Brilliant first analysis: A real-world study of characteristics and safety about brigatinib as first-line for Chinese patients with *ALK*+ NSCLC

POSTER #492

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Background

- Brigatinib is a next-generation tyrosine kinase inhibitor with potent activity against anaplastic lymphoma kinase (*ALK*) and high central nervous system penetration.[1,2]
- In the phase 3 ALTA-1L study (NCT02737501), brigatinib was the first ALK inhibitor that exhibited superior efficacy, tolerability, and significantly improved health-related quality of life than crizotinib in patients with *ALK*-positive (*ALK*+) locally advanced or metastatic non-small cell lung carcer (NSCLC) (depth of response [>75% tumor shrinkage]: 56% vs 34%; complete response: 24% vs 13%).[2-4] Subsequent analysis revealed a median real-world progression-free survival 2 of 74.7 months with first-line (1L) brigatinib followed with lorlatinib.[5]
- Brigatinib has been recommended by authoritative guideline as a preferred choice for 1L treatment in *ALK*+ NSCLC patients.[6]
- There is a lack of real-world data of brigatinib as a 1L therapy and subsequent treatment patterns in the Chinese population.

Objectives

- The aim is to better understand the real-world practice of brigatinib in 1L for Chinese patients with *ALK*+ locally advanced or metastatic NSCLC.

Results

Patient characteristics

- By June 30, 2024, 82 patients were enrolled with a median follow-up of 3.96 months (**Table 1**).
- The median age was 55.5 years (range, 28-80) (**Table 1**).
- 6 patients (7.3%) were at stage Ⅲ and 76 patients (92.7%) at stage Ⅳ. 76 patients (92.7%) were reported having ≥ 2 metastatic sites (**Table 1**).

Table 1. Baseline characteristics

Characteristic	Brigatinib N=82
Median age, years (range)	55.5 (28-80)
Median follow-up time, months	3.96
Median duration of medication, months	4.57
Duration from diagnosis of locally advanced or metastatic NSCLC to first treatment of brigatinib, days	
N	81
Median	9
Min, max	2, 112
Median duration from diagnosis of *ALK*+ to first treatment of brigatinib, days	
N	82
Median	5
Min, max	1, 1704*
Female, n (%)	50 (61.0%)
ECOG performance status, n (%)	
0	8 (9.8)
1	22 (26.8)
2	2 (2.4)
Unknown	50 (61.0)
Smoking history, n (%)	
Never smoked	25 (30.5)
Former smoker	18 (22.0)
Current smoker	2 (2.4)
Unknown	37 (45.1)

Characteristic	Brigatinib N=82
cTNM Stage (at trial entry), n (%)	
Ⅲ	6 (7.3)
ⅢA	3 (50.0)
ⅢC	3 (50.0)
Ⅳ	76 (92.7)
ⅣA	16 (21.1)
ⅣB	30 (39.5)
Unknown	30 (39.5)
Metastatic site, n (%)	
1	6 (7.3)
2	26 (31.7)
3	22 (26.8)
4	18 (22.0)
5	8 (9.8)
>5	2 (2.4)
Histologic type, n (%)	
Adenocarcinoma	67 (81.7)
Squamous-cell carcinoma	1 (1.2)
Unknown	14 (17.1)
ALK testing, n (%)	
FISH	1 (1.2)
PCR	21 (25.6)
IHC	26 (31.7)
NGS	29 (35.4)
Unknown	5 (6.1)

Characteristic	Brigatinib N=82
EML4-ALK fusion, n (%)	
V1	8 (9.8)
V2	2 (2.4)
V3	11 (13.4)
V5	2 (2.4)
Other	13 (15.9)
Unknown	46 (56.1)
T (before first treatment of brigatinib), n (%)	
Tx	5 (6.1)
T0	0
Tis	0
T1	12 (14.6)
T1a	0
T1b	1 (1.2)
T1c	2 (2.4)
T2	16 (19.5)
T2a	3 (3.7)
T2b	0
T3	14 (17.1)
T4	29 (35.4)
N (before first treatment of brigatinib), n (%)	
Nx	2 (2.4)
N0	6 (7.3)
N1	4 (4.9)
N2	23 (28)
N3	47 (57.3)

Characteristic	Brigatinib N=82
M (before first treatment of brigatinib), n (%)	
Mx	0
M0	6 (7.3)
M1	27 (32.9)
M1a	14 (17.1)
M1b	4 (4.9)
TP53 status, n (%)	
Mutant	6 (7.3)
Wild type	2 (2.4)
Unknown	74 (90.2)
Brain metastases, n (%)	
Yes	24 (29.3)
No	58 (70.7)
Previous radiotherapy to brain, n (%)	
Yes	3 (12.5)
No	21 (87.5)
Previous treatment	
Chemotherapy	8 (9.8)
Chemotherapy + VEGFRi	5 (6.1)
No	70 (85.4)

