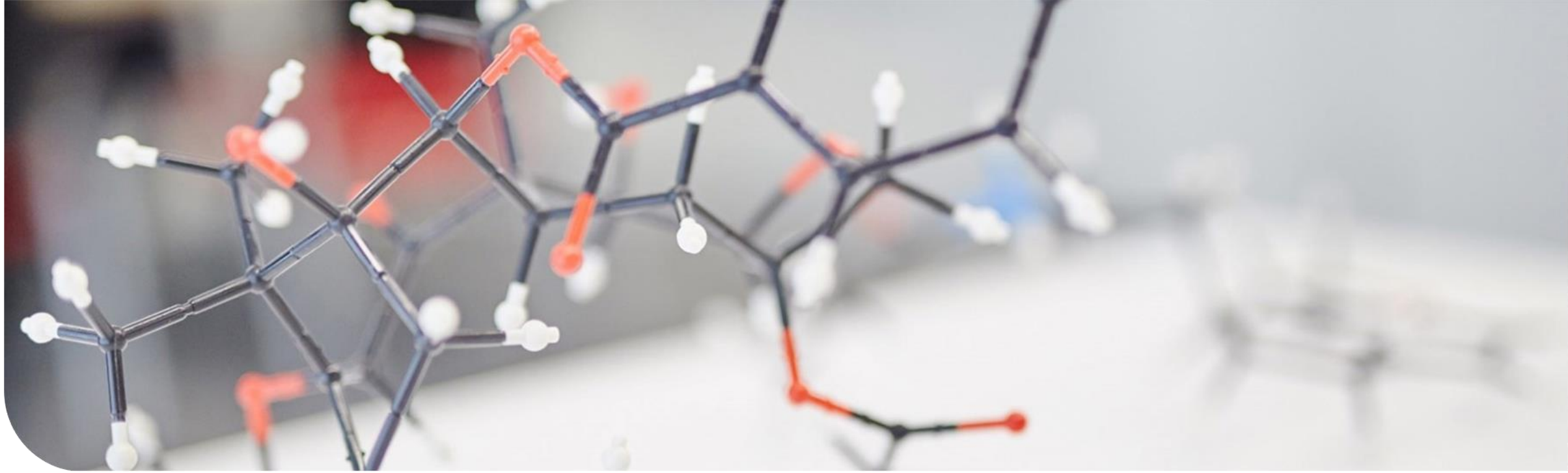


Brigatinib 2025
Post-Congress Reactive Deck

June 2025
VV-MEDMAT-122583
Global/US Medical

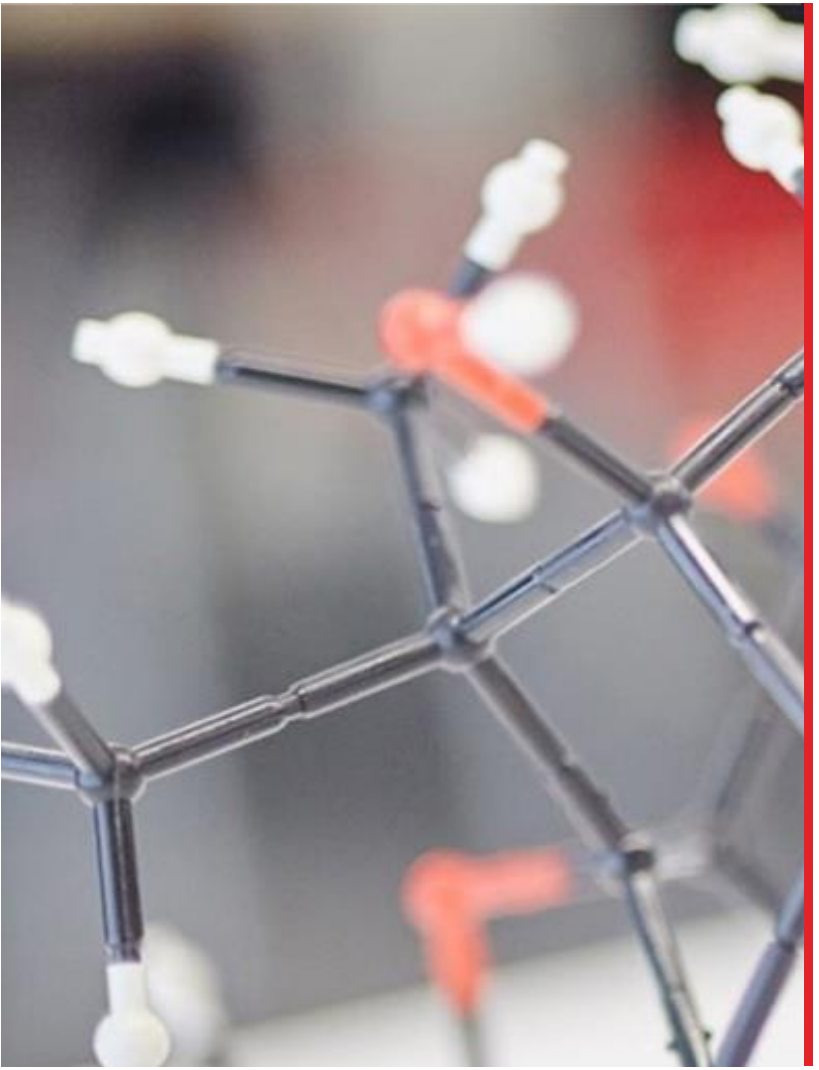
ONCOLOGY

Disclaimers

- Diese Folien wurden zur reaktiven Nutzung durch das Medical-Team im wissenschaftlichen Austausch mit HCPs erstellt, als Antwort auf nicht angeforderte Informationsanfragen zu den hierin enthaltenen Themen.
  - Antworten müssen gezielt auf die nicht angeforderte Anfrage zugeschnitten sein und den entsprechenden Kontext vollständig enthalten.
- Das Medical-Team sollte seine professionelle Einschätzung nutzen, um passende Folien in einer Reihenfolge zu präsentieren, die am besten dazu geeignet ist, die nicht angeforderte Anfrage gezielt zu beantworten.
- Die Verwendung dieser Folien muss im Einklang mit allen geltenden lokalen Gesetzen und Vorschriften erfolgen; alle LOCs müssen dieses Deck lokal für den reaktiven Gebrauch genehmigt haben, um es extern verwenden zu können.
- Dieses Deck darf nicht vom Vertrieb oder für Vertriebs-Training verwendet werden.

HCP, healthcare professional; LOC, local operating company

Contents



Company-sponsored research

Collaborative research

Investigator-initiated research

1L, first-line; ALCL, anaplastic large cell lymphoma; ASCO, American Society of Clinical Oncology; ELCC, European Lung Cancer Congress; IMT, inflammatory myofibroblastic tumor; ITCC, Innovative Therapies for Children and Adolescent Cancer; NSCLC, non-small cell lung cancer; R/R, relapsed/refractory; TKI, tyrosine kinase inhibitor; TTLC, Targeted Therapies of Lung Cancer

CLICK TO RETURN TO TABLE OF CONTENTS

Company-sponsored research

TTLC 2025

Poster PP01.06

Real-world treatment patterns and outcomes of tyrosine kinase inhibitors in anaplastic lymphoma kinase positive metastatic non-small cell lung cancer

Rosalyn I. Marar, [1] Kaushal Parikh,[1] Yin Wan,[2] Christopher Danes,[3] Jianling Peng,[3] Huamao M. Lin,[3] Wei-Jhih Wang,[4] Traci LeMasters,[5] Viktor Chirikov,[5] Kyle Roney,[5] Yuanbin Chen[6]

[1]Mayo Clinic College of Medicine, Rochester, MN, USA; [2]Previously Employed at Takeda Development Center Americas, Inc., Cambridge, MA, USA; [3]Takeda Development Center Americas, Inc., Cambridge, MA, USA; [4]Previously employed at OPEN Health, Bethesda, MD, USA; [5]OPEN Health, Bethesda, MD, USA; [6]Cancer & Hematology Centers of Western Michigan, Grand Rapids, MI, USA

Background, methods, and 2L treatment patterns

STUDY DESIGN

Retrospective observational study using **Komodo Healthcare Map secondary claims data** from 1,476 adult US patients with *ALK*+ advanced NSCLC who initiated 1L brigatinib, alectinib, crizotinib, or lorlatinib monotherapy (Jan 2016 – Mar 2023)

BRIGATINIB · CRIZOTINIB · ALECTINIB · LORLATINIB

Start of study: Jan 1, 2016

Index date: start of 1L ALK TKI

End of study: Mar 31, 2023

Baseline of ≥6 months before index

Examination of patient characteristics

Follow-up period

Examination of treatment patterns and clinical outcomes

OUTCOMES

- **Time to treatment discontinuation**
- **Overall survival**

OBJECTIVE:

To characterize treatment patterns and outcomes of individual 1L ALK TKIs in patients with *ALK*+ metastatic NSCLC

2L treatment patterns

1L brigatinib n=43

Received 2L, n=9
2L lorlatinib (55.6%), chemo/IO (33.3%), alectinib (11.1%)

1L alectinib n=938

Received 2L, n=291
2L lorlatinib (47.4%), chemo/IO (16.2%), brigatinib (15.5%)

1L lorlatinib n=29

Received 2L, n=8
2L brigatinib (50.0%), chemo/IO (25.0%), ceritinib (25.0%)

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

1L, first-line; 2L, second-line; ALK, anaplastic lymphoma kinase; chemo, chemotherapy; IO, immunotherapy; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor; TTLC, Targeted Therapies of Lung Cancer

Marar RI, et al. TTLC 2025 [poster #PP01.06]

Baseline characteristics

BASELINE CHARACTERISTICS		BRIGATINIB (n=43)	ALECTINIB (n=938)	CRIZOTINIB (n=466)	LORLATINIB (n=29)
Median (IQR) age at TKI initiation, years		57.0 (45.0–64.0)	58.0 (49.0–64.0)	60.0 (53.0–65.0)	57.0 (47.0–64.0)
Male, n (%)		20 (46.5)	405 (43.2)	195 (41.8)	16 (55.2)
White race, n (%)		12 (27.9)	316 (33.7)	186 (39.9)	9 (31.0)
Commercial payer type, n (%)		30 (69.8)	600 (64.0)	271 (58.2)	18 (62.1)
Charlson comorbidity index score, n (%)	0	14 (32.6)	247 (26.3)	117 (25.1)	7 (24.1)
	1	16 (37.2)	293 (31.2)	138 (29.6)	8 (27.6)
	2	6 (14.0)	165 (17.6)	80 (17.2)	6 (20.7)
	3+	7 (16.3)	233 (24.8)	131 (28.1)	8 (27.6)
Mean (StD) number of metastasis sites		2.91 (1.76)	2.56 (1.62)	2.37 (1.64)	3.24 (1.88)
Selected site of metastasis, n (%)	Brain	21 (48.8)	367 (39.1)	128 (27.5)	16 (55.2)
	Liver	13 (30.2)	209 (22.3)	85 (18.2)	7 (24.1)
	Bone	18 (41.9)	402 (42.9)	185 (39.7)	15 (51.7)
Median (IQR) length of follow-up, months		19.4 (12.0–34.8)	24.2 (10.0–44.1)	24.8 (6.8–54.3)	6.7 (1.9–24.1)
Median (IQR) time from metastasis to 1L treatment initiation, months		1.8 (1.1–14.7)	1.2 (0.8–1.9)	1.3 (0.8–2.4)	3.4 (1.2–14.4)

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

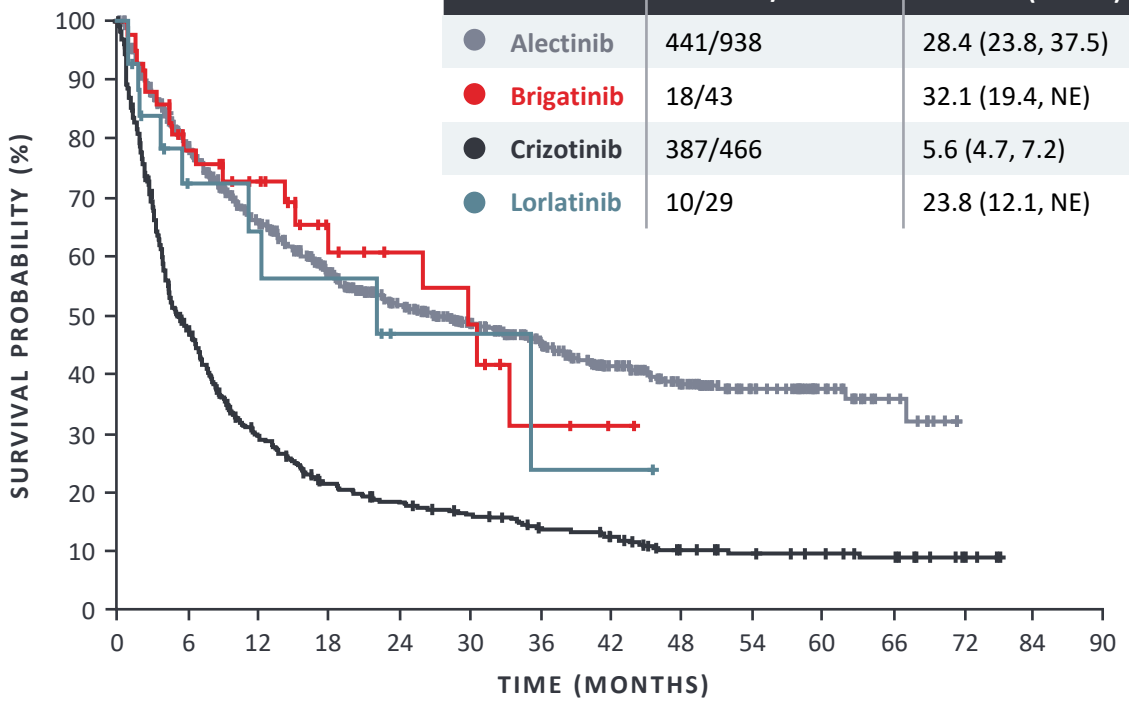
1L, first-line; IQR, interquartile range; StD, standard deviation; TKI, tyrosine kinase inhibitor; TTLC, Targeted Therapies of Lung Cancer

