

Treatment administration and decision making

- Most (60%) patients reported engaging in shared decision making with their healthcare provider.
- Some physicians (40%) indicated the frequency/number of pills being burdensome for patients, which can impact treatment adherence; however, few patients (30%) mention dissatisfaction with the frequency/number of pills of treatment.
- Oncologists reported that efficacy (60%), safety (60%), and quality of life (20%) were important factors in their treatment decisions; however, most (80%) reported that treatments depended on patient factors, such as brain metastasis, performance status, and comorbidities.

Figure 1. Representative quotes related to treatment benefits

Patient quotes on treatment benefits

Progression free survival: *" if you were surviving longer and if you're going further with progression free survival then [preventing the spreading of cancer] automatically happens" (P004)*

Brain metastasis: *"I'm petrified every time I go for an MRI. Every time I get a headache, I don't know if it's spread...I can't live my life worrying where it spread...I can only pray that the medication that I'm on is doing its job." (P012)*

"[prevent] the cancer from spreading to other parts of the body…I've seen people who get brain cancer and it's a horrible, horrible thing to watch" [P013]

Improve quality of life: *"Preventing the spread of the cancer will kind of relate to the improved symptoms and improved quality of life." (P010)*

Oncologist quotes on treatment benefits

Progression free survival: *"Overall survival. Usually that is my go-to efficacy endpoint. But in this case, because there's an overall survival can be many years, PFS would be an adequate endpoint as well." (PH071)*

Brain metastasis: *"ALK inhibitors are better than chemotherapy in the first-line setting. My preference would be to use an ALK inhibitor in almost all patients. Again, if I have brain metastasis or very heavy disease burden, I would probably make sure that the drug I'm choosing is active against the brain metastasis." (PH084)*

Improve quality of life: *"You want to extend life but not compromise things that they want to do." (PH056)*

Figure 3. Representative quotes related to treatment risks

Patient quotes on treatment risks

"This new TKI that I'm on, that one has fatigue, which when I just started it, it was very problematic. I mean, I've found ways to cope. So, for the most part, I think, it's been doing its job and it's been okay." (P010)

"I can deal with symptoms if I get them, as long as I know it's working" (P015)

"I've always been active […] when I started this new TKI, most of the pain was out of this world. And it prevented me from continuing working out because working out made it worse. And then, of course, I think that that also contributed to me gaining weight." (P010)

Oncologist quotes on treatment risks

"Once the honeymoon of your first TKI ALK directed therapy is over, well now, the danger is closer to your doorstep. So, you are willing to put up with greater toxicity and greater tolerability concerns, with later lines of therapy, given that the danger of the disease is now much greater." (PH051)

"…the low-grade ones, honestly, not ever too super concerning for me. It's the higher-grade ones we worry about I suppose. The cognitive effects are bothersome for the patient and that's something that we don't want to see." (PH056)

"Some patients tolerate whatever if they can get more time[…] But I would say, in general, most patients want to just see the efficacy and then they'll look at the safety and tolerability just like us." (PH056)

Figure 5. Representative quotes related to decision making

Patient quotes on treatment administration and decision making

Administration: *"I would rather not have to take medications, but yeah [the number of pills is] fine" (P010).*

Decision making: *"Those first few decisions were really out of my hands, I just went with whatever they said but once I started being able to research stuff on my own then ever since then I've been very involved in all the decisions and ultimately my doctor completely leaves it up to me." (P017)*

Shared decision-making: *"It was a shared decision…my doctor knows about ALK, but he's not an ALK specialist. And I was going to my ALK community, and…getting support…that helped me feel comfortable to move forward and take the medication, then we work together on the dosing, and we started at a lower dose so that I could acclimate my body to taking the medication. And thankfully, my oncologist will meet me halfway. (P019)*

Oncologist quotes on treatment administration and decision making

Administration: *"And after [6 months to a year], they start asking, "Do I have to take these pills?" Because they have to take a few not just one pill, sometimes they have to take three or four, twice a day" (PH071).*

Decision making: *"Patient factors like brain metastasis, their performance status, and any comorbidities that would affect the performance." (PH084)*

Shared decision-making: *"I always have the discussion with them, what are your goals because even some of our older patients maybe they have an important anniversary they want to meet in a couple of years or some landmark event, they need to try and make it to. So, some older patients even want, "Ah, doc, I'm really looking to make it four or five years. I want to do everything within my power to get there." So, you always have that discussion with patients." (PH055)*