Drivers of Treatment Choice in ALK-Positive Metastatic Non-Small Cell Lung Cancer From Patients' and Caregivers' Perspectives

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Background

- As available anaplastic lymphoma kinase (ALK) inhibitors for the treatment of ALK+ non-small cell lung cancer (NSCLC) differ in terms of safety, efficacy and dosing regimens,[1,2] patients and caregivers face a choice among diverse treatment profiles, requiring them to carefully weigh benefits and risks of treatment.
- Data on the treatment experience and expectations of patients with ALK+ NSCLC and their caregivers are scarce.[3] A better understanding of patients' and caregivers' preferences for treatment in ALK+ NSCLC is needed to facilitate shared decision-making among treatment options.

Objectives

- This study aimed to identify drivers of treatment choice from the perspective of patients and caregivers in the US.

Methods

- Adults with stage 4, ALK+ NSCLC (≤5 years since diagnosis) in the US, who had received ALK inhibitors for NSCLC for ≥6 months and informal, current or recent (within 1 year) caregivers of such patients participated in the study.
- The study received ethical approval from Ethical & Independent Review Services, a fully accredited, US-based central institutional review board (study number 23154 - 01).
- Semi-structured, qualitative interviews (**Table 1**) were conducted, with the interview guide developed based on concepts identified from a targeted literature review of qualitative and quantitative preference studies in NSCLC. Interview discussions were facilitated by open-ended questions in addition to ranking/rating exercises.
- Interview data were analyzed using descriptive and content analysis.

Table 1: Qualitative interview structure

Diagnosis and treatment experience
Patients' experience with symptoms prior to diagnosis and experience with treatments to date
Treatment expectation and desires
• Desired treatment benefits and reasons for seeking them • Ranking of 4 efficacy measures based on perceived meaningfulness in evaluating treatment benefit
Concerns about treatment risks
• Concerning side effects and rated how worrisome the pre-specified side effects were • Perceptions of treatment discontinuation and dose reduction due to AEs, AE management and monitoring • Selection of 2 AEs that were most important to avoid
Views on treatment regimens
Oral dose frequency, number of pills and food requirements

AE, adverse event; OS, overall survival; PFS, progression-free survival.

Results

Baseline patient characteristics

- Twenty participants (8 patient-caregiver dyads, 2 additional patients, and 2 additional caregivers) were included in the study (**Table 2**).
- Patients were 35.3 years old on average and were mostly female (70%) and White (60%) (**Table 2**).
- Average time since NSCLC diagnosis was 2.3 years; 4 (40%) patients had brain metastasis (**Table 3**).
- Patients and patients of caregivers had received alectinib (100%), brigatinib (30%), lorlatinib (30%) (**Table 3**).

Table 2: Sociodemographic characteristics

Characteristics, n (%)	Patients (n = 10)	Caregivers (n = 10)
Mean (SD) age, years	35.3 (9.3)	36.0 (12.4)
Min-Max	23–56	20–56
Sex at birth		
Male	3 (30)	5 (50)
Female	7 (70)	5 (50)
Racial background[a]		
White	6 (60)	6 (60)
Asian or Asian American	2 (20)	3 (30)
Hispanic or Latino	2 (20)	1 (10)
Black/ African American	1 (10)	1 (10)
Patient-caregiver relationship		
Caregiver = partner/spouse	8 (80)	8 (80)
Caregiver = relative/grandparent/sibling	1 (10)	1 (10)
Caregiver = parent	0	1 (10)
No caregiver	1 (10)	0

Among patients of caregivers (n = 10), the mean (SD) age was 35.9 (8.9) years; 5 of them were female, and 8 of them also participated in the study as patients. [a]Answers not mutually exclusive. SD, standard deviation.

Table 3: Clinical characteristics

Characteristics, n (%)	Patients (n = 10)	Patients of caregivers[a] (n = 10)
Mean (SD) time since NSCLC diagnosis, yrs	2.3 (1.6)	2.5 (1.7)
Min-Max	1–5	1–5
Cancer metastasis to other areas[b]		
Tissue around lungs (lymph nodes)	8 (80)	7 (70)
Brain	4 (40)	3 (30)
Liver	3 (30)	3 (30)
Other metastasis, not mentioned above	6 (60)	6 (60)
Targeted therapies received[b]		
Alectinib	10 (100)	10 (100)
Brigatinib	3 (30)	3 (30)
Lorlatinib	3 (30)	3 (30)