Marar RI, et al. TTLC 2025 [poster #PP01.06]

Time to treatment discontinuation

Time to treatment discontinuation

COHORT	EVENTS/TOTAL	MEDIAN (95% CI)
Alectinib	441/938	28.4 (23.8, 37.5)
Brigatinib	18/43	32.1 (19.4, NE)
Crizotinib	387/466	5.6 (4.7, 7.2)
Lorlatinib	10/29	23.8 (12.1, NE)



No. at risk

Alectinib	938	666	500	402	314	256	197	147	110	72	52	26	10	0	-
Brigatinib	43	31	24	16	11	9	3	2	0	-	-	-	-	-	-
Crizotinib	466	213	129	90	69	61	53	44	31	23	19	16	10	4	0
Lorlatinib	29	12	9	7	5	3	3	1	1	0	-	-	-	-	-

Propensity-score weighted Cox regression model results: Brigatinib versus alectinib or lorlatinib

OUTCOME	UNWEIGHTED		WEIGHTED*	
TIME TO TREATMENT DISCONTINUATION	HR (95% CI)	P VALUE	HR (95% CI)	P VALUE
Brigatinib vs alectinib	0.959 (0.612, 1.501)	0.854	0.971 (0.613, 1.538)	0.900
Brigatinib vs lorlatinib	0.826 (0.384, 1.777)	0.625	0.760 (0.333, 1.734)	0.514

Adjusted time to treatment discontinuation† versus crizotinib‡

COHORT	HR (95% CI)	P VALUE
Alectinib	0.347 (0.298, 0.404)	<0.001
Brigatinib	0.326 (0.209, 0.508)	<0.001
Lorlatinib	0.415 (0.227, 0.760)	0.004

- Real-world time to discontinuation was similar for 1L brigatinib versus 1L alectinib or 1L lorlatinib
- 1L brigatinib, alectinib, and lorlatinib had improved time to discontinuation compared with 1L crizotinib

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

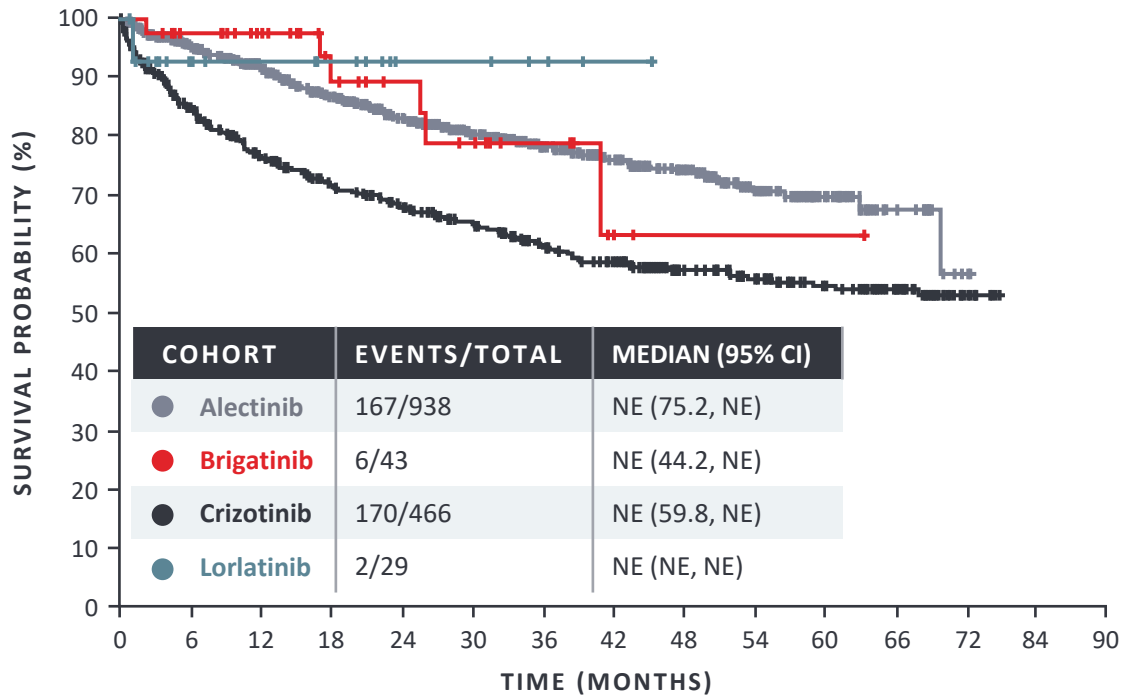
*Propensity-score weights were calculated using adjustment on age, gender, race, region, payer type, CCI, number of metastatic sites, selected sites of metastasis (brain, liver, bone), and time from metastasis to 1L treatment initiation as independent variables. Adjustment was made to the larger treatment group for each comparison. In the alectinib comparison, n=43 for brigatinib and weighted effective sample size was 472 for alectinib. In the lorlatinib comparison, weighted effective sample size was 26 for brigatinib and n=29 for lorlatinib; †Using backwards selection criteria, adjusted for age, region, CCI, and selected sites of metastasis (brain, liver, bone); ‡In a sensitivity analysis, TTNT multivariable analysis indicated similar findings as those for time to treatment discontinuation: alectinib (HR 0.341; 95% CI 0.289, 0.402), brigatinib (HR 0.317; 95% CI 0.195, 0.515), and lorlatinib (HR 0.654; 95% CI 0.344, 1.245) versus crizotinib

1L, first-line; CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; NE, not estimable; TTLC, Targeted Therapies of Lung Cancer; TTNT, time to next treatment

Marar RI, et al. TTLC 2025 [poster #PP01.06]

Overall survival

Overall survival



COHORT	EVENTS/TOTAL	MEDIAN (95% CI)
Alectinib	167/938	NE (75.2, NE)
Brigatinib	6/43	NE (44.2, NE)
Crizotinib	170/466	NE (59.8, NE)
Lorlatinib	2/29	NE (NE, NE)

No. at risk

Alectinib	938	793	670	570	475	390	319	252	195	137	85	45	18	0	-
Brigatinib	43	37	32	25	18	15	10	5	1	1	1	1	0	-	-
Crizotinib	466	357	299	263	237	207	185	164	140	117	97	83	57	11	0
Lorlatinib	29	16	12	11	8	5	4	2	1	0	-	-	-	-	-

Propensity-score weighted Cox regression model results: Brigatinib versus alectinib or lorlatinib

OUTCOME	UNWEIGHTED		WEIGHTED*	
OVERALL SURVIVAL	HR (95% CI)	P VALUE	HR (95% CI)	P VALUE
Brigatinib vs alectinib	0.913 (0.419, 1.990)	0.820	0.984 (0.432, 2.243)	0.970
Brigatinib vs lorlatinib	1.243 (0.273, 5.665)	0.779	2.198 (0.504, 9.582)	0.295

Adjusted overall survival† versus crizotinib

COHORT	HR (95% CI)	P VALUE
Alectinib	0.458 (0.362, 0.579)	<0.001
Brigatinib	0.453 (0.221, 0.928)	0.030
Lorlatinib	0.292 (0.061, 1.387)	0.121

- Real-world OS was similar for 1L brigatinib versus 1L alectinib or 1L lorlatinib
- 1L brigatinib and alectinib had improved overall survival compared with 1L crizotinib

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

*Propensity-score weights were calculated using adjustment on age, gender, race, region, payer type, CCI, number of metastatic sites, selected sites of metastasis (brain, liver, bone), and time from metastasis to 1L treatment initiation as independent variables. Adjustment was made to the larger treatment group for each comparison. In the alectinib comparison, n=43 for brigatinib and weighted effective sample size was 472 for alectinib. In the lorlatinib comparison, weighted effective sample size was 26 for brigatinib and n=29 for lorlatinib;
†Using backwards selection criteria, adjusted for age, region, payer type, CCI, number of metastases, bone and liver metastases, and time from metastasis to 1L treatment initiation

1L, first-line; CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; TTLC, Targeted Therapies of Lung Cancer

Marar RI, et al. TTLC 2025 [poster #PP01.06]

Authors' conclusions

This study summarized 1L real-world treatment patterns and health outcomes for metastatic NSCLC patients in the US and found that patients treated with brigatinib had better outcomes than those treated with crizotinib, and similar outcomes to those treated with alectinib or lorlatinib[1]

Our findings were consistent with previous studies, which reported similar time to discontinuation adjusted HRs for alectinib and brigatinib in comparison to crizotinib[1-3]

This study was conducted using claims data that did not contain certain clinical data such as a confirmed *ALK* gene rearrangement mutation, lung cancer subtype, or smoking history[1]

Given the small sample sizes for some cohorts, the results should be interpreted with caution; future research using real-world data is needed to assess clinical treatment outcomes among larger sample sizes over longer follow-up periods[1]

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

1L, first-line; HR, hazard ratio; NSCLC, non-small cell lung cancer; TTLC, Targeted Therapies of Lung Cancer

1. Marar RI, et al. TTLC 2025 [poster #PP01.06]; 2. Chen Y, et al. J Thorac Oncol 2024;19):S641 [abstract #EP.12B.02]; 3. Zhang Q, et al. JTO Clin Res Rep 2023;4:100483

ELCC 2025

Poster 939

Clinical characteristics, treatment patterns, and outcomes of first-line brigatinib in patients with advanced *ALK*+ NSCLC: A multinational real-world study

Sharmistha Ghosh,[1] Chul Kim,[2] Hollie Bailey,[3] Cameron Forshaw,[3] Yin Wan,[4,*] Huamao M. Lin,[4] Julian Kretz,[5,*] Martin Metzenmacher[6]

[1]Guy's and St Thomas' NHS Foundation Trust, London, UK; [2]Department of Hematology Oncology, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA; [3]Adelphi Real World, Bollington, UK; [4]Takeda Development Center Americas, Inc., Cambridge, MA, USA; [5]Takeda Pharmaceuticals International AG, Zurich, Switzerland; [6]Department of Medical Oncology, West German Cancer Center, University Hospital Essen, University Duisburg-Essen, Essen, Germany

*At the time of study

Background

Lung cancer, which accounts for about 12% (2.5 million new cases) of all new cancer diagnoses, is the leading cause of cancer deaths globally, with an estimated 1.8 million cancer deaths in 2022[1]

ALK rearrangement (*ALK*+) is seen in approximately 4–5% of all NSCLC cases in Western populations and represents an estimated 40,000 new cases worldwide per year[2]

The treatment landscape for advanced NSCLC has evolved considerably over recent decades, particularly with the advent of targeted therapies for patients with oncogenic driver mutations[3]

Availability of treatments targeting the *ALK* rearrangement have resulted in significant therapeutic responses and has changed the treatment landscape in patients with *ALK*+ advanced NSCLC[4]

Brigatinib was approved as a 1L treatment for *ALK*+ NSCLC patients by the European Commission in April 2020,[5] by the FDA in May 2020,[6] and by NICE in November 2020[7]

In the real-world setting, there is a need to gain a holistic understanding of brigatinib and its place in the current treatment landscape[8]

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials.
No study-specific limitations were presented in the poster

1L, first-line; ELCC, European Lung Cancer Congress; FDA, US Food and Drug Administration; HR, hazard ratio; NICE, National Institute for Health and Care Excellence; NSCLC, non-small cell lung cancer

1. Bray F, et al. CA Cancer J Clin 2024;74:229-63; 2. Itchins M, et al. Front Oncol 2022;12:959637; 3. Michelotti A, et al. Int J Mol Sci 2022;23:6748; 4. Majeed U, et al. J Hematol Oncol 2021;14:1-20; 5. Chazan G, et al. Transl Lung Cancer Res 2023;12:369; 6. Camidge DR, et al. Lung Cancer 2025;201:108424; 7. NICE. Available at: https://www.nice.org.uk/guidance/TA670 (accessed May 2025); 8. Ghosh S, et al. ELCC 2025 [poster #939]

Methods

STUDY DESIGN

Retrospective cross-sectional study using data drawn from the **Adelphi NSCLC Disease-Specific Programme™** between December 2023 and August 2024 across the US, Germany, and the UK for 331 patients with advanced *ALK*+ NSCLC treated with 1L brigatinib

A geographically representative sample of oncologists and pulmonologists responsible for treating patients with advanced *ALK*+ NSCLC with 1L brigatinib were recruited

Physician inclusion criteria

- Medical/clinical oncologist or pulmonologist actively involved in the management of patients with advanced NSCLC
- Sees ≥4 patients/month and ≥1 patient currently receiving or has received 1L brigatinib

Physicians completed a patient record form reporting:

- **Patient demographics**
- **Clinical characteristics**
- **Treatment patterns**
- **Treatment outcomes**

