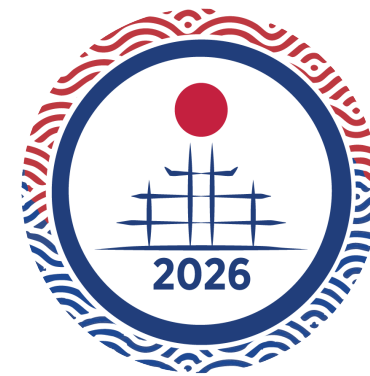


Real-World Outcomes of Polish Patients with ALK-Positive NSCLC Treated with Brigatinib: 1-Year Results (ENTIRETY Study)

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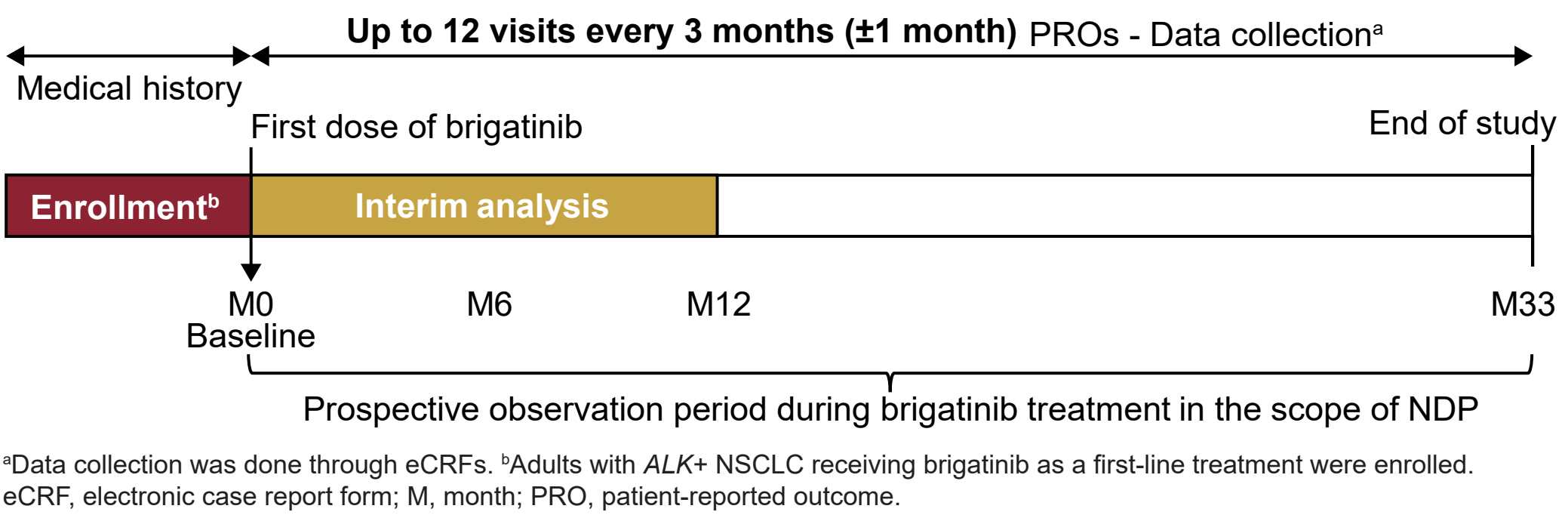
INTRODUCTION

- Non small cell lung cancer (NSCLC) accounts for over 85% of lung cancer cases^{1,2}
 - Anaplastic lymphoma kinase (*ALK*) gene rearrangement occurs in 4.5% of NSCLC cases and is associated with an increased risk of metastases into the central nervous system (CNS)³
- Brigatinib, a next-generation *ALK* tyrosine kinase inhibitor (TKI), demonstrated enhanced efficacy vs crizotinib, a first-generation TKI, in *ALK*-TKI-naïve patients with advanced/metastatic *ALK*-positive (*ALK*+) NSCLC in the global phase III ALTA-1L trial⁴⁻⁶
- However, real-world evidence on the safety and effectiveness of brigatinib in Polish patients with *ALK*+ NSCLC is limited
- Thus, the overall objective of the study was to evaluate the real-world effectiveness of brigatinib as a first-line treatment in patients with *ALK*+ NSCLC in Poland

METHODS

- ENTIRETY (NCT05735327), a prospective, multicenter, noninterventional, open-label study, enrolled TKI-naïve patients (aged ≥18 years) with *ALK*+ NSCLC in Poland receiving brigatinib as first-line therapy in the scope of the National Drug Program (NDP; **Figure 1**)
 - This prespecified interim analysis covered a 12-month observation period for each patient (between May 2023 and July 2025) following treatment initiation

Figure 1: ENTIRETY study design



*Data collection was done through eCRFs. *Adults with *ALK*+ NSCLC receiving brigatinib as a first-line treatment were enrolled. eCRF, electronic case report form; M, month; PRO, patient-reported outcome.

