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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 (CNS) penetration for patients with locally advanced/ metastatic *ALK*-positive non-small cell lung cancer (NSCLC)^{1,2}.
- The phase III ALTA-1L trial established brigatinib as an effective first-line treatment for *ALK*-positive advanced NSCLC, supporting its FDA approval in 2020³.
- It is recommended as a preferred first-line treatment in NCCN and CSCO guidelines^{4,5}.
- Real-world evidence for brigatinib as a first-line treatment in the Chinese population remains limited.

Objectives

- To evaluate the real-world effectiveness and safety of first-line brigatinib in Chinese patients with *ALK*-positive locally advanced or metastatic NSCLC and to assess its clinical performance in routine practice.

Methods

- Study Design:** Ambispective (retrospective and prospective), multicenter, non-interventional real-world study conducted across 21 sites in China.
- Clinical Trial Identifier:** NCT05721950
- Inclusion Criteria:** Adults with *ALK*-positive locally advanced or metastatic NSCLC who initiated first-line brigatinib from September 2022 onward.
- ALK* positivity was confirmed using validated testing methods, including IHC, FISH, or NGS.

Results

Data cutoff: August 29, 2025

Patient Characteristics:

In the full analysis set (FAS) population, 154 patients were included, and in the efficacy analysis set (EAS) population, 137 patients were included.

The median age was 55.0 years (range: 28–80), with a median follow-up duration of 14.0 months (range: 0.2–34.5; IQR: 9.1-18.4).

The mean (SD) with median (Q1, Q3) time to brigatinib initiation was:

- From NSCLC diagnosis to brigatinib: 69.9 (268.36) with 14.0 (7.0, 22.0) days
- From advanced/metastatic NSCLC diagnosis to brigatinib: 28.0 (125.91) with 11.0 (5.0, 18.5) days
- From first *ALK*-positive status to brigatinib: 44.8 (204.13) with 5.0 (3.0, 12.0) days

Characteristic	Category	n (%)
Gender	Female	82 (53.2)
	Male	72 (46.8)
Disease Stage at Baseline	Stage III	18 (11.7)
	Stage IV	136 (88.3)
Number of Brain Lesions (n=39)	1 lesion	22 (56.4)
	2 lesions	2 (5.1)
	3 lesions	2 (5.1)
	Other	12 (30.8)
	Missing	1 (2.6)
Co-mutations	Present	64 (41.6)
<i>ALK</i> Status	<i>ALK</i> -positive	154 (100.0)
<i>ALK</i> Fusion	Any <i>ALK</i> fusion	142 (92.2)
EML4- <i>ALK</i> Fusion Subtype (n=116)	V1	27 (23.3)
	V2	6 (5.2)
	V3	26 (22.4)
	V5	2 (1.7)

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Disclosures

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Question

How effective and safe is first-line brigatinib in routine practice for Chinese patients with *ALK*-positive locally advanced or metastatic NSCLC?

Study design

Population

Adult with *ALK*+ve locally advanced or metastatic NSCLC

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1L Brigatinib Treatment

90mg orally QD for first 7 days followed by 180mg orally QD

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Analysis Sets

Full Analysis Set (n=154)
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Efficacy Analysis Set (n=137)

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Primary Endpoint

rwTTD

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Secondary Endpoint

• rwPFS and rwOS
• 1-, 2-year rwPFS and OS rates
• rwORR and rwDOR
• rwTTD2 and Safety