The patients for whom the physician provided information were asked to complete a voluntary self-completion survey to collect toxicity information

Patient inclusion criteria

- Age ≥18 years
- Confirmed *ALK*+ NSCLC
- Receiving or have received treatment with 1L brigatinib

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials.
No study-specific limitations were presented in the poster

1L, first-line; ELCC, European Lung Cancer Congress; NSCLC, non-small cell lung cancer

Ghosh S, et al. ELCC 2025 [poster #939]

Baseline characteristics and 1L brigatinib dosing

ELCC 2025
Poster 939

BASELINE CHARACTERISTICS		ALL COUNTRIES (N=331)	US (n=107)	GERMANY (n=100)	UK (n=124)
Mean (StD) age, years		64 (9.20)	65 (9.78)	66 (6.79)	61 (9.70)
Male, n (%)		180 (54)	59 (55)	68 (68)	53 (43)
Smoking status, n (%)	Current	17 (5)	4 (4)	6 (6)	7 (6)
	Former	148 (45)	58 (54)	54 (54)	36 (29)
	Never	152 (46)	32 (30)	40 (40)	80 (65)
Histology, n (%)	Adenocarcinoma	287 (87)	79 (74)	85 (85)	123 (99)
	Squamous cell carcinoma	33 (10)	22 (21)	11 (11)	0
	Large cell carcinoma	10 (3)	6 (6)	3 (3)	1 (1)
ECOG PS at initiation of 1L brigatinib, n (%)	0	83 (25)	29 (27)	12 (12)	42 (34)
	1	182 (55)	44 (41)	62 (62)	76 (61)
	2	49 (15)	19 (18)	24 (24)	6 (5)
	3	12 (4)	10 (9)	2 (2)	0

90% of patients received the optimal brigatinib dose of 180 mg/d*

92% of patients completed treatment without a change in dose

87% of patients completed treatment without a dose interruption

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials.
No study-specific limitations were presented in the poster

*Of this 90%, 71% received 90 mg for 7 days and then increased to 180 mg, while the remaining 19% were given 180 mg from treatment initiation

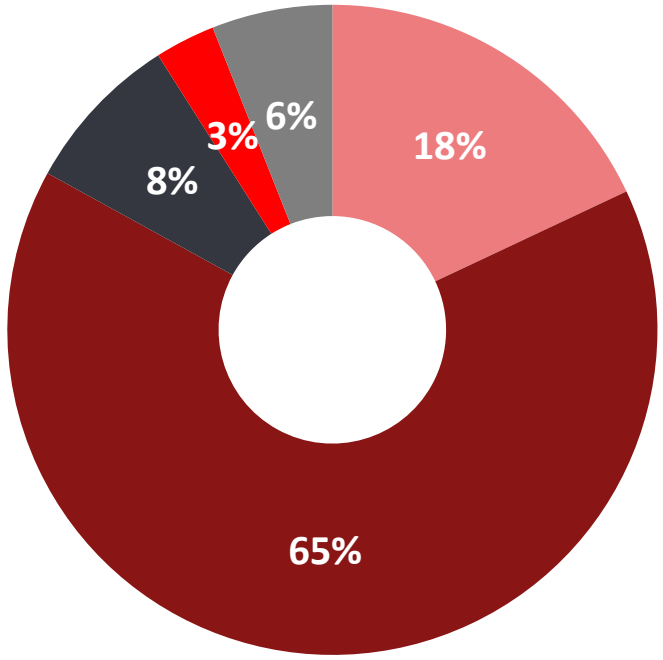
1L, first-line; d, day; ECOG PS, Eastern Cooperative Oncology Group performance status; ELCC, European Lung Cancer Congress; StD, standard deviation

Ghosh S, et al. ELCC 2025 [poster #939]

Efficacy and safety profile of 1L brigatinib

ELCC 2025
Poster 939

Best response to 1L brigatinib (N=331)



- CR (n=60)
- PD (n=11)
- PR (n=216)
- Unknown (n=19)
- SD (n=25)

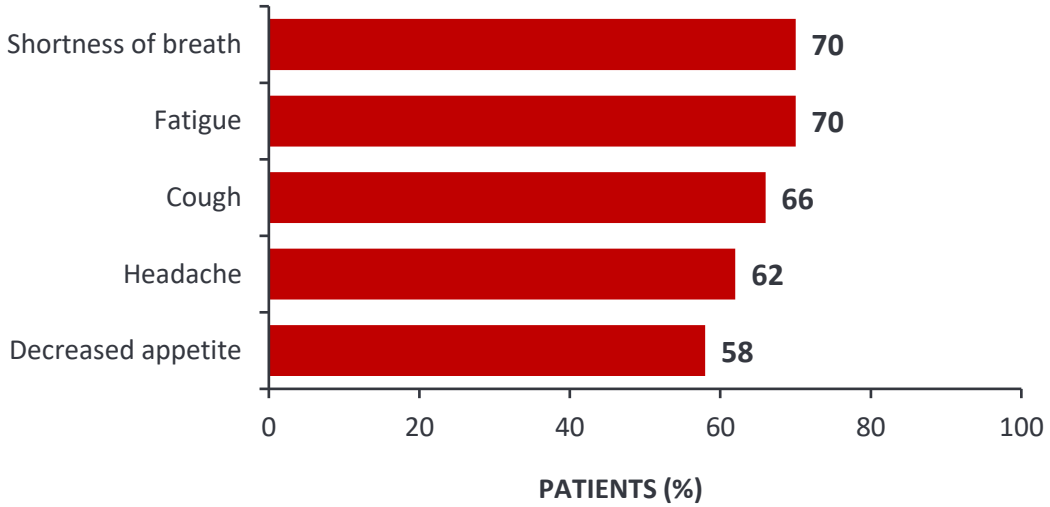
rwORR
83%

rwDCR
91%

Median rwTTD (95% CI)
24.2 months (23.1, 29.5)

Median rwTTP (95% CI)
27.2 months (24.1, 44.0)

Most common patient-reported AEs on 1L brigatinib (n=53)*



Gastrointestinal toxicities were reported in 34 (64%) patients

Most common were:
- Nausea (77%)
- Vomiting (56%)
- Diarrhea (56%)

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials.
No study-specific limitations were presented in the poster

*In patients who provided a self-completion survey and whose 1L brigatinib treatment was ongoing at the time of data collection

1L, first-line; AE, adverse event; CI, confidence interval; CR, complete response; DCR, disease control rate; ELCC, European Lung Cancer Congress; ORR, objective response rate; PD, progressive disease; PR, partial response; rw, real-world; SD, stable disease; TTD, time to treatment discontinuation; TTP, time to progression

Ghosh S, et al. ELCC 2025 [poster #939]

1L radiotherapy and 2L treatment patterns

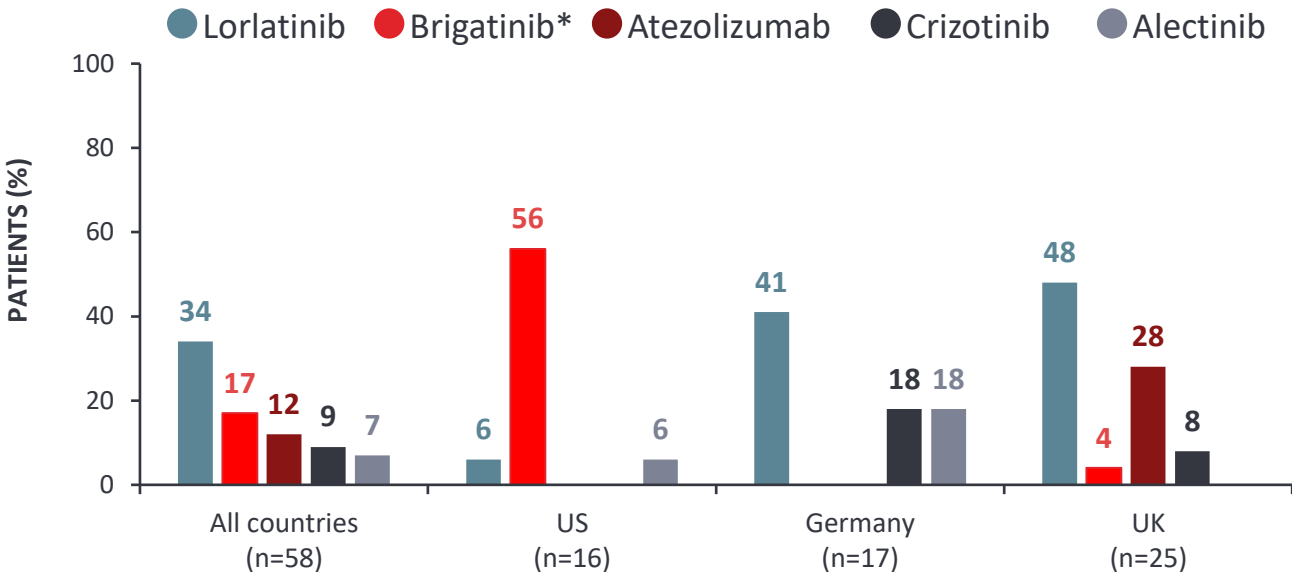
ELCC 2025
Poster 939

1L radiotherapy

19% of patients received radiotherapy as concurrent treatment with 1L brigatinib

SITE, n (%)	ALL COUNTRIES (n=64)	US (n=27)	GERMANY (n=30)	UK (n=7)
Lymph nodes	26 (41)	9 (33)	17 (57)	0
Bone	17 (27)	10 (37)	4 (13)	3 (43)
Contralateral lung	15 (23)	5 (19)	10 (33)	0
Liver	13 (20)	5 (19)	7 (23)	1 (14)
Brain	9 (14)	4 (15)	2 (7)	3 (43)
Pleura	9 (14)	6 (22)	3 (10)	0
Adrenal glands	4 (6)	4 (15)	0	0
CNS	3 (5)	1 (4)	2 (7)	0
Visceral/soft tissue	2 (3)	1 (4)	1 (3)	0

2L treatment patterns



Of the patients who completed 1L brigatinib, 58 patients went on to receive 2L treatment; lorlatinib was the most commonly prescribed

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials.
No study-specific limitations were presented in the poster

*2L brigatinib was defined as a repeat of the previous brigatinib regimen ≥90 days after completion of the original course due to non-response or relapse

1L, first-line; 2L, second-line; CNS, central nervous system; ELCC, European Lung Cancer Congress

Ghosh S, et al. ELCC 2025 [poster #939]

Authors' conclusions

Results from this real-world, multinational study were in line with data captured from the Phase 3 ALTA-1L trial and mirrored previous trials, such as NCT01449461 and NCT02094573

The majority of patients with advanced ALK+ NSCLC who received 1L brigatinib did not require a treatment interruption while receiving 1L brigatinib treatment, highlighting brigatinib's tolerability

Brigatinib's effectiveness was also supported by the high response rate observed in this study, with the majority of patients having a partial or complete response to 1L brigatinib treatment

Future research examining the drivers of choosing brigatinib as a 1L treatment will provide further understanding into its place in the advanced NSCLC treatment landscape

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials.
No study-specific limitations were presented in the poster

1L, first-line; ELCC, European Lung Cancer Congress; NSCLC, non-small cell lung cancer

Ghosh S, et al. ELCC 2025 [poster #939]

ELCC 2025

Poster 88P

Real-world occurrence of early-onset pulmonary events with brigatinib for advanced *ALK*+ NSCLC

Maximilian J. Hochmair,[1] Grant Stewart,[2] Markus Rauter,[3] Michael Studnicka,[4] Bilal Khokhar,[5] Ronald Gounden,[5] Yu Yin,[5] Robert J. Fram,[5,*] Thomas Egenod[6]

[1]Karl Landsteiner Institute for Lung Research and Pulmonary Oncology, Klinik Floridsdorf, Vienna, Austria; [2]Royal Cornwall Hospital, Truro, UK;
[3]Klinikum Klagenfurt am Wörthersee, Klagenfurt am Wörthersee, Austria; [4]LKH-Universitätsklinikum der PMU, Salzburg, Austria;
[5]Takeda Development Center Americas, Inc., Cambridge, MA, USA; [6]CHU de Limoges-Hôpital Dupuytren, Limoges, France

*At the time of study

Background

ILD and pneumonitis are known AEs with TKIs used to treat *ALK*+ NSCLC, including brigatinib[1-3]

In brigatinib clinical trials, pulmonary AEs (eg, ILD, pneumonitis, dyspnea, hypoxia) occurring within 14 days of starting brigatinib were termed EOPEs[4]

In order to minimize EOPE occurrence observed in early-phase trials, a step-up dosing regimen for brigatinib (180 mg QD with a 7-day lead-in at 90 mg QD) was implemented[4-6]

In patients with advanced NSCLC, symptoms of drug-related pulmonary AEs may be similar to those of the underlying cancer and other lung diseases, making assessment of causality challenging

This post-authorization safety study evaluated EOPE rates with brigatinib in a real-world setting[7]

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials.
No study-specific limitations were presented in the poster

AE, adverse event; ELCC, European Lung Cancer Congress; EOPE, early-onset pulmonary event; ILD, interstitial lung disease; NSCLC, non-small cell lung cancer; QD, once daily; TKI, tyrosine kinase inhibitor