Interim analysis outcomes

- Primary endpoint: Real-world progression-free survival (PFS) from the time of the first dose of brigatinib
- Secondary endpoints: Real-world overall survival (OS) and overall response rate (ORR)
- Exploratory endpoints: Safety, real-world intracranial PFS (iPFS), and quality of life (QoL) assessed by EuroQol 5-Dimension 5-Level (EQ-5D-5L) utility score, EQ-5D-5L Visual Analog Scale (VAS), and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)

DISCUSSION AND CONCLUSION

- First-line brigatinib treatment demonstrated effectiveness across real-world PFS, iPFS, ORR, and OS outcomes over the 12-month observation period, with no new safety signals observed
 - These findings were independent of baseline CNS metastases
- Health-related QoL significantly improved from baseline to Month 12
- The rate of real-world PFS was slightly lower than that observed in the ALTA-1L study at 12 months,⁴ which may be attributed to the differences in patient populations
 - Most patients (61.5%) in the ENTIRETY study were current or former smokers vs 39% of patients in the ALTA-1L study⁴
 - All patients in the ENTIRETY study were Caucasian; 43% of patients in the ALTA-1L study were Asian⁴

Interim analysis results of the ENTIRETY study demonstrated sustained effectiveness and safety of first-line brigatinib in Polish patients with *ALK*+ NSCLC in the real-world setting

RESULTS

Baseline characteristics

- Of the 52 patients enrolled (May 2023–July 2024), 27 completed the 12-month visit; 25 discontinued owing to lack of effectiveness (n=10), death (n=8), adverse events (AEs; n=5), and other reasons (n=2)
- Most patients (61.5%) smoked or had a smoking history; all were Caucasians
- At baseline, 9 patients (17.3%) had CNS metastases
 - Baseline characteristics were generally comparable between those with and without CNS metastases (**Table 1**)

Table 1: Baseline patient demographics and disease characteristics

	Overall (n=52)	With CNS metastases (n=9)	Without CNS metastases (n=43)
Age, median (Q1, Q3), years	63 (56.8, 70.2)	51 (44.0, 60.0)	64 (58.0, 71.5)
Male	32 (61.5)	3 (33.3)	29 (67.4)
Smoking status			
Smoked or with smoking history	32 (61.5)	5 (55.6)	27 (62.8)
Did not smoke	20 (38.5)	4 (44.4)	16 (37.2)
BMI, mean (SD), kg/m ²	26.0 (5.2)	25.9 (7.0)	26.0 (4.8)
Caucasian	52 (100.0)	9 (100.0)	43 (100.0)
Time from diagnosis, mean (SD), months	8.0 (15.8)	6.5 (9.2)	8.3 (16.9)
ALK gene rearrangement detection method			
FISH	12 (23.1)	4 (44.4)	8 (18.6)
NGS	21 (40.4)	1 (11.1)	20 (46.5)
IHC	19 (36.5)	4 (44.4)	15 (34.9)
ECOG grade			
0	14 (26.9)	4 (44.4)	10 (23.3)
1	30 (57.7)	3 (33.3)	27 (62.8)
≥2	8 (15.4)	2 (22.2)	6 (14.0)
Disease stage at screening			
≤3	7 (13.5)	0 (0.0)	7 (16.3)
4A	13 (25.0)	2 (22.2)	11 (25.6)
4B	32 (61.5)	7 (77.8)	25 (58.1)
Disease localization			
Liver	14 (26.9)	2 (22.2)	12 (27.9)
Bones	18 (34.6)	3 (33.3)	15 (34.9)
Other	24 (46.2)	2 (22.2)	22 (51.2)
Previous therapy			
Radiotherapy	14 (26.9)	5 (55.6)	9 (20.9)
Chemotherapy, as part of radical treatment	8 (15.4)	2 (22.2)	6 (14.0)

Data are presented as n (%) unless otherwise specified.
ALK, anaplastic lymphoma kinase; BMI, body mass index; CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; NGS, next-generation sequencing; Q, quartile; SD, standard deviation.