Results

Figure 1A: 1-Year rwPFS Rate by Brain Metastasis Status

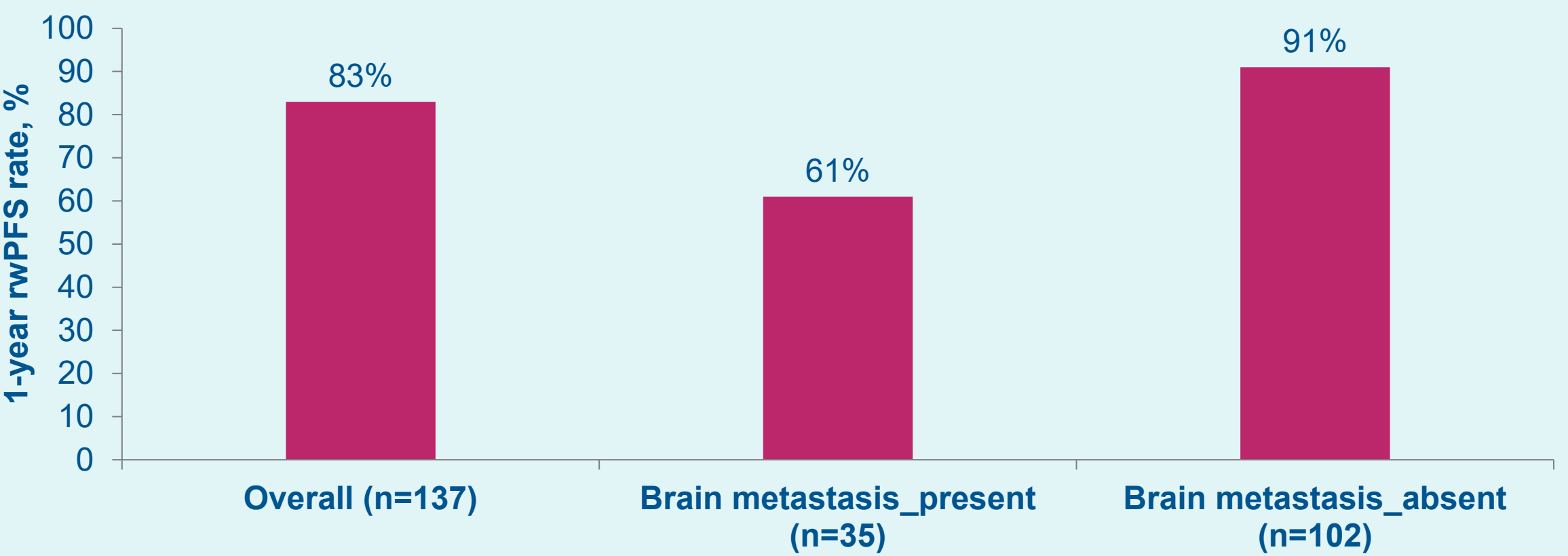


Figure 1B: 2-Year rwPFS Rate by Brain Metastasis Status