[a]Eight patients of caregivers also participated in the study as patients. [b]Answers not mutually exclusive. NSCLC, non-small cell lung cancer; SD, standard deviation.
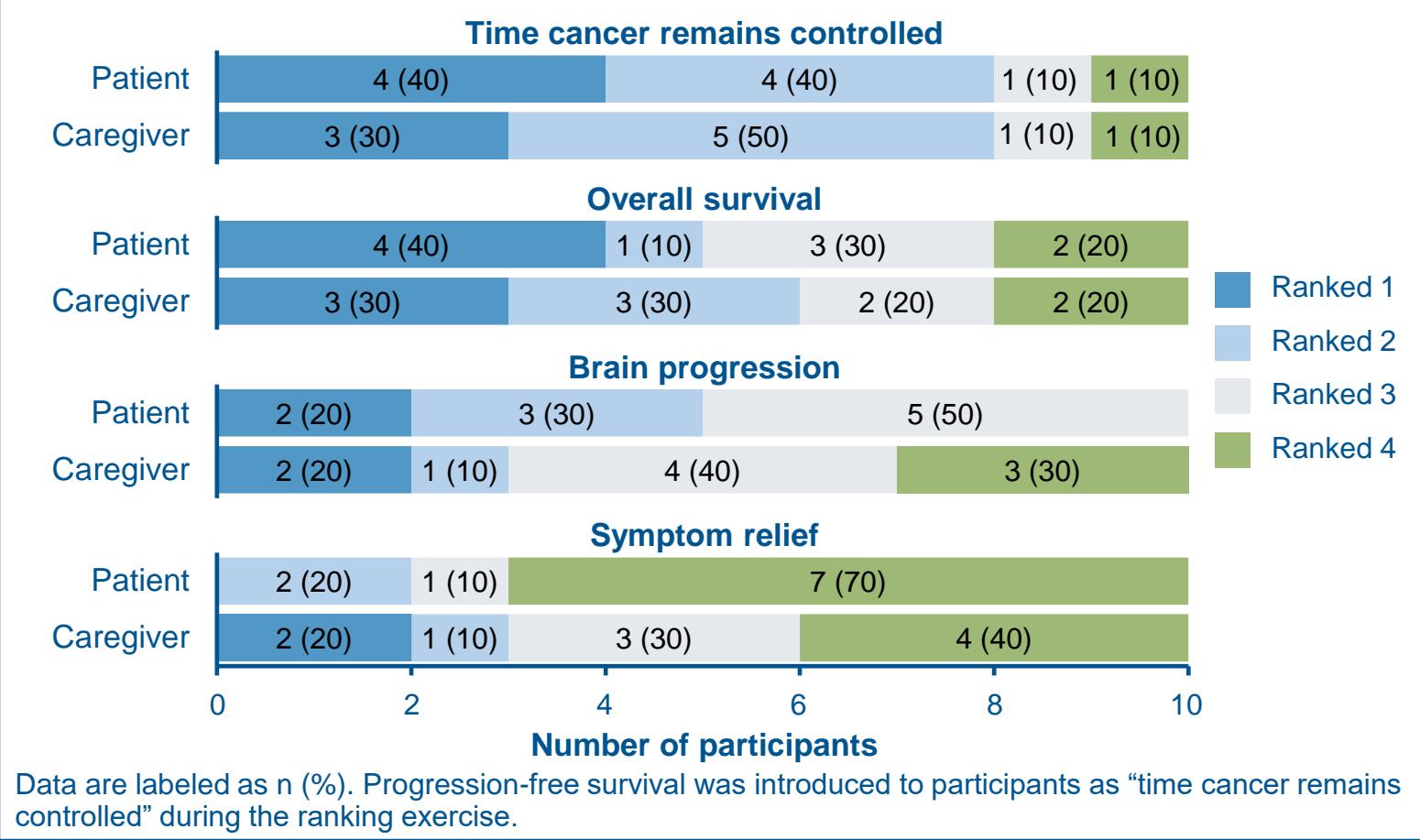
Disease-related symptoms

- Shortness of breath (SOB; 80%), cough (70%), fatigue (60%), and pain (80%) were the most common symptoms that patients had experienced, with pain, cough, and SOB particularly prior to and/or at diagnosis.
- Pain (patient 70%; caregiver 50%), fatigue (50%; 60%), cough (40%; 50%), and SOB (40%; 50%) were also the disease-related symptoms that participants most commonly desired to improve.