Survival outcomes

Real-world progression-free survival

- At 12 months, the median PFS was not reached, with PFS rates at 59.5% (overall), 77.8% (with CNS metastases), and 55.8% (without CNS metastases; **Figure 2**)
 - Similarly, median iPFS was not reached by 12 months, with iPFS rates at 67.3% (overall), 77.8% (with CNS metastases), and 65.2% (without CNS metastases; **Figure 3**)

Figure 2: Real-world PFS in patients treated with brigatinib

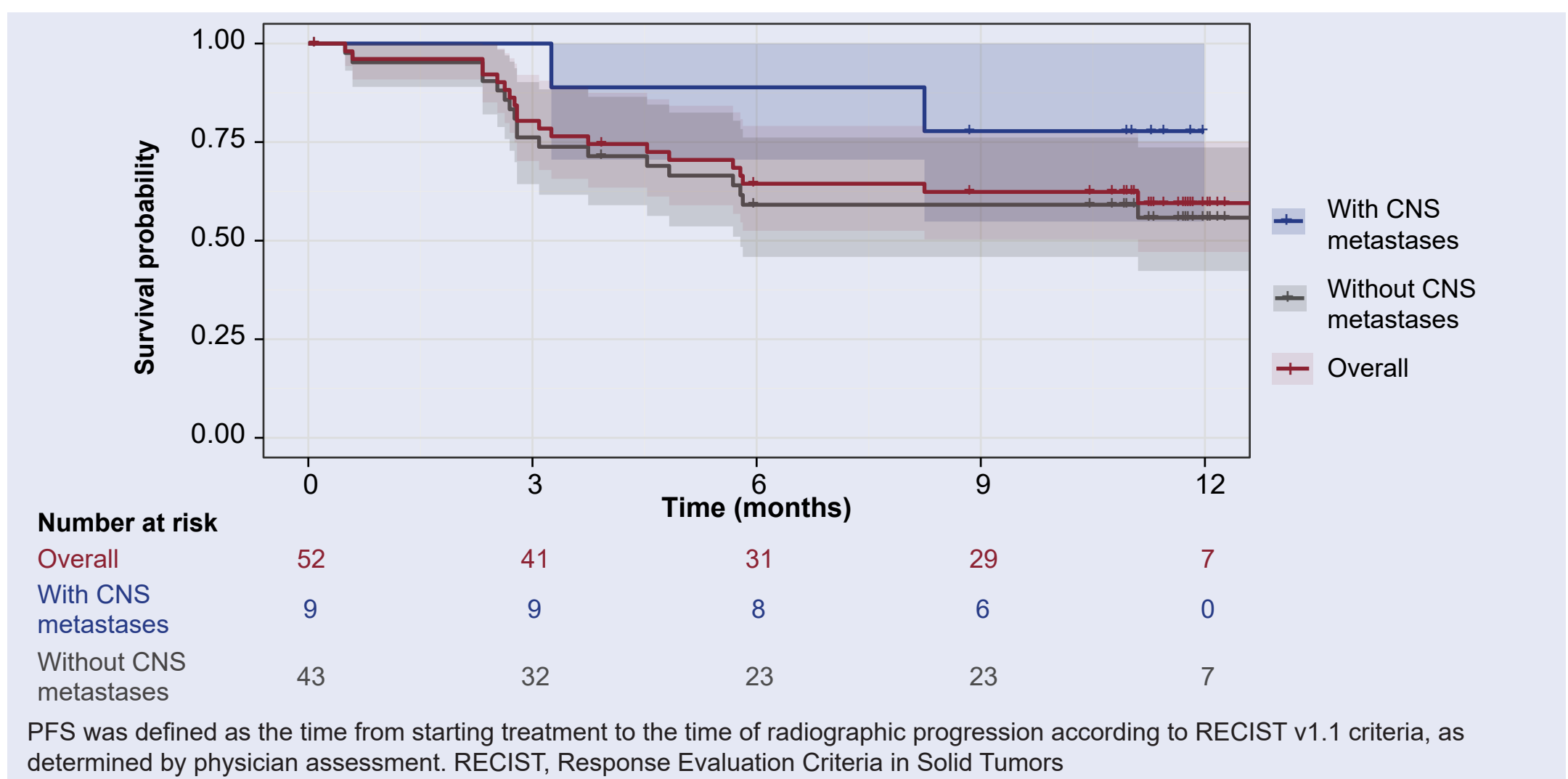
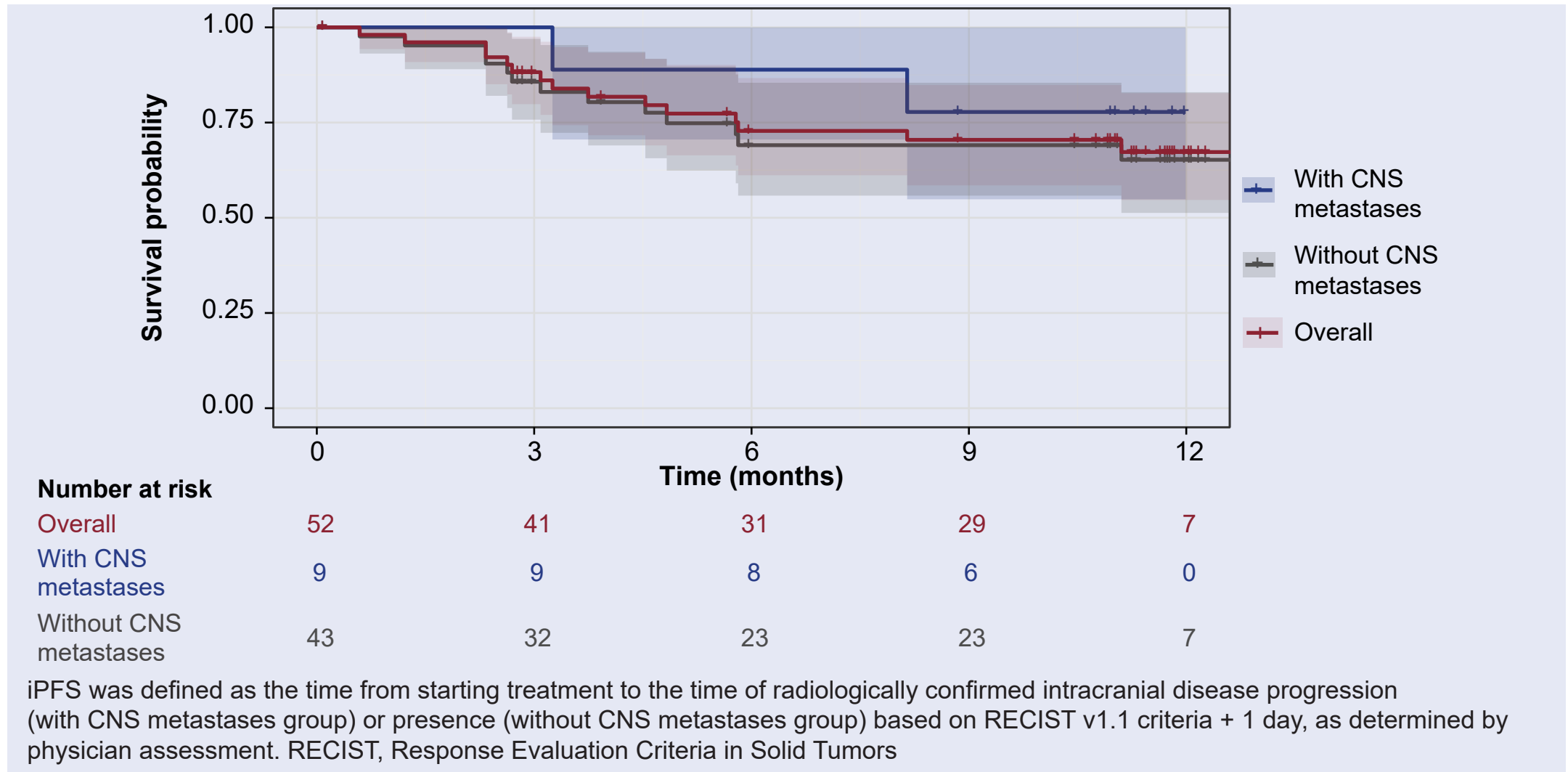