1. Zhou F, et al. ESMO Open 2023;8:101560; 2. Suh CH, et al. Lung Cancer 2019;132:79-86; 3. Dong J, et al. Front Pharmacol 2024;15:1361443; 4. Ng TL, et al. J Thorac Oncol 2020;15:1190-9; 5. Gettinger SN, et al. Lancet Oncol 2016;17:1683-96; 6. Kim D-W, et al. J Clin Oncol 2017;35:2490-8; 7. Hochmair MJ, et al. ELCC 2025 [poster #88P]

Methods

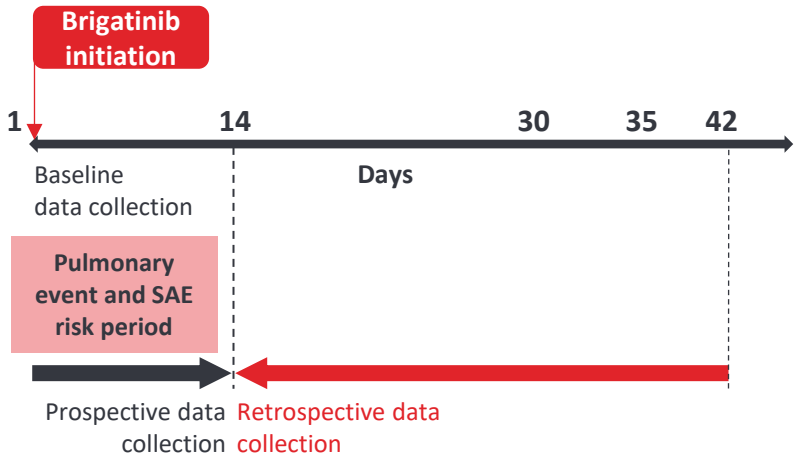
STUDY DESIGN

Real-world, observational, single-arm, multicenter,* Phase 4 cohort study following 98 adult patients with advanced *ALK*+ NSCLC during the first 42 days of brigatinib monotherapy

Inclusion criteria

- Advanced *ALK*+ NSCLC
- Aged ≥18 years
- Initiating brigatinib monotherapy according to routine local practice

Safety data reporting period



Electronic case report forms captured:

- Diagnosis
- Description of pulmonary event
- Grade of event
- Relevant clinical information
  - Lab results
  - Imaging reports/copies of images
  - Histopathology findings

OBJECTIVE:

Assess the occurrence of confirmed EOPEs within 14 days after initiation of brigatinib therapy

ADJUDICATION OF EOPEs

An independent adjudication committee of five physicians with expertise in pulmonary medicine, radiology, and thoracic oncology reviewed all reports of AESIs to determine if they met EOPE criteria†

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials.
No study-specific limitations were presented in the poster

*29 sites in Europe; †Charter-defined criteria for a pulmonary event: presence of a temporal relationship (defined as signs and symptoms beginning within 14 days of starting brigatinib), evidence of a pneumonitis-like process supported by imaging or pathology (such as ground glass opacities on computed tomography/x-ray or diffuse alveolar damage on histopathology), and determination that other etiology (such as infection or tumor progression) was unlikely. Procedures related to the independent adjudication of AESIs were conducted by an IQVIA Clinical Event Validation and Adjudication group. Committee members were trained on the predefined EOPE adjudication process outlined in the adjudication charter. Adjudication committee members were able to request additional information (eg, imaging) from the clinical site to thoroughly evaluate each event and complete their assessments

AESI, adverse event of special interest; ELCC, European Lung Cancer Congress; EOPE, early-onset pulmonary event; NSCLC, non-small cell lung cancer; SAE, serious adverse event

Hochmair MJ, et al. ELCC 2025 [poster #88P]

Baseline characteristics and brigatinib treatment patterns

ELCC 2025
Poster 88P

BASELINE CHARACTERISTICS	BRIGATINIB (N=98)
Median (range) age, years	59.5 (26–88)
Female, n (%)	49 (50)
Disease stage at entry	n=90
IIIA or IIIB / IV, n (%)	10 (11) / 80 (89)
Smoking status	n=93
Never / former / current, n (%)	49 (53) / 38 (41) / 6 (6)
Prior anticancer therapy, n (%)	28 (29)
1 prior line / ≥2 prior lines	19 (68) / 9 (32)
Prior ALK TKI, n (%)	10 (10)
Alectinib	10 (10)
Crizotinib	4 (4)
Lorlatinib	2 (2)
Median (range) time from diagnosis,* mos	1 (0–69)
History of ILD or pneumonitis, n (%)	3 (3)
Other pulmonary condition or disease,† n (%)	10 (10)
Pulmonary embolism	2 (2)
Asthma	1 (1)
COPD	1 (1)
Dyspnea	1 (1)
Other‡	7 (7)

DOSE PATTERN, n (%)		BRIGATINIB (N=98)
Within the first 7 days (dose given once daily)	90 mg	90 (92)
	90 mg → 180 mg / 0 mg	3 (3) / 2 (2)
	Other§	3 (3)
During the entire study period (dose given once daily)	90 mg → 180 mg	77 (79)
	90 mg	4 (4)
	90 mg → 180 mg → 0 mg → 90 mg	3 (3)
	90 mg → 0 mg → 90 mg → 180 mg	2 (2)
	90 mg → 180 mg → 120 mg	2 (2)
	Other§	8 (8)
Dose modifications during the entire study¶	Dose increased	93 (95)
	Dose reduced	4 (4)
	Dose interrupted	12 (12)
	Physician intervention	11 (92)
	Patient decision/action	1 (8)
	Drug withdrawn	11 (11)
	Switch to new therapy	7 (64)
Reason for dose adjustment¶	Adverse event	7 (7)
	Lack of efficacy	3 (3)
	Other	94 (96)
	Standard of care	92 (98)
	PI decision	1 (1)
	Planned dose increase	1 (1)

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. No study-specific limitations were presented in the poster

*Of advanced disease to brigatinib first dose (n=90); †Other than ILD or pneumonitis within 180 days before brigatinib; ‡Hyper-responsive bronchial system (n=1), cough and hoarseness (n=1), asthma-COPD overlap (n=1), relapse (n=1), shortness of breath on exertion and when speaking fast (n=1), cough (n=1), respiratory desaturation and febrile cough (n=1); §See slide notes for details of 'Other' categories; ¶There could be more than one dose modification and reason for dose adjustment per patient.

See slide notes for abbreviations

Hochmair MJ, et al. ELCC 2025 [poster #88P]

EOPEs and pulmonary AESIs within 14 days after brigatinib initiation

ELCC 2025
Poster 88P

Adverse events

	BRIGATINIB (N=98)
Confirmed EOPE, n	**0**
Pulmonary AESI, n (%) [no. events]	10 (10) [11]
Cough	4 (4) [4]
Dyspnea	2 (2) [2]
Atypical pneumonia	1 (1) [1]
Pneumonia	1 (1) [1]
Pneumonitis	1 (1) [1]
Productive cough	1 (1) [1]
NSCLC	1 (1) [1]

- Ten patients experienced a total of 11 pulmonary AESIs during the first 14 days of brigatinib treatment
- Three AESIs in three patients were serious AEs*
  - Pneumonia requiring or prolonging hospitalization
  - Dyspnea requiring or prolonging hospitalization
  - NSCLC disease progression
- None of the serious AEs were considered related to treatment

Unlike ALTA-1L, all pulmonary AESIs in this study were reviewed by the independent expert adjudication committee, and none were adjudicated as confirmed EOPEs

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. No study-specific limitations were presented in the poster

*An additional two serious AEs were reported: pleural effusion requiring or prolonging hospitalization in patient who had AESI of dyspnea (n=1); death due to unknown cause (n=1)

AE, adverse event; AESI, adverse event of special interest; ELCC, European Lung Cancer Congress; EOPE, early-onset pulmonary event; NSCLC, non-small cell lung cancer

Hochmair MJ, et al. ELCC 2025 [poster #88P]

Authors' conclusions

In this real-world study, most patients (79%) received brigatinib at doses consistent with recommended step-up dosing

There were no confirmed EOPEs after review by the independent adjudication committee

With the inclusion of an independent adjudication committee, this study may provide a more accurate representation of EOPE incidence than previous studies

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials.
No study-specific limitations were presented in the poster

ELCC, European Lung Cancer Congress; EOPE, early-onset pulmonary event

Hochmair MJ, et al. ELCC 2025 [poster #88P]

ASCO 2025
Poster 97

Patient and caregiver treatment preferences for *ALK*+ non-small cell lung cancer in the United States

Christopher G. Danes,[1] Jaein Seo,[2] Myrto Trapali,[3] Harrison Clarke,[2] Jennifer A. Whitty,[3] Anirudh Sethi,[1] Dasha Cherepanov,[4] Summer Farmen,[5] Kenneth W. Culver[5]

[1]Takeda Oncology, Cambridge, MA, USA; [2]Patient-Centered Research, Evidera, Wilmington, NC, USA; [3]Patient-Centered Research, Evidera, London, UK; [4]Takeda Development Center Americas, Inc., Cambridge, MA, USA; [5]ALK Positive, Atlanta, GA, USA

Background and objectives

Background

New-generation ALK TKIs, such as alectinib, brigatinib, and lorlatinib, have been FDA approved as first-line therapies for *ALK*+ NSCLC[1]

Treatments for *ALK*+ NSCLC have distinct benefits and risks.[2,3] As patients often use ALK TKIs for years, balancing these considerations is crucial

Yet, there is a paucity of evidence regarding how these benefits and risks influence treatment preferences from the perspectives of patients and caregivers

OBJECTIVES

To elicit patient and caregiver preferences for *ALK*+ NSCLC treatments, this study[4]:

- Quantified the trade-offs they were willing to make between benefit and risk attributes
- Explored the extent to which caregiver preferences are aligned with those of patients
- Assessed preference differences by sociodemographic/clinical characteristics

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

ALK, anaplastic lymphoma kinase; ASCO, American Society of Clinical Oncology; FDA, US Food and Drug Administration; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor

1. Zheng B, et al. Cancer Med 2023;12:15983-97; 2. Parvaresh H, et al. Biomedicines 2024;12:297; 3. Bearz A, et al. Int J Mol Sci 2025;26:308; 4. Danes CG, et al. ASCO 2025 [poster #97]; see the abstract

Methods

STUDY DESIGN

US adults with Stage IV *ALK*+ NSCLC (diagnosed since 2018) who had received ≥1 ALK TKI for >6 months and their current or recent (within 1 year) caregivers were recruited via physician referrals and ALK Positive patient advocacy group to complete an online discrete choice experiment (DCE) survey developed in a mixed-methods research process

Through 10 DCE choice tasks, participants chose between two hypothetical treatment profiles described by seven benefit/risk attributes,* each with one of three plausible clinical levels (see example). These levels were varied across the choice tasks to elicit trade-offs

A mixed logit model was used to assess the relative impact of each attribute on preferences, by estimating **relative attribute importance (RAI)** and **maximum acceptable reduction in the probability of having 3-year PFS** in exchange for reduced risks of adverse events

Treatment A	Treatment B
 • **30 out of 100 patients** would be **progression-free** for at least 3 years • **15 out of 100 patients** would have **tumor progression anywhere other than the brain** within 3 years • **55 out of 100 patients** would have **tumor progression in the brain** within 3 years	 • **45 out of 100 patients** would be **progression-free** for at least 3 years • **45 out of 100 patients** would have **tumor progression anywhere other than the brain** within 3 years • **10 out of 100 patients** would have **tumor progression in the brain** within 3 years
 **3 out of 100 (3%)** develop severe lung complications	 **6 out of 100 (6%)** develop severe lung complications
 **25 out of 100 (25%)** develop cognitive/ mood effects	 **15 out of 100 (15%)** develop cognitive/ mood effects
 **15 out of 100 (15%)** develop severe abnormal lab results	 **15 out of 100 (15%)** develop severe abnormal lab results
 **10 out of 100 (10%)** develop myalgia	 **20 out of 100 (20%)** develop myalgia
 **20 out of 100 (20%)** develop severe weight gain	 **10 out of 100 (10%)** develop severe weight gain

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

*Treatment attributes were selected based on a targeted literature review, Phase 3 trial data of ALK TKIs, consultations with a patient advocacy group representative, and qualitative interviews with ten patients and ten caregivers

ALK, anaplastic lymphoma kinase; ASCO, American Society of Clinical Oncology; DCE, discrete choice experiment; NSCLC, non-small cell lung cancer; PFS, progression-free survival; RAI, relative attribute importance; TKI, tyrosine kinase inhibitor

Danes CG, et al. ASCO 2025 [poster #97]; see the abstract

Participant characteristics (1/2)

PATIENT PARTICIPANTS (n=205)

Mean (StD) age: 61.9 (10.3) years

Gender

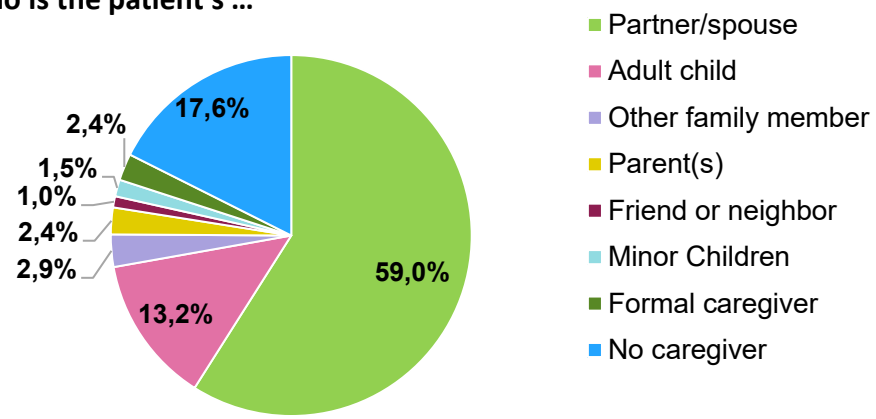
46.3% females

53.2% males

Transgender: n=1 (0.5%)

