

# Integrated efficacy and safety of brigatinib in patients with ALK TKI-naïve advanced *ALK*+ NSCLC in the ALTA-1L and J-ALTA studies

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## Introduction

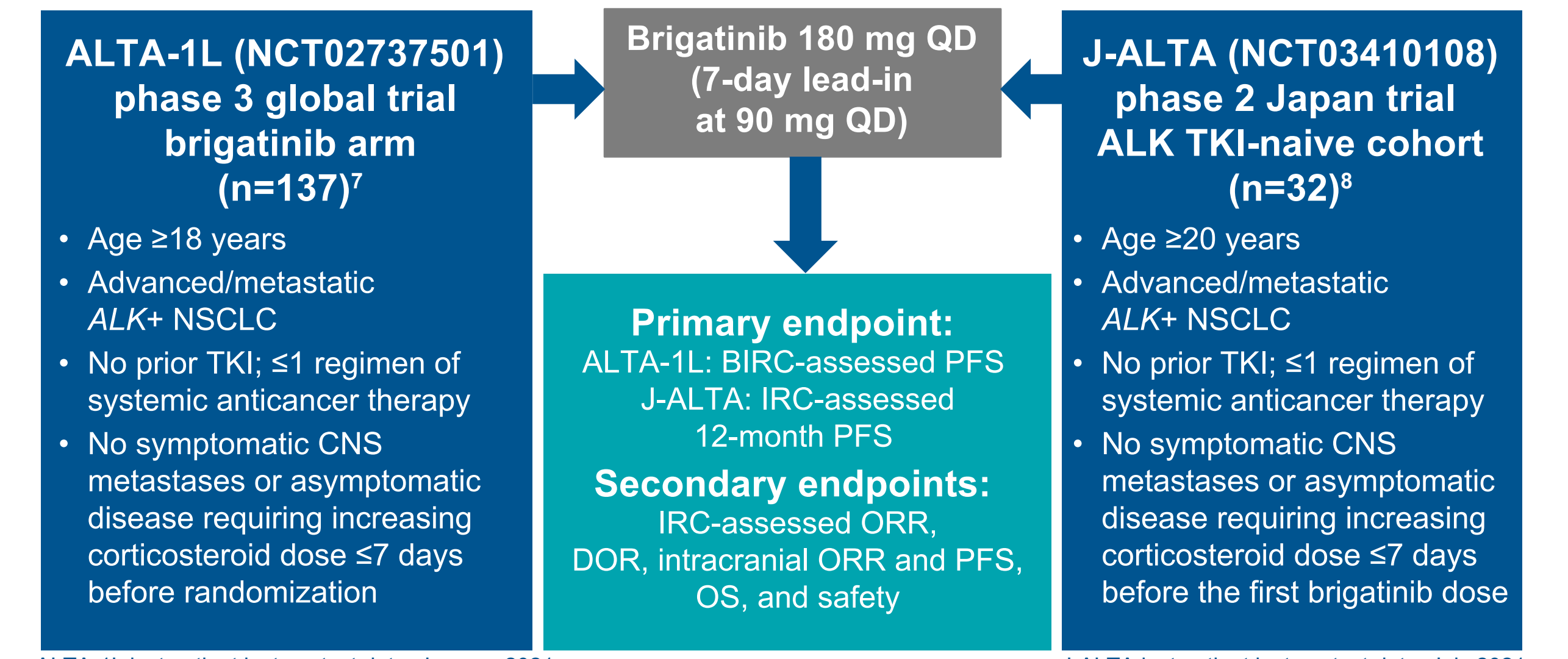
- Approximately 3%–8% of patients with non-small cell lung cancer (NSCLC) harbor rearrangements in the anaplastic lymphoma kinase (*ALK*) gene<sup>1–3</sup>
- Brigatinib is a potent, next-generation, oral tyrosine kinase inhibitor (TKI) against the *EML4-ALK* fusion gene, with demonstrated activity against *ALK* resistance mutations<sup>4–6</sup>
- The clinical efficacy of brigatinib was demonstrated in patients with TKI-naïve advanced or metastatic *ALK*+ NSCLC in the phase 3 ALTA-1L and phase 2 J-ALTA trials<sup>7,8</sup>
  - ALTA-1L: median progression-free survival (PFS) with brigatinib 24.0 months vs crizotinib 11.1 months; hazard ratio (HR), 0.48 (95% confidence interval [CI]: 0.35–0.66); log-rank *P* < 0.0001<sup>7</sup>
  - J-ALTA TKI-naïve cohort: 12-month PFS rate 93.0% (90% CI: 79.2–97.8)<sup>8</sup>