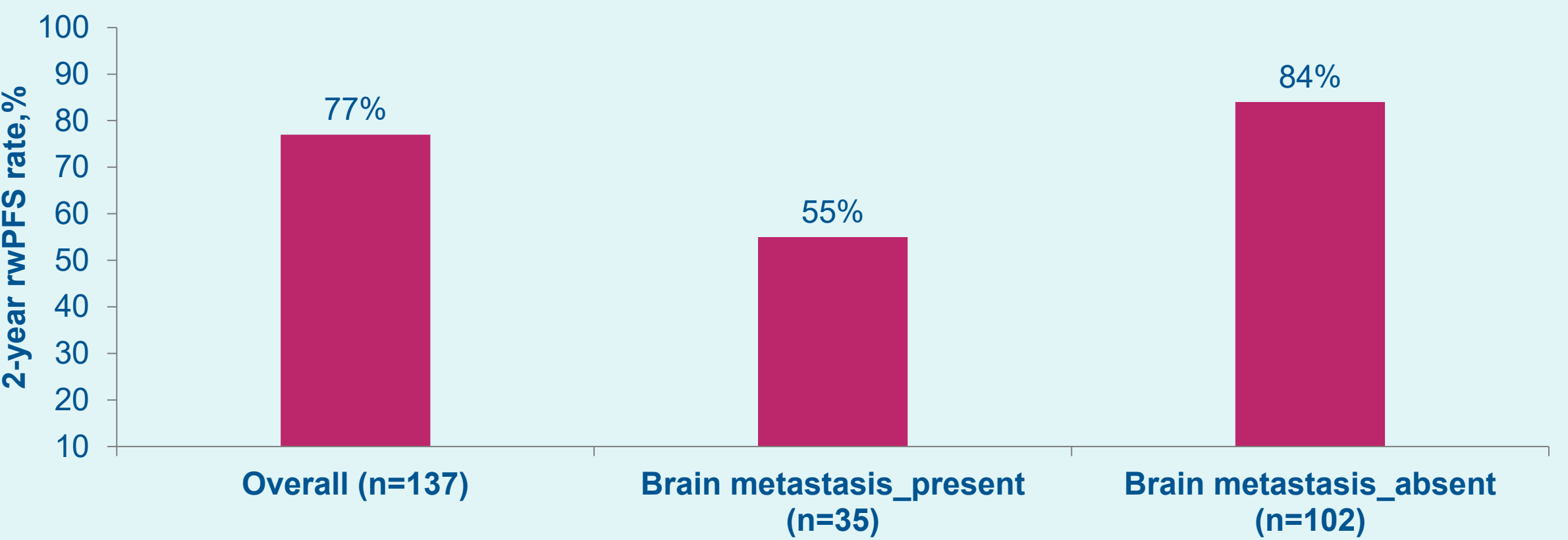


Figure 1C: 1-Year rwPFS Rate by Age

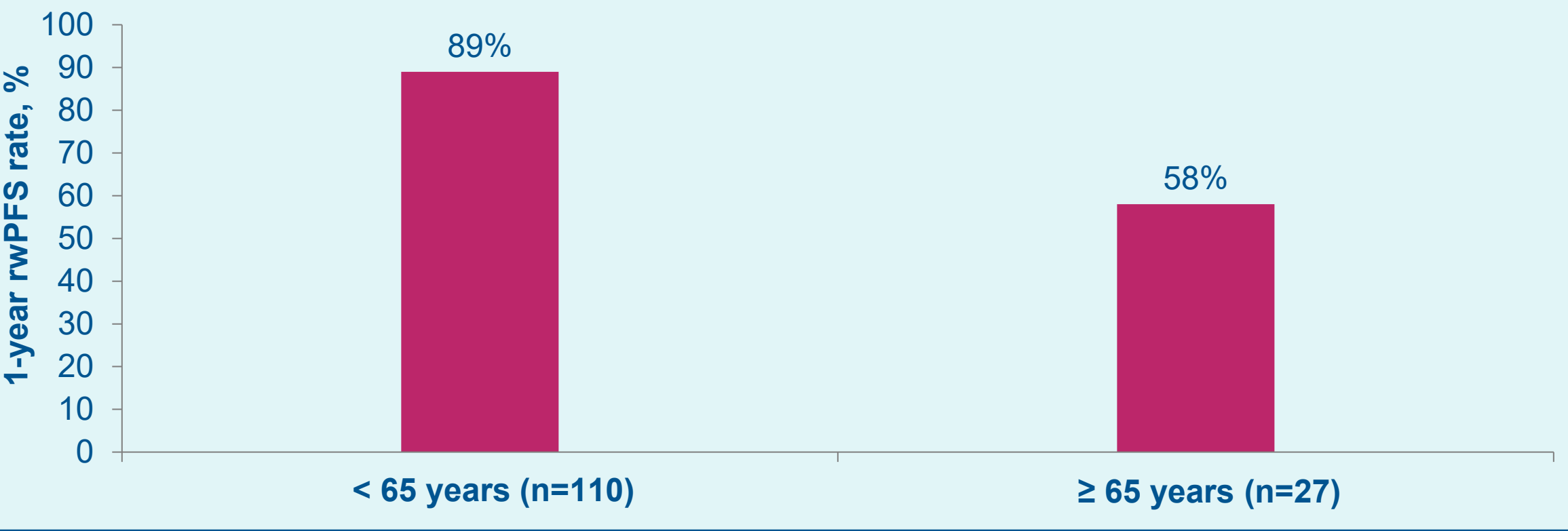
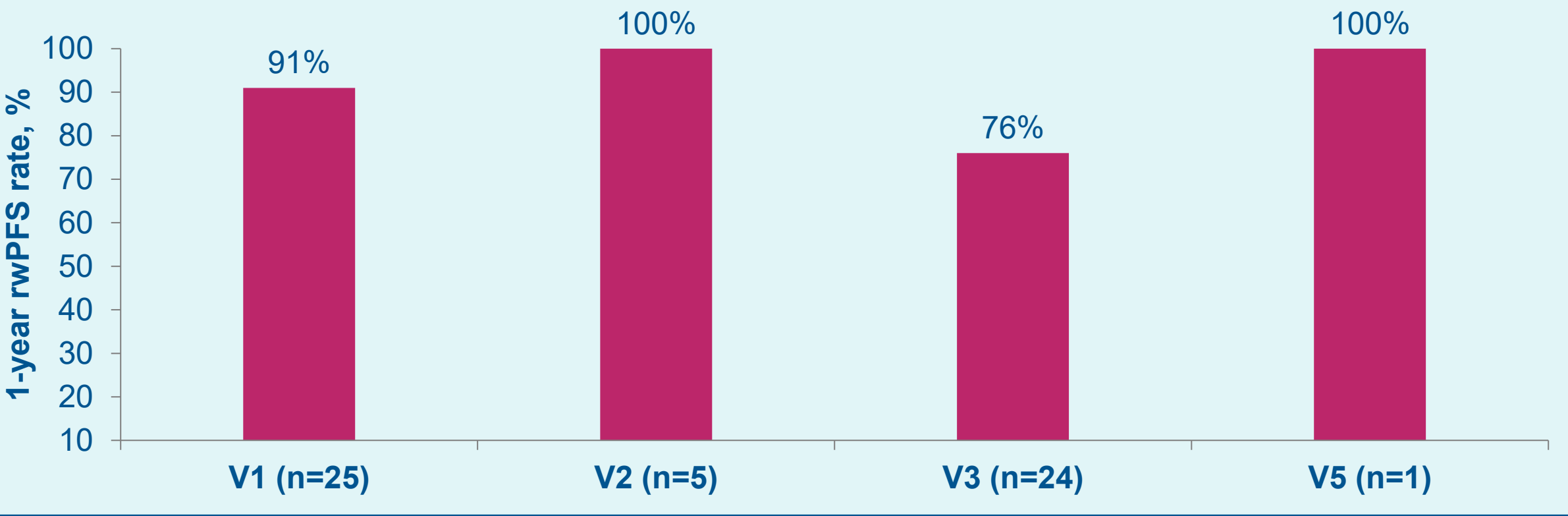