Employment status

Patient has a caregiver who is the patient's …



CAREGIVER PARTICIPANTS (n=125)

Caregivers

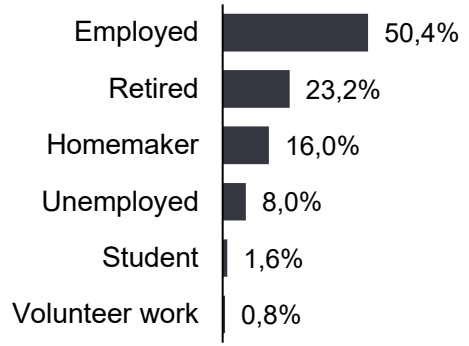
Mean (StD) age: 58.7 (11.7) years

Gender

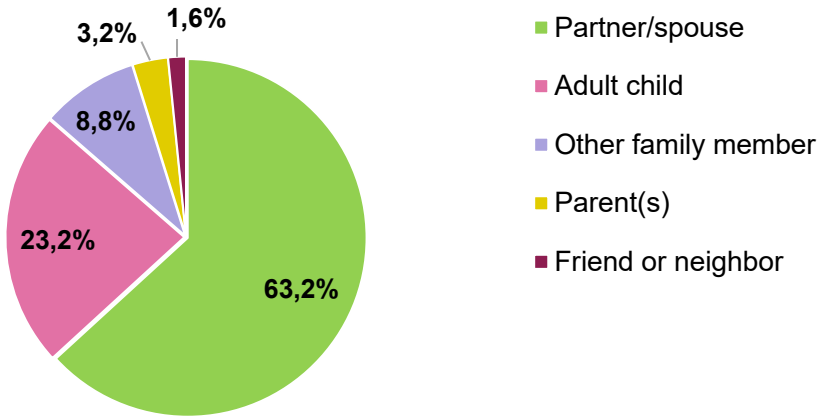
72.8% females

27.2% males

Employment status



Caregiver is patient's …



Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

ASCO, American Society of Clinical Oncology; StD, standard deviation

Danes CG, et al. ASCO 2025 [poster #97]; see the abstract

Participant characteristics (2/2)

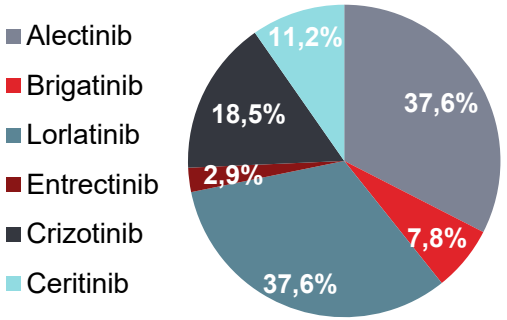
PATIENT PARTICIPANTS (n=205)

Mean (StD) time since NSCLC diagnosis:
2.7 (1.6) years

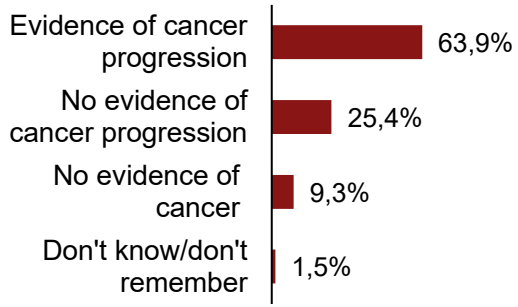
Health status (ECOG score)

Fully active	16.6%
Restricted	38.0%
Ambulatory	28.8%
Limited	13.7%
Completely disabled	2.9%

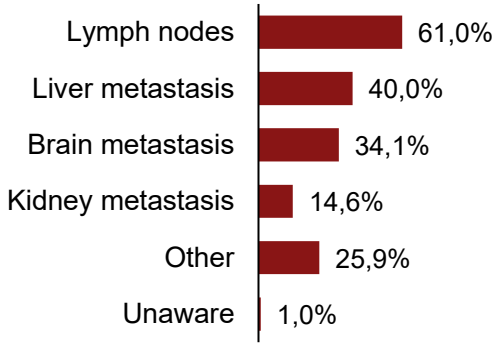
Targeted therapy received*



Status of NSCLC



Cancer metastasis*,†



CAREGIVER PARTICIPANTS (n=125)

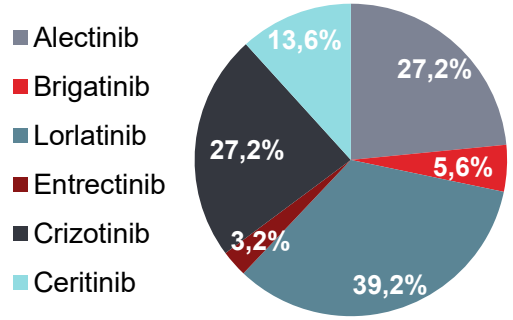
Caregivers' patients

Mean (StD) time since NSCLC diagnosis:
2.8 (1.5) years

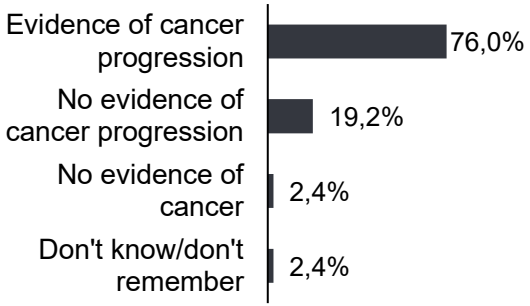
Health status (ECOG score)

Fully active	6.4%
Restricted	36.0%
Ambulatory	34.4%
Limited	20.0%
Completely disabled	3.2%

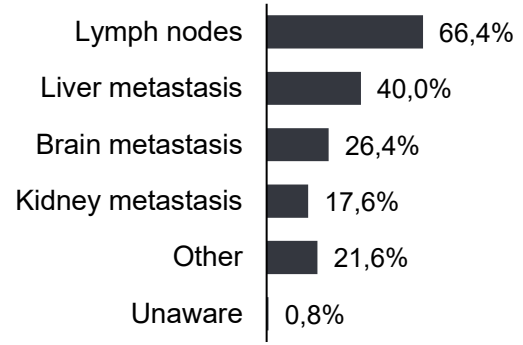
Targeted therapy received*



Status of NSCLC



Cancer metastasis*,†



Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

*Options were not mutually exclusive; †The "Unaware" option was self-reported as 'don't know/don't remember'

ASCO, American Society of Clinical Oncology; ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small cell lung cancer; StD, standard deviation

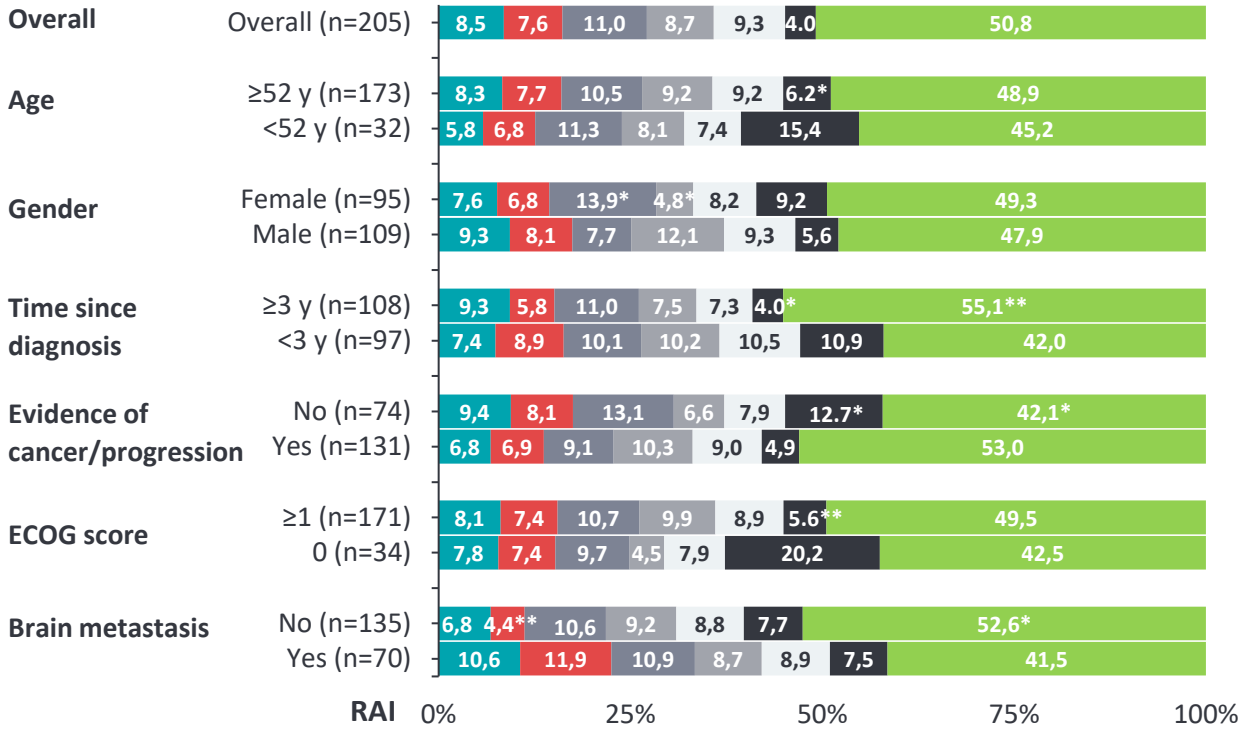
Danes CG, et al. ASCO 2025 [poster #97]; see the abstract

Variation of RAIs in patients and caregivers

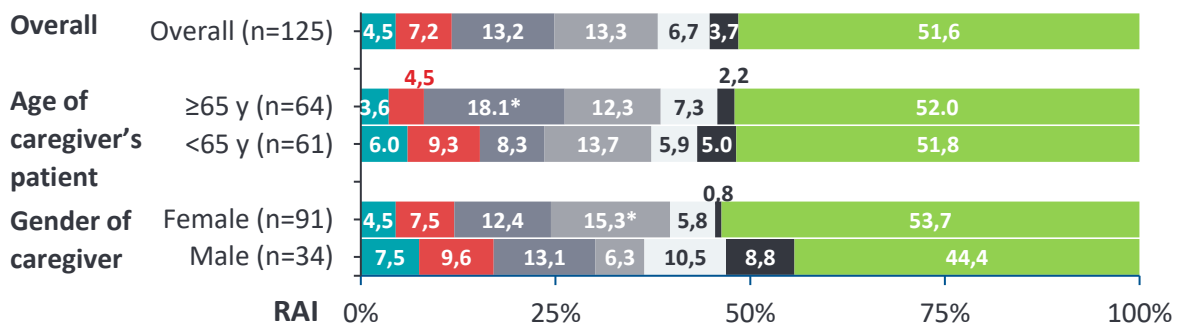
ASCO 2025
Poster 97

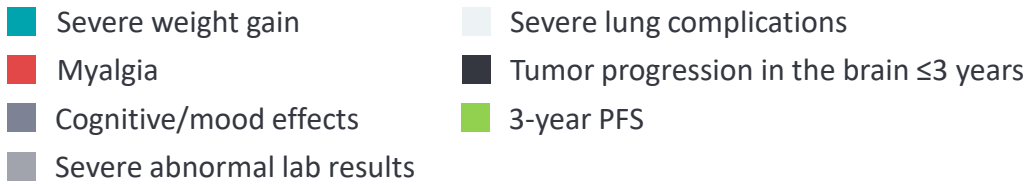
29.8% of patients and 33.6% of caregivers chose treatments based solely on 3-year PFS

Patients



Caregivers





- Improving the chance of reaching 3-year PFS was most important to both patients and caregivers
- Patients placed similar values on reducing risks across different AEs whereas caregivers prioritized reducing severe abnormal lab results and cognitive/mood effects
- Preferences varied among patients and caregivers

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

Significance was determined using independent two-sided z-tests: *p<0.05, **p<0.01 between subgroups