## Objective

- To conduct an integrated analysis of the efficacy and safety of brigatinib in the ALTA-1L and J-ALTA trials in patients with ALK TKI-naïve advanced *ALK*+ NSCLC

## Methods

Figure 1: Integrated study design



Response was assessed using RECIST v1.1 criteria<sup>9</sup>  
BIRC, blinded independent review committee; CNS, central nervous system; DOR, duration of response; IRC, independent review committee; ORR, objective response rate; OS, overall survival; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors

## Results

- The median duration of follow-up for the integrated population was 35.8 months (range, 0.2–52.5)
  - Median durations of follow-up for ALTA-1L and the J-ALTA TKI-naïve cohort were 40.5 months (range, 0.2–52.5) and 22.2 months (range, 3.2–27.7), respectively
- Most patients had stage IV disease at study entry and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 (Table 1)

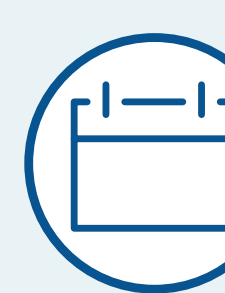
Table 1: Demographic and baseline characteristics

Characteristic	Integrated population (N=169)	ALTA-1L (n=137)	J-ALTA TKI-naïve cohort (n=32)
Median age, years (range)	58 (27–86)	58 (27–86)	60.5 (29–85)
Female, n (%)	86 (51)	69 (50)	17 (53)
Median time from diagnosis, months (range)	1.5 (0.1–231.6)	1.7 (0.1–145.3)	1.1 (0.3–231.6)
Stage IV disease at study entry, n (%)	161 (95)	129 (94)	32 (100)
ECOG performance status, n (%)			
0	70 (41)	54 (39)	16 (50)
1	91 (54)	76 (55)	15 (47)
2	8 (5)	7 (5)	1 (3)
Smoking history, n (%)			
Never	104 (62)	84 (61)	20 (63)
Current	3 (2)	3 (2)	0
Former	62 (37)	50 (36)	12 (38)
Intracranial CNS metastases, n (%)	47 (28)	40 (29)	7 (22)
Prior chemotherapy in the advanced or metastatic setting, n (%)	44 (26)	36 (26)	8 (25)
Prior radiotherapy to the brain, n (%)	21 (12)	18 (13)	3 (9)

## Question

What is the efficacy and safety of brigatinib in patients with ALK TKI-naïve advanced *ALK*+ NSCLC?

## Investigation



Advanced/metastatic ALK TKI-naïve *ALK*+ NSCLC (N=169)



Integrated analysis of ALTA-1L (n=137) and J-ALTA (n=32)