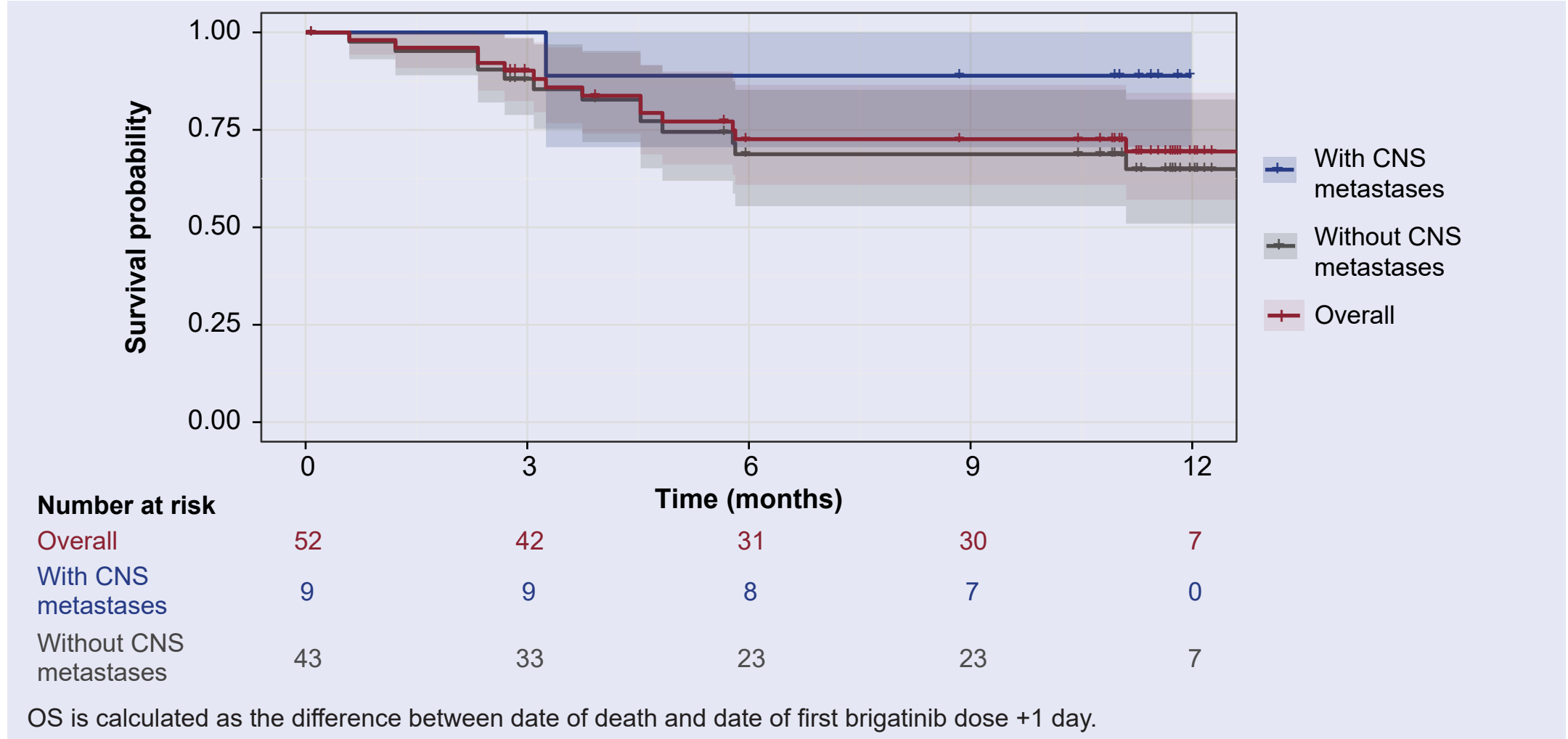
Figure 3: Real-world iPFS in patients treated with brigatinib



Real-world overall survival

- At 12 months, the median OS was not reached, with OS rates at 69.4% (overall), 88.9% (with CNS metastases), and 64.9% (without CNS metastases; **Figure 4**)