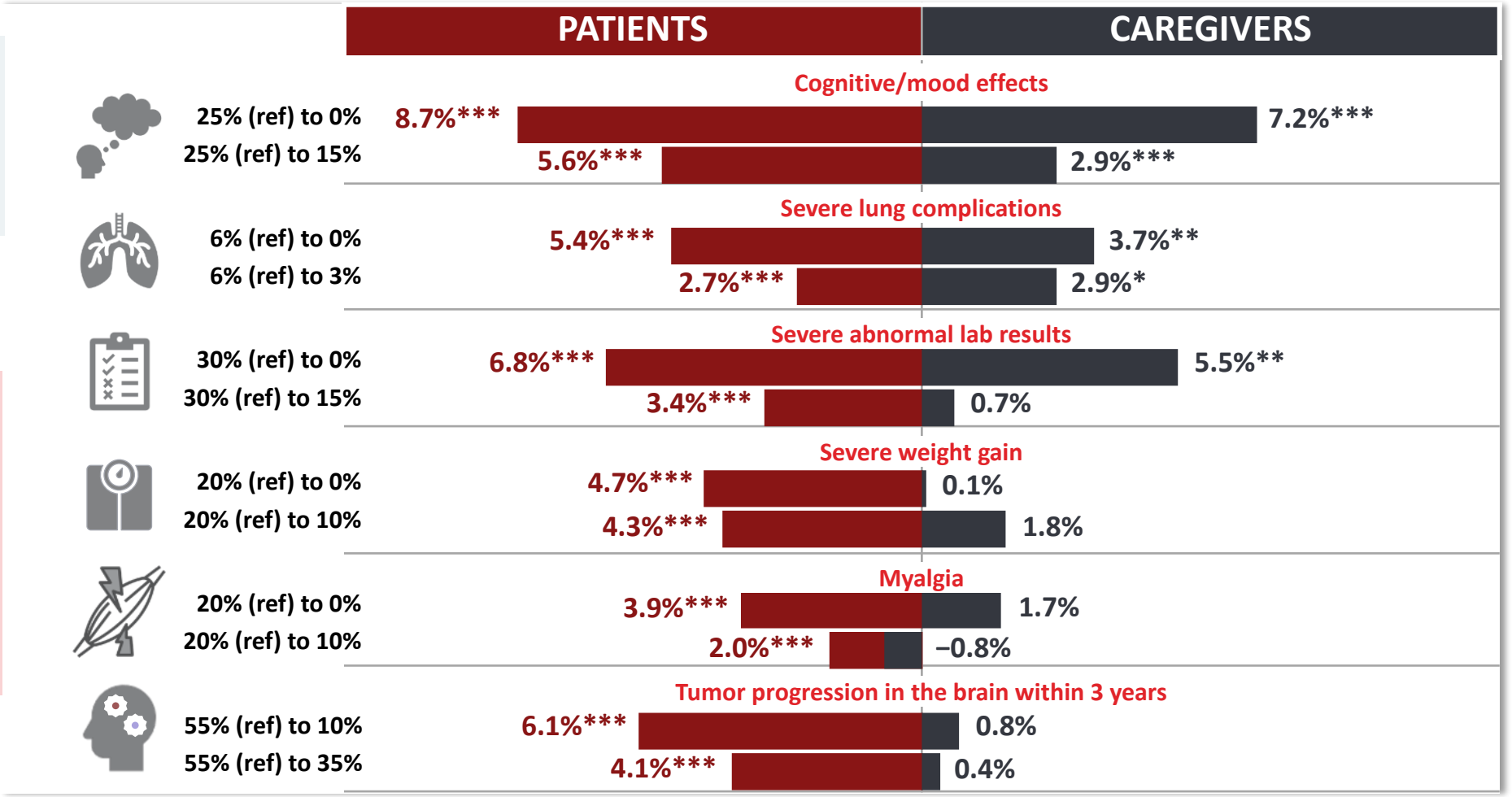
AE, adverse event; ASCO, American Society of Clinical Oncology; ECOG, Eastern Cooperative Oncology Group; RAI, relative attribute importance; PFS, progression-free survival; y, year

Danes CG, et al. ASCO 2025 [poster #97]; see the abstract

Average maximum acceptable reduction in 3-year PFS

While holding all other attributes constant, patients/caregivers were willing to accept a reduced chance of 3-year PFS in exchange for reducing risks

While caregivers were unwilling to accept reductions in the chance of 3-year PFS to reduce the risks of any-grade myalgia, severe weight gain, or tumor progression in the brain within 3 years since treatment initiation, patients were more willing to do so



Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

Significance, determined using independent two-sided z-tests, indicates the difference in the maximum acceptable reduction in achieving 3-year PFS to lower the risk of each listed attributes from their reference level to the other two lower-risk levels: *p<0.05; **p<0.01; ***p<0.001

ASCO, American Society of Clinical Oncology; PFS, progression-free survival; ref, reference level

Danes CG, et al. ASCO 2025 [poster #97]; see the abstract

Authors' conclusions

Patients and caregivers weigh the benefits and risks of treatment options

- **In this study, increasing the chance of reaching 3-year PFS was the highest priority for both patients and caregivers when choosing treatments; however, both patients and caregivers were willing to trade off the 3-year PFS benefit for reducing the risk of specific AEs at varying levels**

Patients and caregivers care about specific AEs

- **Preference differences within each group were also evident from the varying values placed on each risk attribute**

Future directions warrant identifying groups of patients and caregivers who are risk-sensitive versus those who want to solely maximize PFS benefits, along with the underlying characteristics of these groups. This can improve shared decision-making between physicians, patients, and caregivers in managing patient care in *ALK*+ NSCLC

Real-world analyses are often nonrandomized, observational, retrospective, or prospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data. Observational, retrospective, and prospective analyses are not intended for direct comparison with clinical trials. See slide notes for study limitations

AE, adverse event; ASCO, American Society of Clinical Oncology; NSCLC, non-small cell lung cancer; PFS, progression-free survival

Danes CG, et al. ASCO 2025 [poster #97]; see the abstract

Collaborative research

ITCC Scientific Days 2025

Poster

Brigatinib monotherapy in children with R/R *ALK*+ ALCL, IMT, or other solid tumors: Updated results from the BrigaPED (ITCC-098) Phase 1 dose-escalation study

Charlotte Rigaud,[1,*] Kim P. J. Schellekens,[2,3,*] Veronique Minard-Colin,[1] Christine Damm-Welk,[4] Pascal Chastagner,[5] Stéphane Ducassou,[6] Natasha K. A. van Eijkelenburg,[2] Nathalie Garnier,[7] Michael J. Hanley,[8] Alwin D. R. Huitema,[2,9,10] Nicole Scobie,[11] Florin Vranceanu,[8] Wilhelm Woessmann,[4] Christian M. Zwaan,[2,3,†] Reineke A. Schoot[2,†]

[1]Department of Children and Adolescent Oncology, Gustave Roussy Cancer Campus, Université Paris-Saclay, Villejuif, France;
[2]Princess Máxima Center for Pediatric Oncology, Utrecht, the Netherlands; [3]Department of Pediatric Oncology, Erasmus Medical Center, Rotterdam, the Netherlands;
[4]Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany;
[5]Children University Hospital, Vandoeuvre-lès-Nancy, University of Nancy, Nancy, France; [6]Department of Pediatric Hemato-Oncology, Bordeaux, France;
[7]Institut d'Hematologie et d'Oncologie Pediatrique, Hospices Civils de Lyon, Lyon, France; [8]Takeda Development Center Americas, Cambridge, MA, USA;
[9]Department of Pharmacy and Pharmacology, The Netherlands Cancer Institute-Antoni Van Leeuwenhoek Hospital, Amsterdam, the Netherlands;
[10]Department of Clinical Pharmacy, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands; [11]Zoé4Life, Sullens, Switzerland

*Shared first authors; †Shared last authors

Background, methods, and objectives

Background

ALK+ ALCL:

- Aggressive non-HL subtype
- *ALK*+ in >90% of pediatric cases[1]
- Promising efficacy of ALK inhibitors[2-5]

Brigatinib:

- Second-generation ALK inhibitor
- Approved for *ALK*+ NSCLC (7-day lead-in: 90 mg QD, followed by 180 mg QD)
- Good CNS penetration

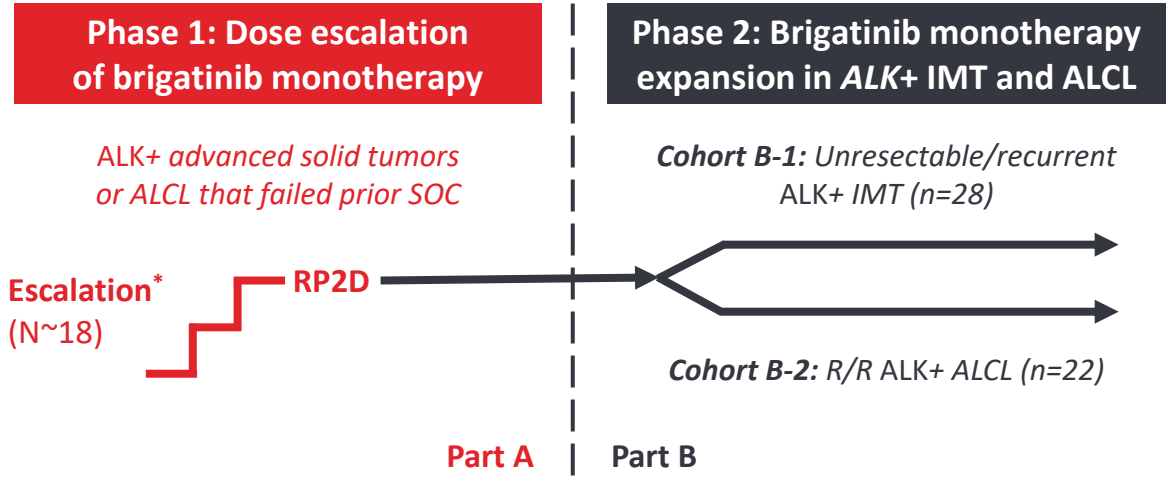
Methods[6]

STUDY DESIGN

Multicenter, nonrandomized, open-label Phase 1/2 trial, conducted in ITCC sites (NCT04925609; EUCT:2024-513412-10-00)

Key inclusion criteria (Phase 1)

- Aged 1–17 years
- R/R disease, including:
  - ALCL: 1L MRD positivity after first chemotherapy course
  - IMT: 1L metastatic and/or unresectable disease
- Previous treatment with other ALK TKIs allowed
- Adequate organ function/ clinical condition



OBJECTIVES

To assess the safety and efficacy of brigatinib monotherapy in children and adolescents with *ALK*+ malignancies, with a focus on†:

- *ALK*+ IMT
- *ALK*+ ALCL

Pharmacokinetics modeling/analysis and dose finding results from the study were presented at NVKFB 2025; *Maximum of three dose levels (rolling 6 design); †Study in the context of a Pediatric Investigation Plan

1L, first-line; ALCL, anaplastic large cell lymphoma; ALK, anaplastic lymphoma kinase; CNS, central nervous system; HL, Hodgkin lymphoma; IMT, inflammatory myofibroblastic tumor; ITCC, Innovative Therapies for Children and Adolescent Cancer; MRD, minimal residual disease; NSCLC, non-small cell lung cancer; NVKFB, Dutch Society for Clinical Pharmacology and Biopharmacy; QD, once daily; R/R, relapsed/refractory; RP2D, recommended Phase 2 dose; SOC, standard of care; TKI, tyrosine kinase inhibitor

1. Brugières L, et al. Blood 1998;92:3591-8; 2. Mossé YP, et al. J Clin Oncol 2017;35:3215-21; 3. Brugières L, et al. Eur J Cancer 2023;191:112984; 4. Fischer M, et al. Lancet Oncol 2021;22:1764-76;
5. Fukano R, et al. Cancer Sci 2020;111:4540-7; 6. Rigaud C, et al. ITCC Scientific Days 2025 [poster]

Baseline characteristics

BASELINE CHARACTERISTICS		PHASE 1 PATIENTS (N=10)
Median (range) age, years		9 (6–17)
ALCL, n (%)	Frontline MRD+	3 (30)
	Relapsed/refractory	6 (60)
Other *ALK*+ solid tumor,* n (%)		1 (10)
Previous LOT, median (range)		1 (1–5)
Previous treatment with ALK TKI, n (%)		3 (30)
Weight, n (%)	<18 kg	1 (10)
	18–40 kg	6 (60)
	>40 kg	3 (30)

Data cutoff: Jun 21, 2024. Pharmacokinetics modeling/analysis and dose finding results from the study were presented at NVKFB 2025

*Sarcoma NOS with *PLEKHH2*::*ALK* fusion

ALCL, anaplastic large cell lymphoma; ALK, anaplastic lymphoma kinase; ITCC, Innovative Therapies for Children and Adolescent Cancer; LOT, line of treatment; MRD, minimal residual disease; NOS, not otherwise specified; NVKFB, Dutch Society for Clinical Pharmacology and Biopharmacy; TKI, tyrosine kinase inhibitor

Rigaud C, et al. ITCC Scientific Days 2025 [poster]

Safety profile of brigatinib

ITCC Scientific Days 2025
Poster

Dose-limiting toxicities

10 patients were treated in the dose-escalation phase

- DL1 (n=4): no DLT
- DL2 (n=6): one DLT (Grade 3 neutropenia; >7 days, recovered after interruption and dose reduction)

Common TRAEs

AE,* n (%)	TOTAL (N=10)		DL1 (n=4)		DL2 (n=6)	
	GRADE 1/2	GRADE ≥3	GRADE 1/2	GRADE ≥3	GRADE 1/2	GRADE ≥3
CPK increased	6 (60)	2 (20)	2 (50)	1 (25)	4 (67)	1 (17)
Nausea/vomiting	7 (70)	0	2 (50)	0	5 (83)	0
Abdominal pain	6 (60)	0	2 (50)	0	4 (67)	0
Elevated AST/ALT	4 (40)	0	2 (50)	0	2 (33)	0

Ten patients received a median of 18 cycles (range 10–23)

Data cutoff: Jun 21, 2024. Pharmacokinetics modeling/analysis and dose finding results from the study were presented at NVKFB 2025

*Maximum AE grade per patient

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, Creatine phosphokinase; DL, dose level; DLT, dose-limiting toxicity; ITCC, Innovative Therapies for Children and Adolescent Cancer; NVKFB, Dutch Society for Clinical Pharmacology and Biopharmacy; TRAE, treatment-related adverse event