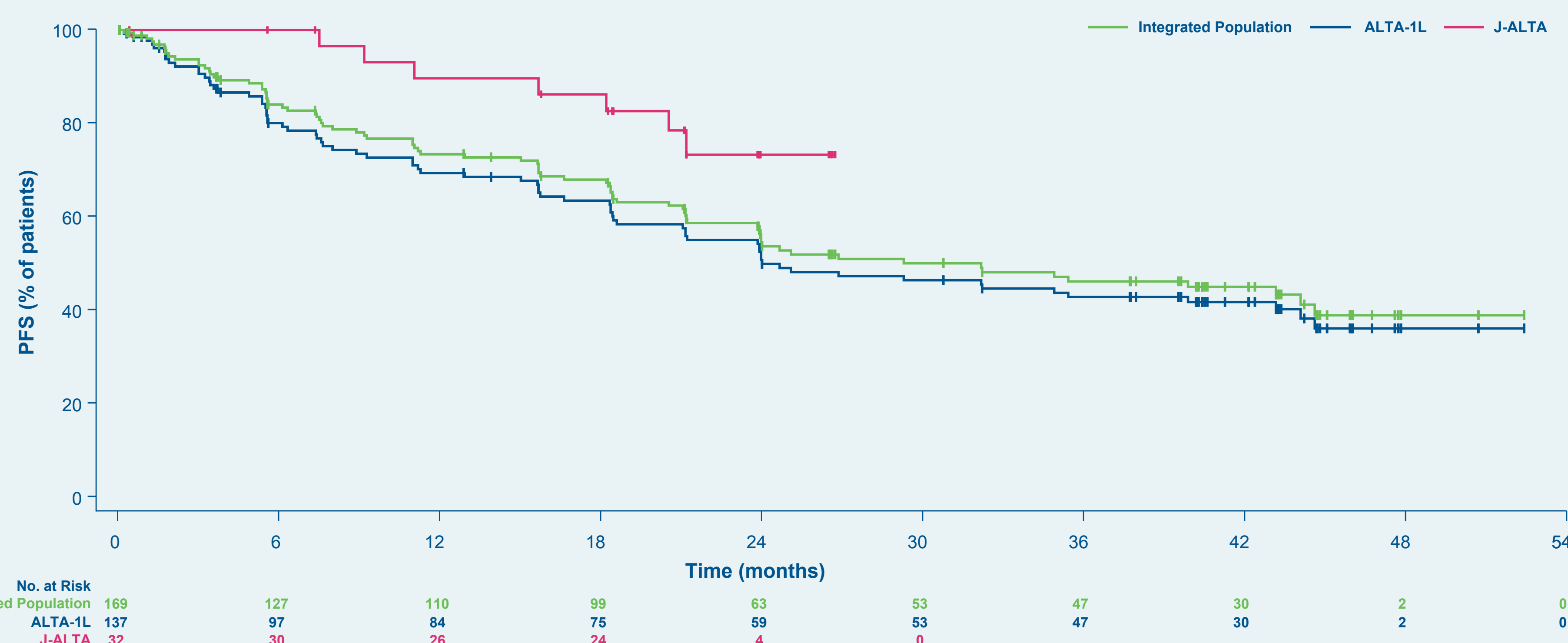


Brigatinib 180 mg QD (7-day lead-in at 90 mg)

Treatment until BIRC-assessed disease progression, toxicity, or other reason for discontinuation

## Results

BIRC-assessed progression-free survival



- With brigatinib treatment, median PFS by IRC was 29.3 months and 2-year PFS was 55%

Patient population	Patients with events, n	Median PFS, months (95% CI)	2-year PFS, % (95% CI)
Integrated population (N=169)	80	29.3 (23.9–44.7)	55 (46–62)
ALTA-1L (n=137)	73	24.0 (18.5–43.2)	51 (41–59)
J-ALTA TKI-naïve cohort (n=32)	7	NE (NE–NE)	73 (51–87)

CI, confidence interval; NE, not evaluable

## Key Takeaways

Treatment with brigatinib demonstrated clinically meaningful systemic and intracranial efficacy in patients with ALK TKI-naïve advanced or metastatic *ALK*+ NSCLC