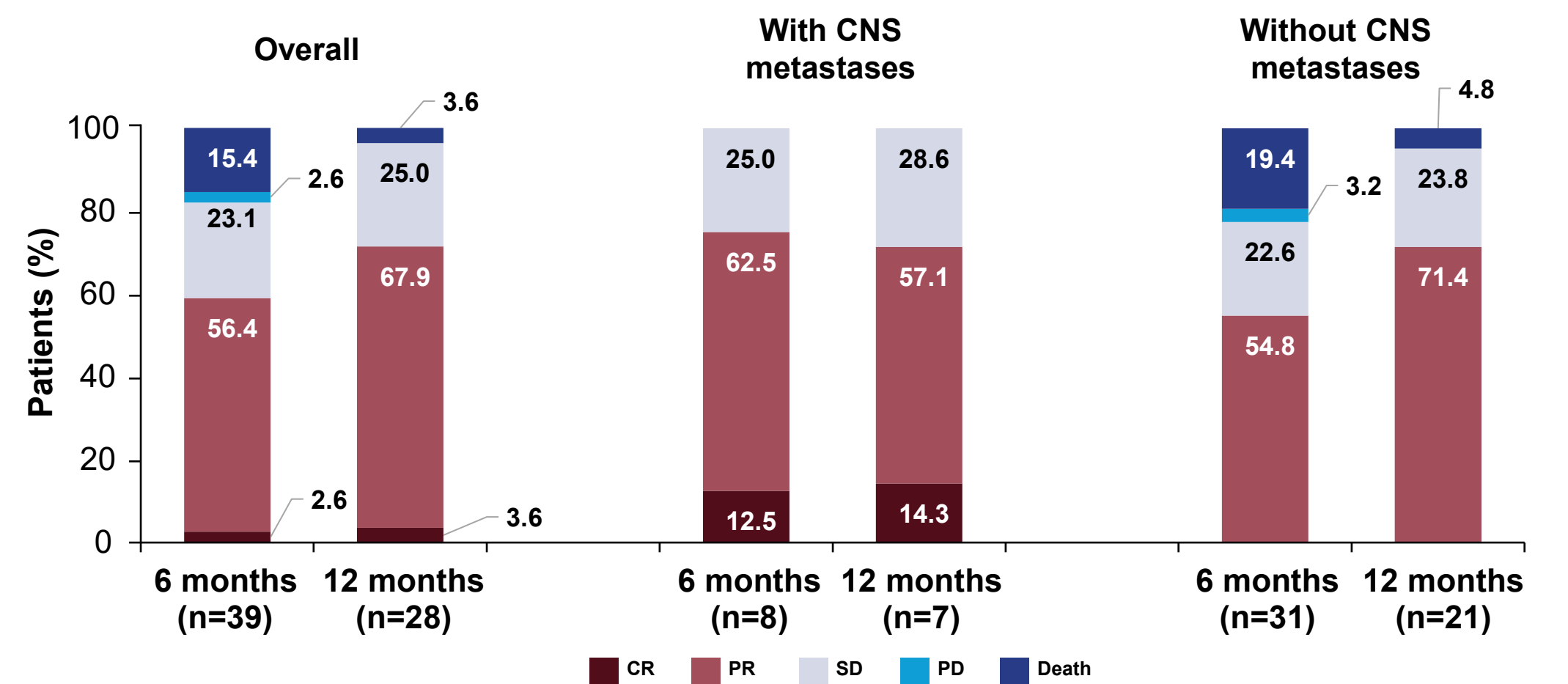
Figure 4: Real-world OS in patients treated with brigatinib



Real-world overall response rate

- For the overall population, an ORR of 41.2% (21/51 patients) was achieved
 - Comparable ORR was observed in patients with vs those without CNS metastases (44.4% [4/9 patients] vs. 40.5% [17/42 patients])
- The best overall response was complete or partial response (CR or PR), observed in 52.9% of patients (27/51)
- Overall, complete and partial responses were achieved in 3.6% and 67.9% of patients, respectively, at 12 months (**Figure 5**)