Rigaud C, et al. ITCC Scientific Days 2025 [poster]

Preliminary efficacy of brigatinib

Time on treatment and radiological response in Phase 1 population

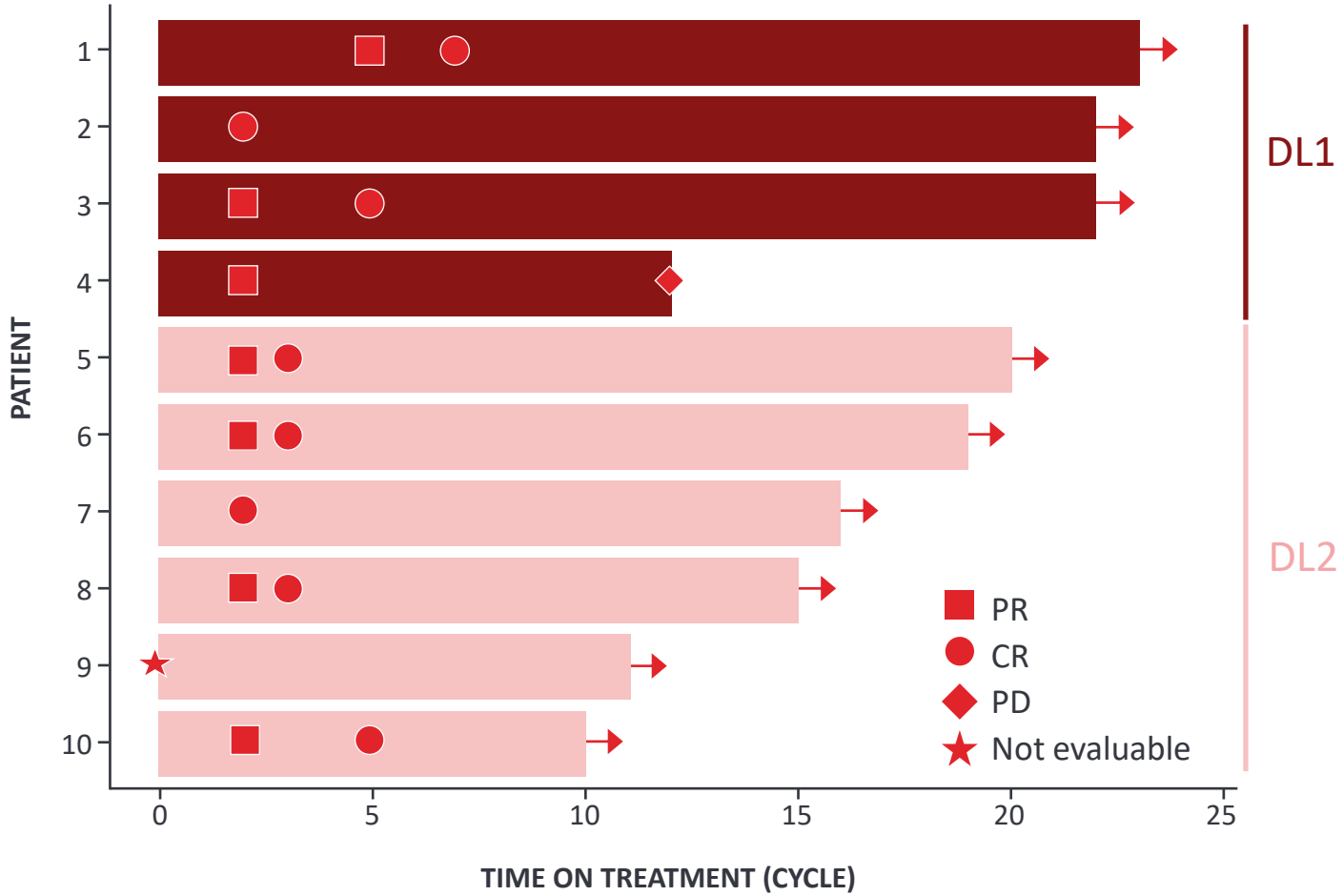
The ORR was 100%
(in nine evaluable patients)

- PR 11% (n=1; sarcoma)
- CR/CRu 89% (n=8; all ALCL)

MRD response in ALCL

Seven patients were MRD+ at screening

- Five patients were MRD− after one cycle
- Two patients became MRD− at a later timepoint



Data cutoff: Jun 21, 2024. Pharmacokinetics modeling/analysis and dose finding results from the study were presented at NVKFB 2025

ALCL, anaplastic large cell lymphoma; CR(u), complete response (unconfirmed); DL, dose level; ITCC, Innovative Therapies for Children and Adolescent Cancer; MRD, minimal residual disease; NVKFB, Dutch Society for Clinical Pharmacology and Biopharmacy; ORR, objective response rate; PD, progressive disease; PR, partial response

Rigaud C, et al. ITCC Scientific Days 2025 [poster]

Authors' conclusions

The RP2D was established at DL2, corresponding to 150 mg (≥18–40 kg) or 240 mg (≥40 kg) QD

Brigatinib monotherapy was well tolerated in children, with no signs of cumulative toxicity

Persistent responses were observed in pediatric patients with *ALK*+ ALCL

The Phase 2 part of the study is currently enrolling patients in two disease-specific cohorts for children and adolescents aged 1–26 years:

- *ALK*+ ALCL (n=22; enrollment completed)
- *ALK*+ IMT (n=28; enrollment ongoing)

A liquid formulation is expected to be implemented soon

Pharmacokinetics modeling/analysis and dose finding results from the study were presented at NVKFB 2025

ALCL, anaplastic large cell lymphoma; DL2, dose level 2; IMT, inflammatory myofibroblastic tumor; ITCC, Innovative Therapies for Children and Adolescent Cancer; NVKFB, Dutch Society for Clinical Pharmacology and Biopharmacy; QD, once daily; RP2D, recommended Phase 2 dose

Rigaud C, et al. ITCC Scientific Days 2025 [poster]

Investigator-initiated research

ASCO 2025
Poster #161

A window of opportunity study for preoperative brigatinib in resectable *ALK*+ NSCLC: WILDERNESS trial (NCT05361564)

Chang Gon Kim,[1] Min Hee Hong,[1] Jaehyung Kim,[1] Moonki Hong,[1] Hyo Sup Shim,[2] Mina Han,[1] Eun Young Kim,[3] Byung Jo Park,[4] Ha Eun Kim,[4] Young Ho Yang,[4] Tae Hee Hong,[4] Chang Young Lee,[4] Hye Ryun Kim[1]

[1]Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea;
[2]Department of Pathology, Yonsei University College of Medicine, Seoul, Republic of Korea;
[3]Division of Pulmonology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea;
[4]Department of Thoracic and Cardiovascular Surgery, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

Background, study design/population and radiologic tumor response

Although ALK TKIs are approved for patients with *ALK*+ recurrent and/or metastatic NSCLC or resected NSCLC, their role as neoadjuvant therapy in resectable NSCLC remains unclear[1]

STUDY DESIGN

Single-arm, open-label, Phase 2 trial evaluating neoadjuvant brigatinib in resectable *ALK*+ NSCLC, aiming to identify the molecular mechanisms underlying innate drug resistance in drug-tolerant persister cells in cancer (NCT05361564)[1,2]

Inclusion criteria[1,2]

- Aged ≥20 years
- Stage I to IIIB NSCLC, according to the AJCC 8th edition
- Documented *ALK* rearrangement
- Amenable to surgical resection
- ECOG PS 0 or 1

Neoadjuvant brigatinib 180 mg/d* → Operation → MRD assessment (6–8 weeks)

Median 45 days (range 38–64 days)

scRNAseq†

OUTCOMES:

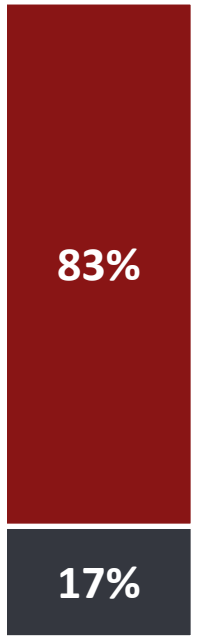
Molecular candidates from scRNAseq;
ORR; MPR rate; DFS; EFS; OS

Study population (N=12)[1]

Median age 49 years | 67% female | 92% ECOG PS 0 | 50% Stage IIIA/B

Radiologic tumor response[1]

ORR: 83%



- PR (n=10)
- Decreasing SD (n=2)

*Following a 7-day lead-in period at 90 mg/d; †Single-cell transcriptomic analyses were performed to characterize the tumor microenvironment according to the achievement of MPR

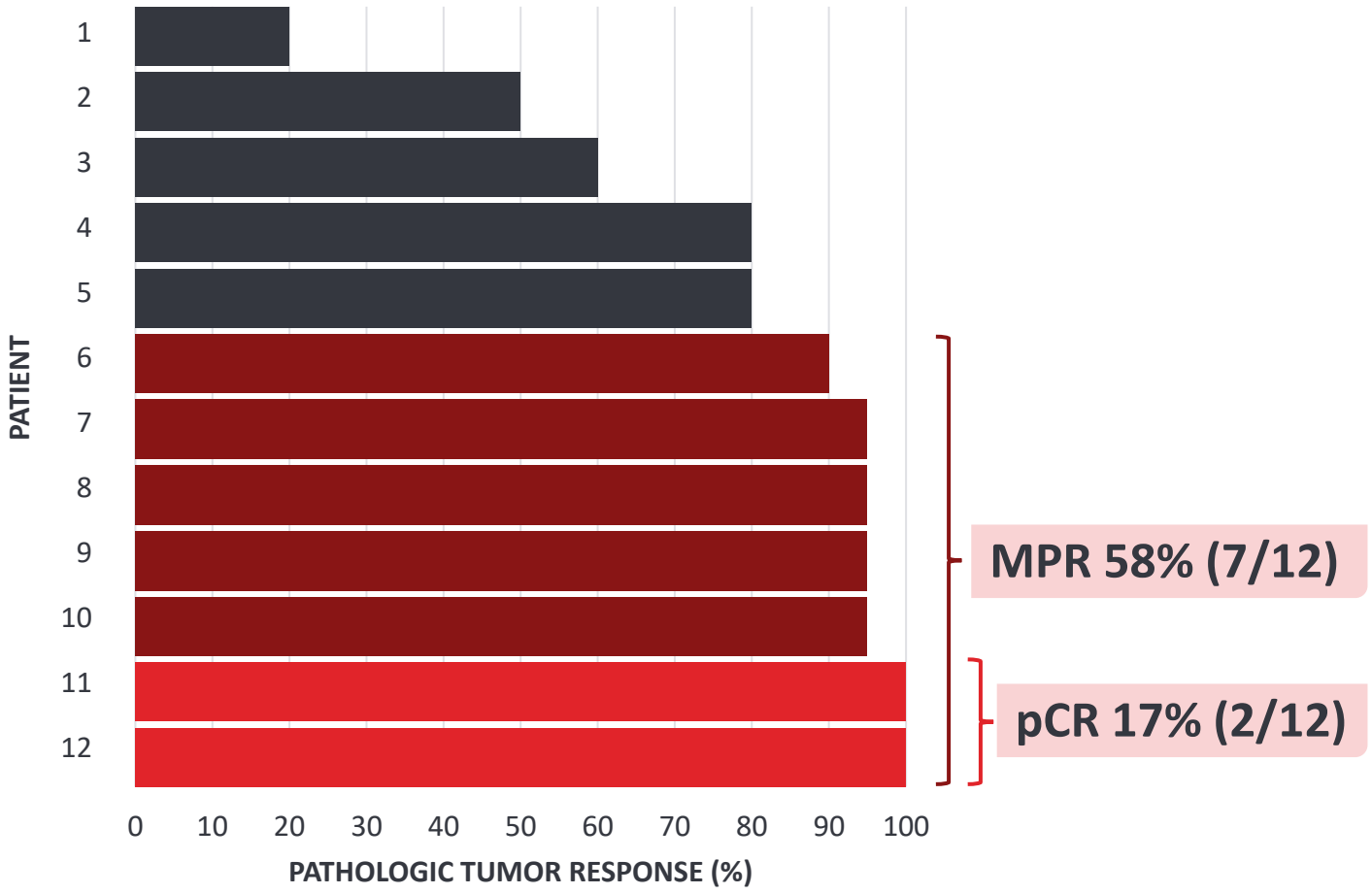
AJCC, American Joint Committee on Cancer; ALK, anaplastic lymphoma kinase; ASCO, American Society of Clinical Oncology; d, day; DFS, disease-free survival; EFS, event-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; MPR, major pathologic response; MRD, minimal residual disease; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PR, partial response; scRNAseq, single-cell RNA sequencing; SD, stable disease; TKI, tyrosine kinase inhibitor