Treatment benefits

- Of the 4 efficacy measures evaluated, progression-free survival (PFS) was more frequently ranked as the most or second-most meaningful benefit measure than overall survival (patient 80% vs 50%; caregiver 80% vs 60%) (**Figure 1**).
  - Participants valued quality of life with less or no symptoms, but many ultimately hoped to buy more time until a new treatment becomes available.
  - Participants believed that achieving progression-free status would mean being metastasis-free and symptom-free.
- Brain metastasis prevention was ranked 3rd by 50% of patients and 40% of caregivers, and symptom relief 4th by 70% and 40%, respectively (**Figure 1**).
  - Prevention of brain metastasis, perceived to be more debilitating and more difficult to treat than lung cancer, was considered a meaningful treatment benefit.

Figure 1: Ranking of 4 efficacy measures

Data are labeled as n (%). Progression-free survival was introduced to participants as "time cancer remains controlled" during the ranking exercise.

Treatment risks

- Among the prespecified treatment-associated AEs, patients were most concerned about lung complications, cognitive/mood effects, myalgia, and weight gain, whereas caregivers were most concerned about lung complications, hypertension, abnormal lab results, and cognitive/mood effects (**Table 4**).
- Participants considered these AEs concerning as the AEs may
  - have limited management options and potential impact on future trial eligibility and the existing lung cancer (lung complications)
  - suggest the need for treatment modification (abnormal lab results)
  - impact patients' functionality (myalgia)
  - impact patient-caregiver relationships (cognitive/mood effects)
  - result in various complications (hypertension, weight gain)
- Participants suggested that AEs could be less concerning when they were aware of available drugs to address them.
- Lung complications (patient 90%; caregiver 80%), abnormal lab results (60%; 30%) and cognitive/mood effects (30%; 30%) were most frequently selected as the most important AEs to avoid.

Treatment regimens

- Assuming treatment was effective, most participants would be indifferent about the number of pills to take (patients 60%, patients of caregivers 80%), but most patients would prefer a once-daily pill regimen (60%).
- Food requirements may influence the preferences of most patients (70%).
- However, neither of these aspects had a significant impact on treatment preferences that would outweigh the potential benefits or risks presented.

Conceptual map

- Drivers of treatment choice for patients and caregivers and topics emerging during interviews are summarized in **Figure 2**.

Efficacy measures

"…Not overall survival, but I would be interested in having *longer period of [...] cancer control* because then I know that I'm not going to get, uh, mets, and I'm not going to get symptoms. So, that's why I had chosen the first box." – PT-01

"… I am… praying and hoping that science and medications will continue to develop, and that *the longer that she stays in the game*, the more of a chance that she's gonna have to *benefit from that*." – CG-04

"… *if the cancer remains* ***controlled***, it means it's *not going to the brain*." – CG-02

Concerning AEs

"'Lung complications', yes, that would be very concerning, because it can actually *exclude him from future clinical trials* and that would be very concerning."– CG-08

"…if the lab results of a particular parameter are out of bounds […] the *treatment needs to be halted or stopped*. …so the concern there obviously is if stage 4 metastatic cancer, if a patient stops treatment, just a matter of time then before *the cancer resumes…*" – PT-05

"I worry about the brain fog that, you know, I'm *not gonna be able to make good decisions*. Like, you know, it's gonna affect my cognition." – PT-03