Figure 1D: 1-Year rwPFS Rate by EML4-ALK Gene Subtype



Key Takeaways

First-line brigatinib showed durable real-world effectiveness and favorable safety, with median rwTTD not reached, median rwPFS of 28.78 months, and 1- and 2-year rwPFS rates of 83% and 77%, supporting sustained long-term disease control in Chinese patients.

Table 2: Effectiveness Data of Brilliant Study

Effectiveness	rwTTD, months, median (95% CI)	rwPFS, months, median (95% CI)	1-year rwPFS rate, % (95% CI)	2-year rwPFS rate, % (95% CI)
Overall (n=137)	NR (28.78, NR)	28.78 (28.78, NR)	83% (0.73, 0.90)	77% (0.64, 0.86)
TP53 mutation status				
TP53 mutation (n=14)	NR (10.91, NR)	NR (9.46, NR)	81% (0.44, 0.95)	NR (NR, NR)
TP53 WT (n=10)	NR (0.16, NR)	NR (NR, NR)	100% (1.00, 1.00)	NR (NR, NR)
Metastatic sites				
1-3 (n=91)	NR (NR, NR)	NR (NR, NR)	85% (0.73, 0.92)	83% (0.70, 0.91)
4-5 (n=27)	28.78 (13.11, NR)	28.78 (11.24, NR)	74% (0.48, 0.88)	54% (0.23, 0.78)
>5 (n=2)	NR (0.16, NR)	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
Co-mutation				
Present (n=54)	NR (20.99, NR)	NR (NR, NR)	88% (0.71, 0.95)	84% (0.66, 0.93)

Table 3: Effectiveness Data of Brilliant Study Across Patient Subgroups

Outcome	Overall (N=137)	Brain Metastases (N=35)	No Brain Metastases (N=102)
rwOS	NR	NR	NR
rwORR (CR+PR)	56.9% (78/137)	45.7% (16/35)	60.8% (62/102)
rwDOR	28.09 months (NR, NR)	28.09 (8.48, NR)	NR
rwTTD2*	NR (12.19, NR)	—	—

*First Sequential Therapy Analysis Set (n = 30)
rwTTD2 was defined as the time from initiation of brigatinib to discontinuation of the first subsequent systemic anticancer therapy or death due to any reason, including disease progression, death, serious AEs, or patient preference

Table 4: Effectiveness Data Across EML4-*ALK* V3 & TP53 Mutation Subgroups

Outcome	rwOS, median (95% CI)
EML4- <i>ALK</i> V3 fusion subtype	18.30 (18.30, NR)
TP53 mutation	18.30 (18.30, NR)

Table 5: Safety Data of Brilliant Study

Category	Brigatinib, n (%)
No. of subjects with ≥1 TEAE	103 (66.9%)
Treatment-related TEAEs	86 (55.8%)
Serious adverse events (SAE)	10 (6.5%)
Treatment-related SAE	6 (3.9%)
TEAE leading to permanent treatment discontinuation	10 (6.5%)
TEAEs	
Grade ≥3	24 (15.6%)
Leading to treatment interruption	7 (4.5%)
Leading to dose reduction	14 (9.1%)
Treatment-related TEAEs, n (%)	
Grade ≥ 3	20 (13.0%)
Leading to treatment interruption	7 (4.5%)
Leading to dose reduction	13 (8.4%)
Elevated aspartate aminotransferase	38 (24.7%)
Elevated serum creatine phosphokinase	37 (24.0%)
Elevated alanine aminotransferase	31 (20.1%)
Elevated blood lactate dehydrogenase	23 (14.9%)
Elevated serum creatinine	13 (8.4%)

- Less frequent TRAEs included hyperuricemia (4.5%), hyperglycemia (3.9%), respiratory, chest, and mediastinal disorders (3.9%), increased markers of myocardial necrosis (2.6%), interstitial lung disease (2.6%), elevated LDL cholesterol (1.9%), and rapid breathing (0.6%).

Conclusions

- Durable real-world effectiveness** of first-line brigatinib in Chinese patients with *ALK*-positive advanced NSCLC.
- Clinical benefit observed across subgroups**, including patients with baseline brain metastases.
- Favorable and predictable safety profile**, with low rates of severe treatment-related adverse events (TRAEs) and treatment discontinuation.
- Supports the long-term use** of brigatinib as a first-line treatment in Chinese patients with *ALK*-positive advanced NSCLC.