1. Kim CG, et al. ASCO 2025 [poster #161]; see the abstract; 2. ClinicalTrials.gov, NCT05361564 (accessed May 2025)

Pathologic tumor response and safety profile

ASCO 2025
Poster #161

Pathologic tumor response



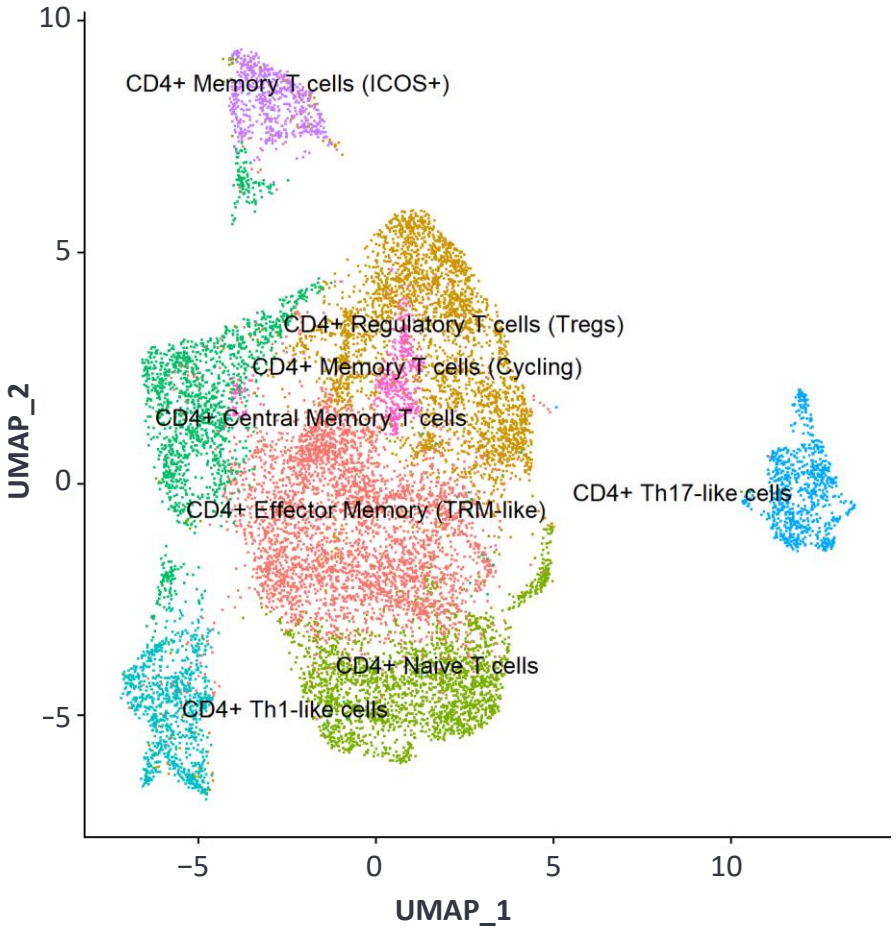
Safety profile

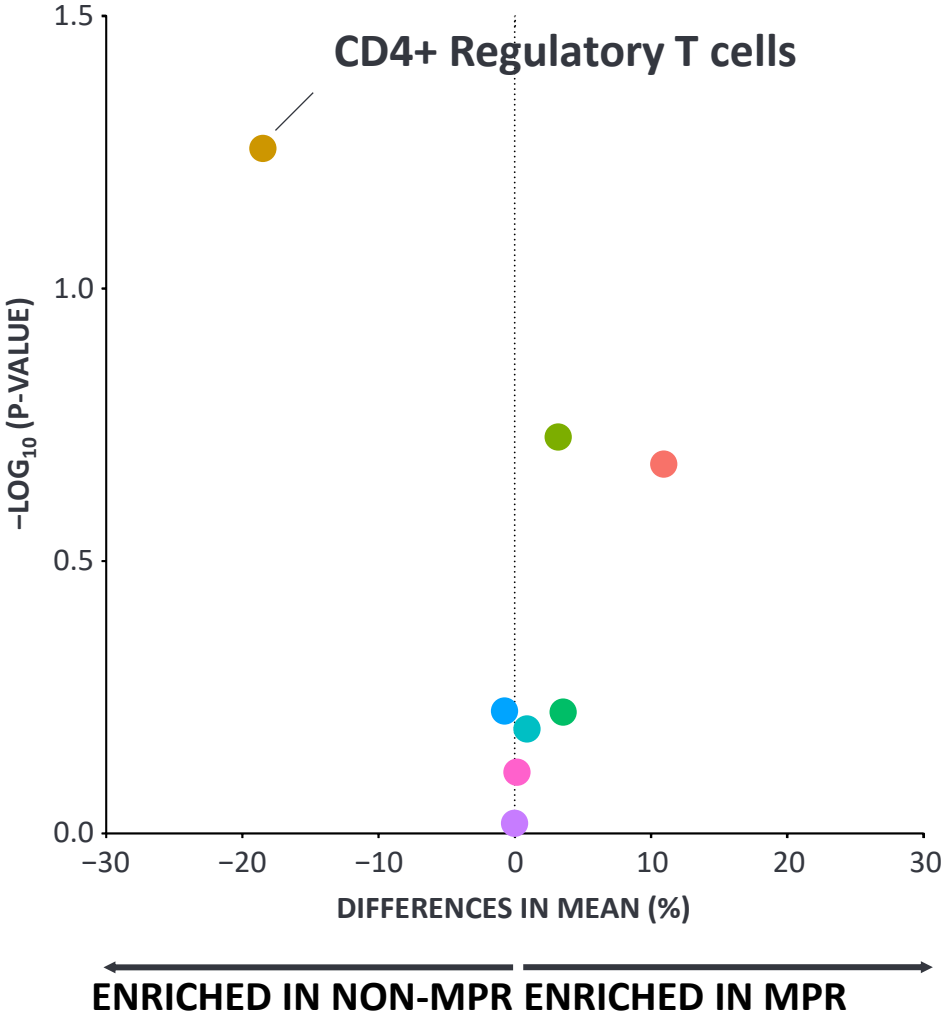
ADVERSE EVENTS, n	ANY GR	GR 1	GR 2	GR 3	GR 4
Any adverse events	12	7	4	1	0
CPK increased	6	3	2	1	0
Cough	3	2	1	0	0
ALT increased	2	2	0	0	0
Amylase increased	2	2	0	0	0
AST increased	2	1	1	0	0
Headache	2	1	1	0	0
Dizziness	1	1	0	0	0
Dyspepsia	1	1	0	0	0
Dyspnea	1	0	1	0	0
Fever	1	1	0	0	0
Hypertension	1	1	0	0	0
Nausea	1	1	0	0	0
Vomiting	1	1	0	0	0

ALT, alanine aminotransferase; ASCO, American Society of Clinical Oncology; AST, aspartate aminotransferase; CPK, creatine phosphokinase; GR, Grade; MPR, major pathologic response; pCR, pathologic complete response

Kim CG, et al. ASCO 2025 [poster #161]; see the abstract

Single cell transcriptomic analysis for tumor-infiltrating CD4+ T cells





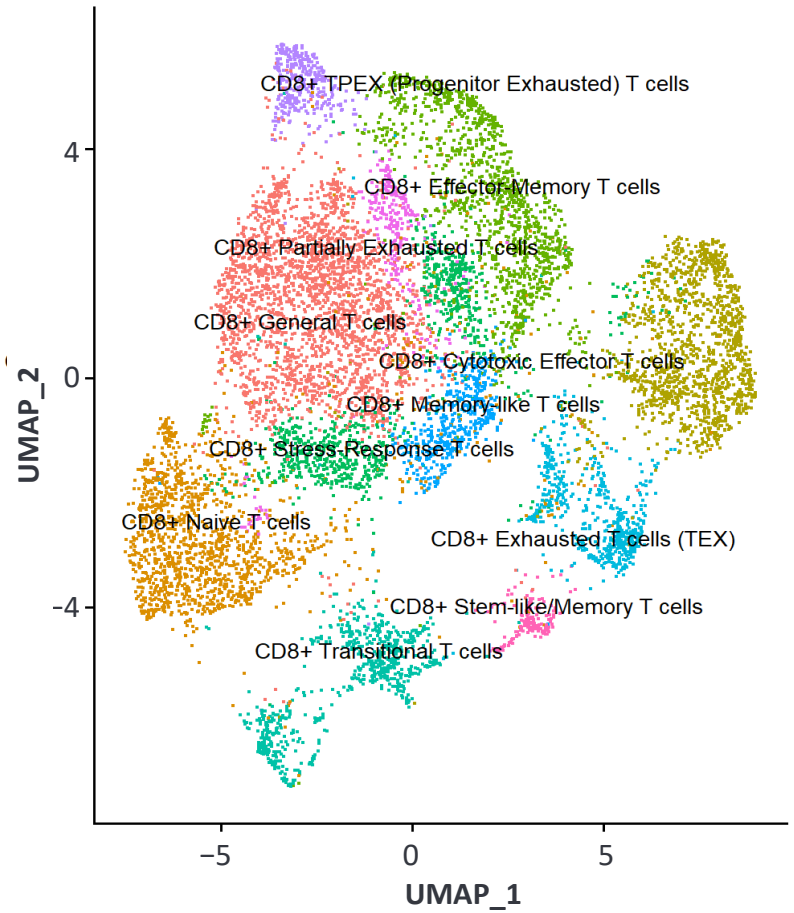
CD4+ T cell type

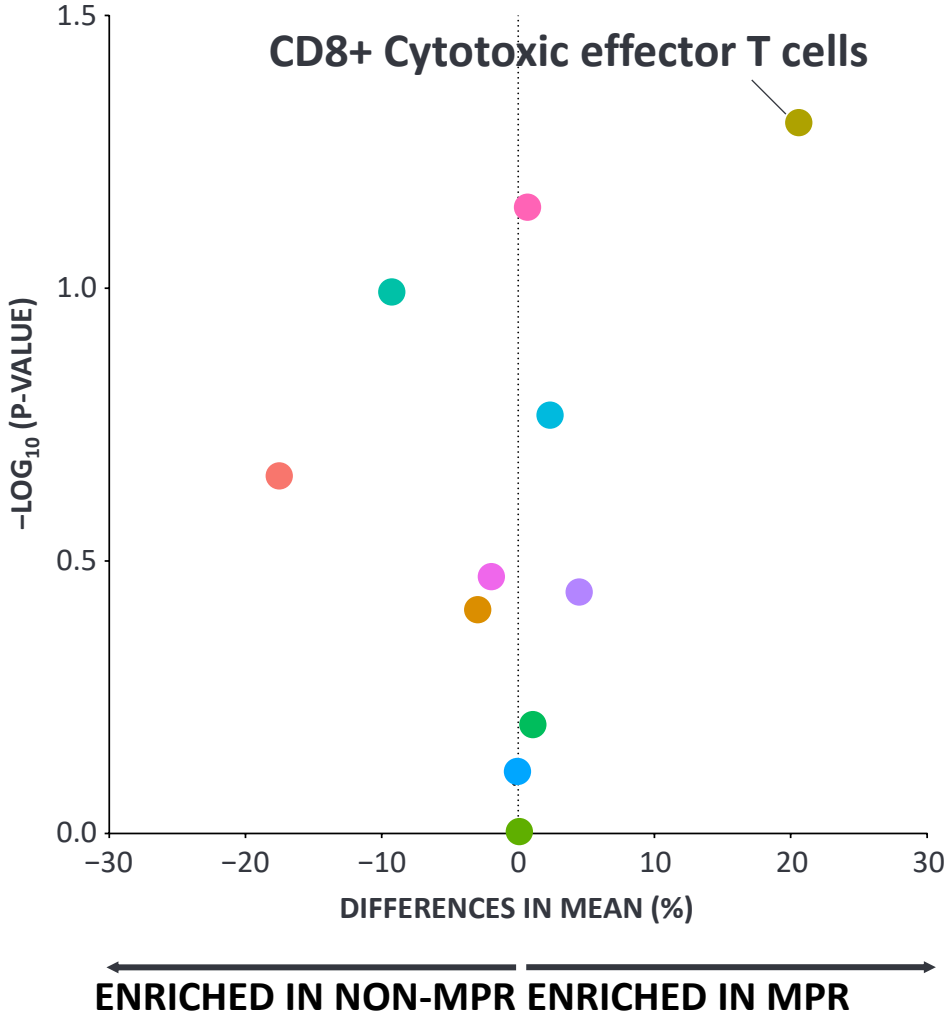
- Effector memory (TRM-like)
- Regulatory T cell
- Naive T cell
- Central memory T cell
- Th1-like cell
- Th17-like cell
- Memory T cell (ICOS+)
- Memory T cell (cycling)

ASCO, American Society of Clinical Oncology; CD, cluster of differentiation; ICOS, inducible costimulator; MPR, major pathologic response; TRM, tissue resident memory; UMAP, uniform manifold approximation and projection

Kim CG, et al. ASCO 2025 [poster #161]; see the abstract

Single cell transcriptomic analysis for tumor-infiltrating CD8+ T cells





CD8+ T cell type

- General T cell
- Naive T cell
- Cytotoxic effector T cell
- Effector-memory T cell
- Stress-response T cell
- Transitional T cell
- Exhausted T cell
- Memory-like T cell
- Progenitor exhausted T cell
- Partially exhausted T cell
- Stem-like/memory T cell

ASCO, American Society of Clinical Oncology; CD, cluster of differentiation; MPR, major pathologic response; UMAP, uniform manifold approximation and projection

Kim CG, et al. ASCO 2025 [poster #161]; see the abstract

Authors' conclusions

Neoadjuvant brigatinib was effective and safe in patients with resectable *ALK*+ NSCLC

Single-cell transcriptomic analysis demonstrated the balance between effector and regulatory T cells as a critical determinant of pathologic response and the clearance of drug-tolerant and persister cancer cells

ASCO, American Society of Clinical Oncology; NSCLC, non-small cell lung cancer
Kim CG, et al. ASCO 2025 [poster #161]; see the abstract