Figure 2: Conceptual map on drivers of treatment choices
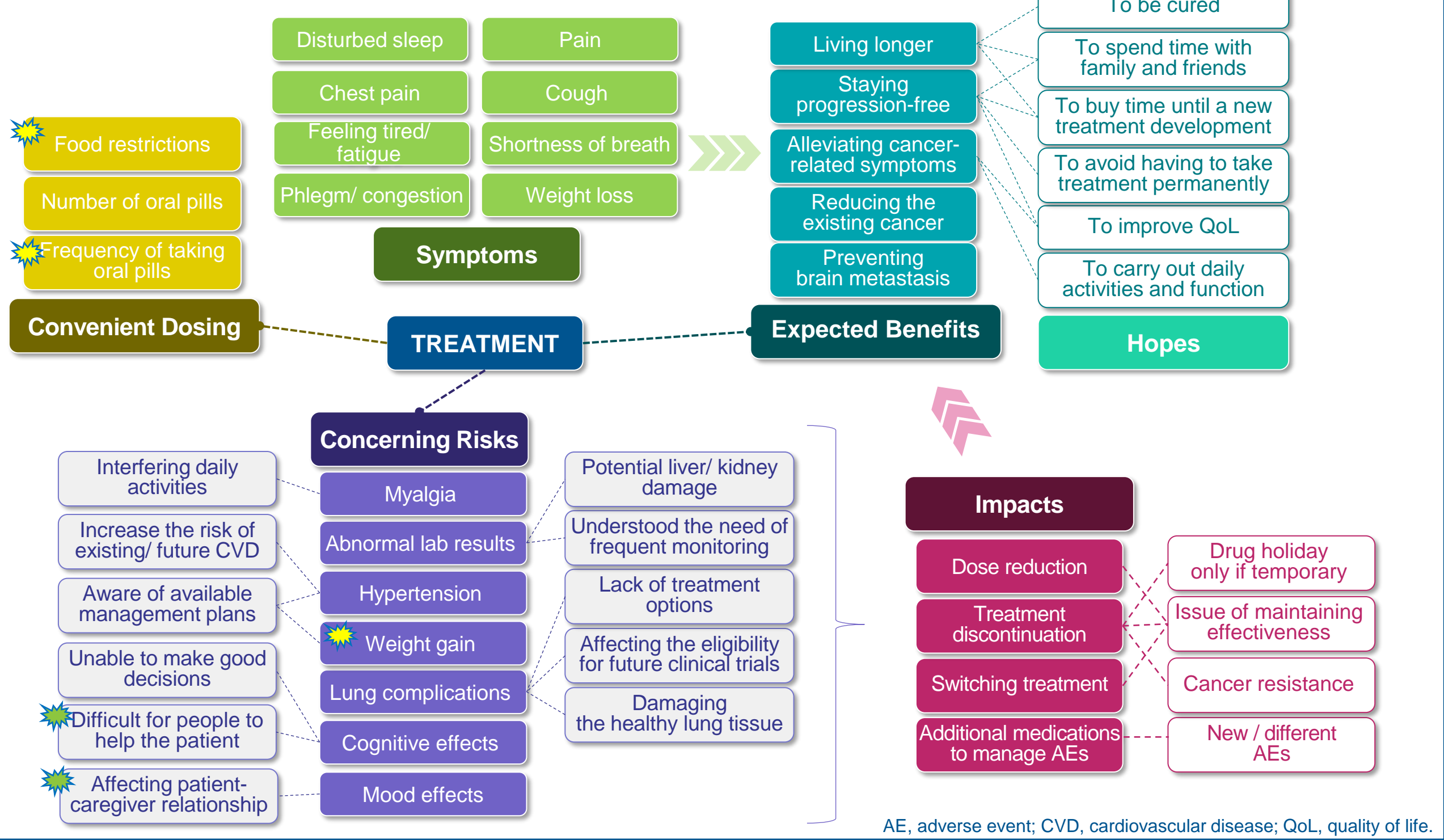
AE, adverse event; CVD, cardiovascular disease; QoL, quality of life.

Table 4: Rating of AEs by degree of concern

Treatment-associated AEs	Mean (SD) rating	
	Patients (n = 10)	Caregivers (n = 10)
Lung complications	8.3 (1.4)	8.3 (2.0)
Cognitive/mood effects	6.8 (1.5)	6.5 (2.4)
Myalgia	6.3 (1.9)	5.6 (1.6)
Weight gain	6.1 (3.0)	4.5 (2.6)
Nausea	6.0 (2.4)	6.1 (1.7)
Fatigue	5.8 (1.9)	5.5 (1.4)
Abnormal lab results	5.6 (2.5)	6.7 (1.5)
Diarrhea	5.3 (2.1)	5.8 (2.7)
Hypertension	4.9 (3.2)	6.9 (2.1)

Rating was based on a scale of 0 (not concerning) to 10 (extremely concerning). AE, adverse event; SD, standard deviation.

Conclusions

- Patients with ALK+ NSCLC and caregivers considered PFS as the most meaningful measure of treatment benefit. Prevention of brain metastasis was also deemed a meaningful treatment benefit given its potential for greater debilitation and increased treatment challenges compared to lung cancer.
- Both patients and caregivers expressed concerns about AEs including lung complications, cognitive/mood effects, myalgia, abnormal lab results, and weight gain, due to their impact on the cancer treatment and daily living.
- Patients and caregivers may not consider the treatment regimen aspects, such as the number of pills, frequency of administration, or food requirements, as significant factors when evaluating the benefits and risks of treatment.
- The extent to which these attributes drive treatment choices will be quantified in a subsequent preference study.

References

1. Parvaresh H, et al. *Biomedicines*. 2024;12:297.
2. Zheng B, et al. *Cancer Med*. 2023;12:15983-15997.
3. Lin HM, et al. *Lung Cancer Manag*. 2020;10:LMT42.