*Three patients with resectable early-stage NSCLC had a duration of more than one year

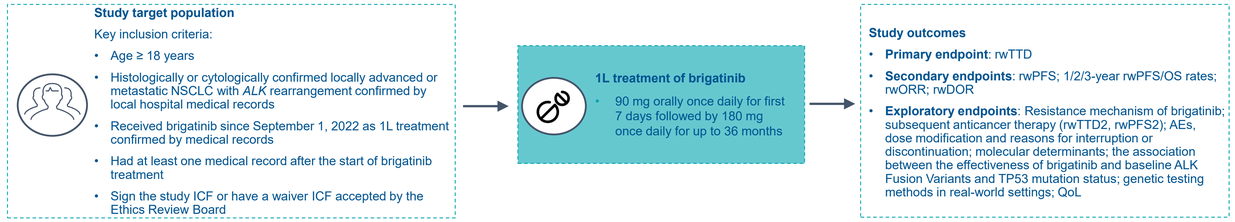
ALK, anaplastic lymphoma kinase; ECOG, Eastern Cooperative Oncology Group; EML4, echinoderm microtubule-associated protein-like 4; FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; N, number of patients; n (%), number and percentage of patients in a specific category; NGS, next-generation sequencing; NSCLC, non-small cell lung carcer; PCR, polymerase chain reaction; TNM, tumor, node, metastasis; TP53, tumor protein 53; VEGFRi, vascular endothelial growth factor receptor inhibitor

Methods

Study design and patients

- The Brilliant study is an ambispective, single arm, observational (retrospective + prospective), multi-center real-world study from 2022 to 2029 (NCT05721950) (**Figure 1**).

Figure 1. Study design



1L, first-line; AEs, adverse events; ALK, anaplastic lymphoma kinase; ICF, informed consent form; NSCLC, non-small cell lung carcer; OS, overall survival; QoL, quality of life; rwDOR, real-world duration of response; rwORR, real-world objective response rate; rwPFS, real-world progression-free survival; rwTTD, real-world time-to-treatment discontinuation

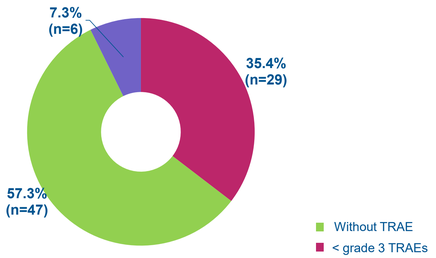
Statistical analyses

- Safety assessments included monitoring treatment-related adverse events (TRAEs), dose modification, and treatment interruption or discontinuation.
- Data analysis will utilize Kaplan-Meier methods for survival curves, the Brookmeyer Crowley method for confidence intervals, and descriptive statistics for baseline characteristics and quality of life assessments.

Safety

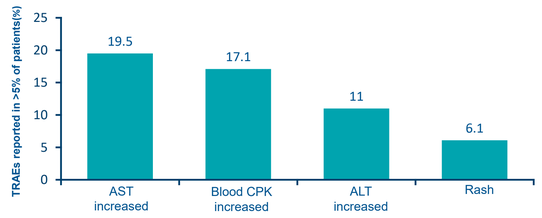
- 82 patients were included in the safety analysis. 51.2% (42 patients) were reported treatment-emergent adverse events.
- Any grade and ≥ grade 3 TRAEs were reported in 35 patients (42.7%) and 6 patients (7.3%) of patients, respectively (**Figure 2**).
- TRAEs leading to dose modification and interruption occurred in 4 (4.9%) and 3 (3.7%) patients, respectively.
- Any grade TRAEs > 5% included increased aspartate aminotransferase (19.5%), increased blood creatine phosphokinase (17.1%), increased alanine aminotransferase (11%), and rash (6.1%) (**Figure 3**).

Figure 2. Overview of TRAEs



n, number of patients in a specific category; TRAEs, treatment-related adverse events

Figure 3. TRAEs reported in >5% of patients



ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; TRAEs, treatment-related adverse events

Conclusions

- The real-world baseline characteristics and safety profile of patients with *ALK*+ locally advanced or metastatic NSCLC treated with brigatinib as 1L therapy in China align with the results of phase 3 ALTA-1L study.
- Patients with locally advanced stage ⅢA and ⅢC received brigatinib treatment in real-world clinical practice.
- This first analysis shows better tolerability of brigatinib in real-world clinical practice, with lower rates of dose modification and interruption than in the ALTA-1L study.
- Real-world effectiveness and post-treatment will continue to be evaluated.

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