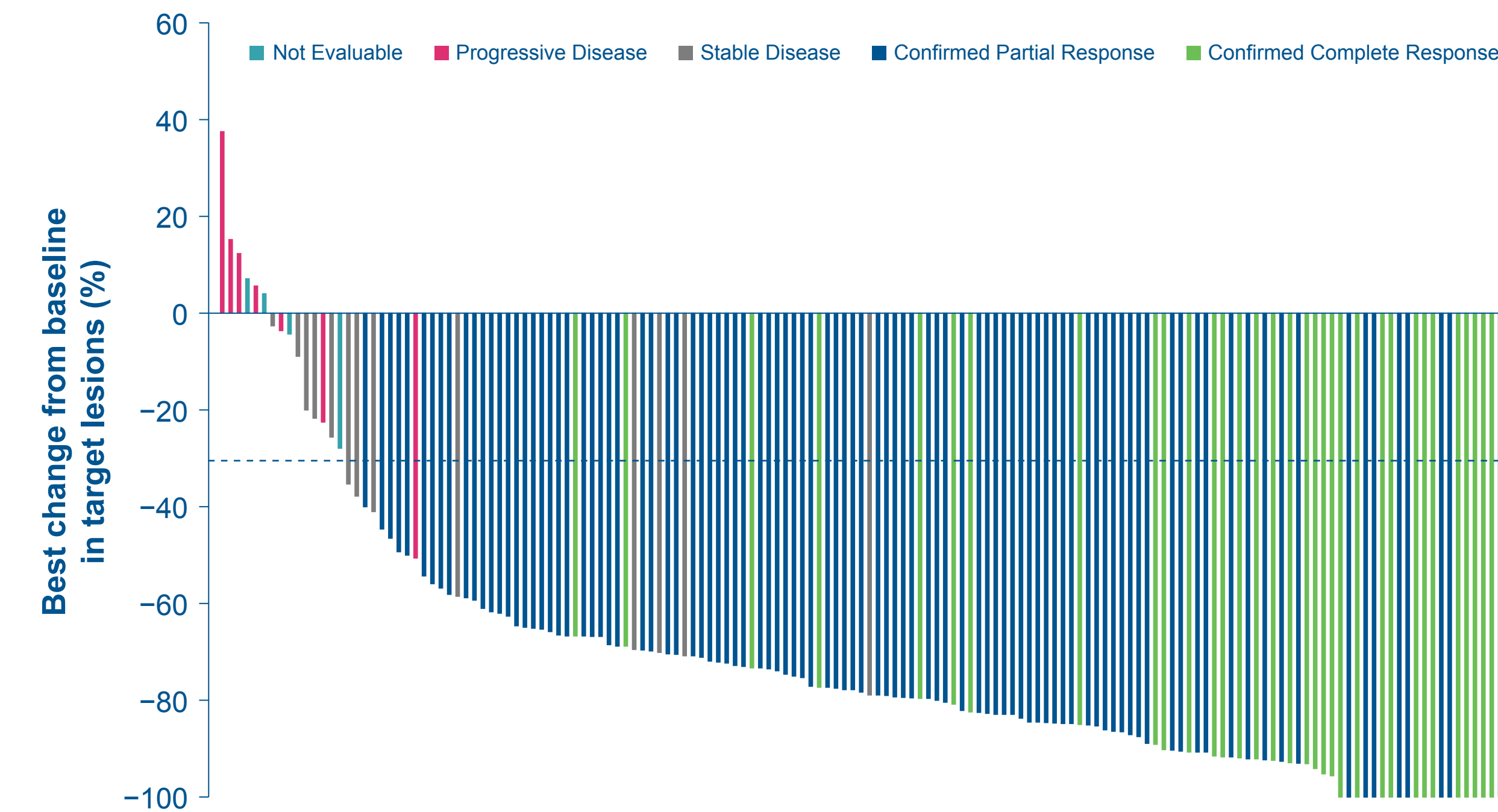
- Confirmed ORR in the integrated population was 79%, with 36 complete responses and 97 partial responses (Table 2 and Figure 2)