Figure 5: Response to treatment in patients receiving brigatinib

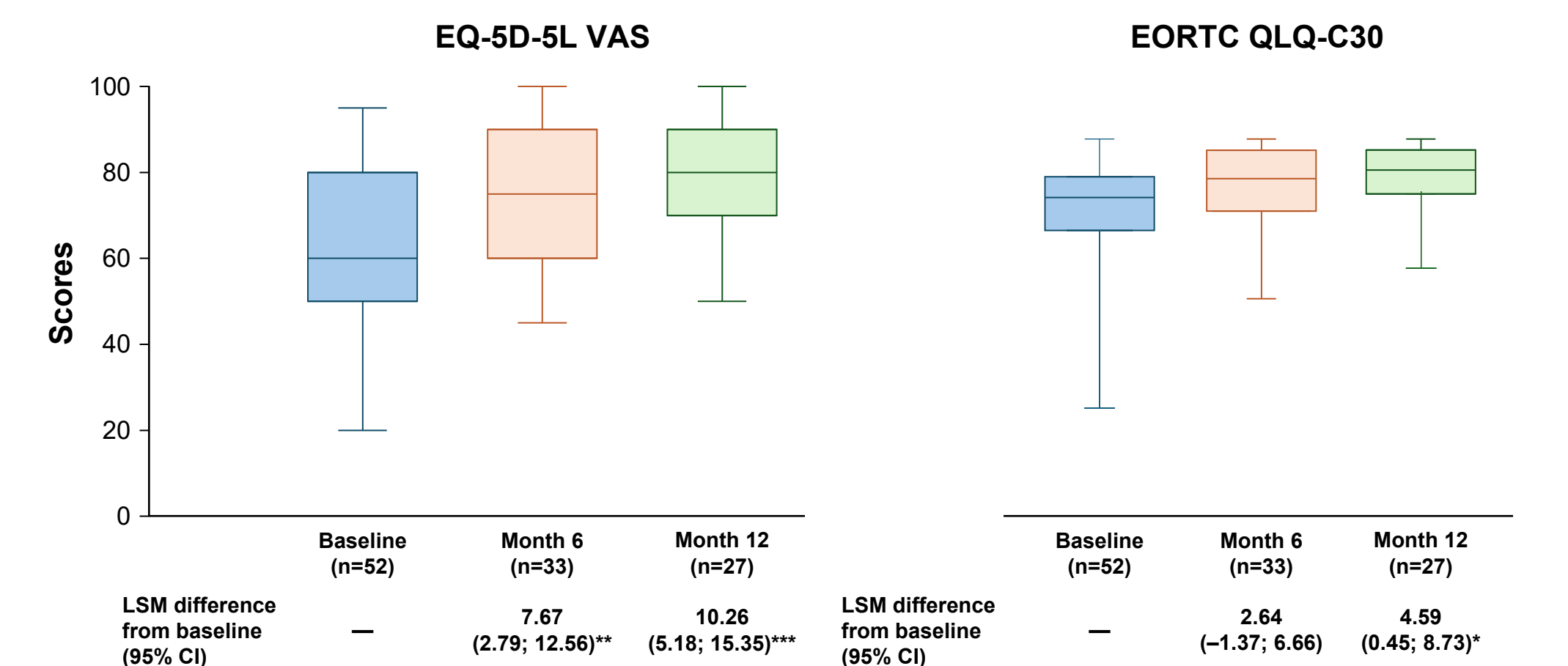


One patient did not have any assessment of response due to early termination; therefore, best response rate is reported for 51 patients. CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

Quality of life

- EQ-5D-5L utility values were high at baseline and remained stable through 12 months (p>0.05)
- At 12 months, the least squares mean (LSM) differences from baseline for both EQ-5D-5L VAS and EORTC QLQ-C30 summary scores were statistically significant (**Figure 6**)
 - Values of the LSM-calculated differences from baseline for EQ-5D-5L VAS scores exceeded the published minimal important difference,⁷ suggesting a clinically meaningful improvement in health-related QoL

Figure 6: Box and whisker plots of EQ-5D-5L VAS and EORTC QLQ-C30 summary scores



*p<0.05; **p<0.01; ***p<0.001. CI, confidence interval.

Safety

- A total of 28 patients experienced ≥1 nonserious AE
 - 18 patients reported ≥1 serious AE (SAE); 3 SAEs (acute interstitial pneumonitis, neuralgia, complex regional pain syndrome) were related to brigatinib treatment in 2 patients
- The most common AEs were abnormal laboratory investigations (44.2%) and general disorders/administration site conditions (23.1%)
- The overall safety profile was consistent with that reported in the Summary of Product Characteristics for brigatinib

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