Table 2: Overall and intracranial objective response

Response parameter	Integrated population	ALTA-1L	J-ALTA TKI-naïve cohort
All patients, n	169	137	32
Patients with a confirmed objective response, n	133	102	31
Confirmed ORR, % (95% CI)	79 (72–85)	74 (66–82)	97 (84–99.9)
Confirmed CR, n (%)	36 (21)	33 (24)	3 (9)
Confirmed PR, n (%)	97 (57)	69 (50)	28 (88)
Median time to response in confirmed responders, months (range)	1.8 (0.4–29.5)	1.8 (1.0–29.5)	1.8 (0.4–12.9)
Intracranial response, all patients			
Confirmed intracranial ORR, % (95% CI)	20 (14–27)	23 (16–31)	9 (2–25)
Confirmed intracranial CR, n (%)	22 (13)	21 (15)	1 (3)
Confirmed intracranial PR, n (%)	12 (7)	10 (7)	2 (6)

CR, complete response; NA, not available; PR, partial response

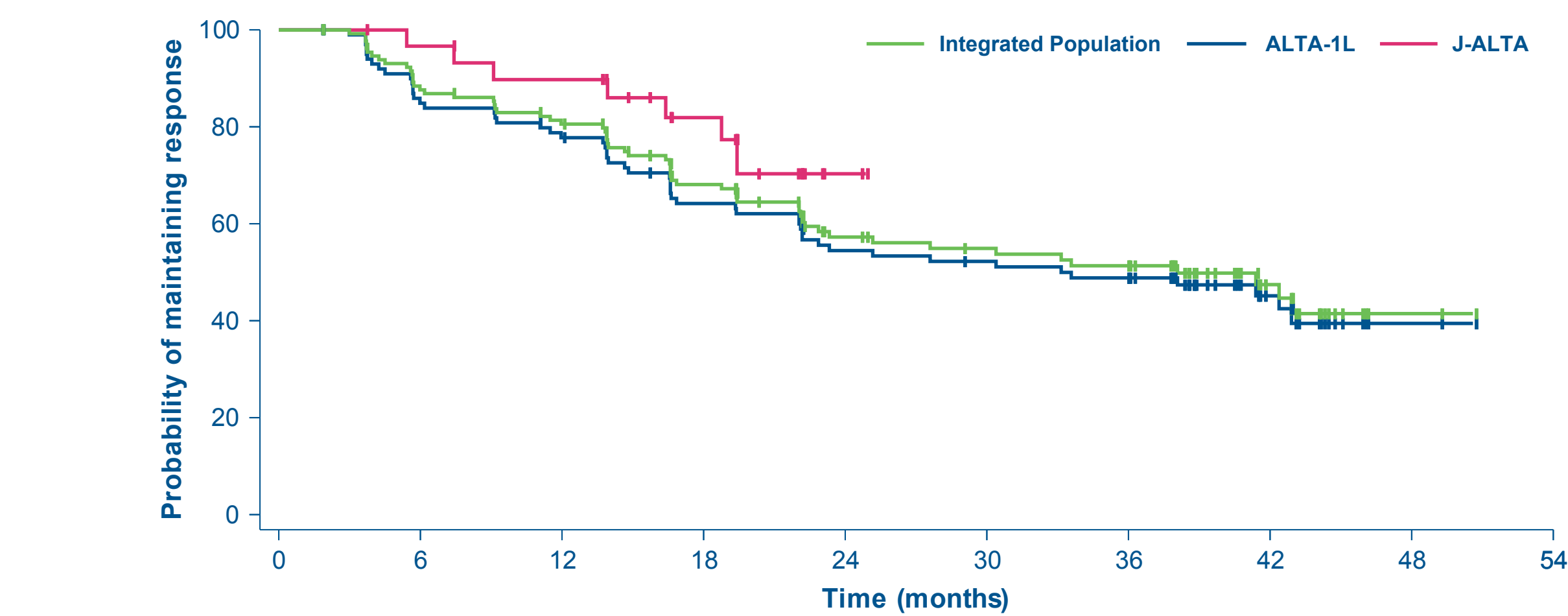
Figure 2: Best percentage change from baseline in sum of target lesions



Dotted line at –30% indicates threshold for partial response per RECIST v1.1

- Median DOR was 38.1 months (95% CI: 22.9 months–NE; Figure 3)

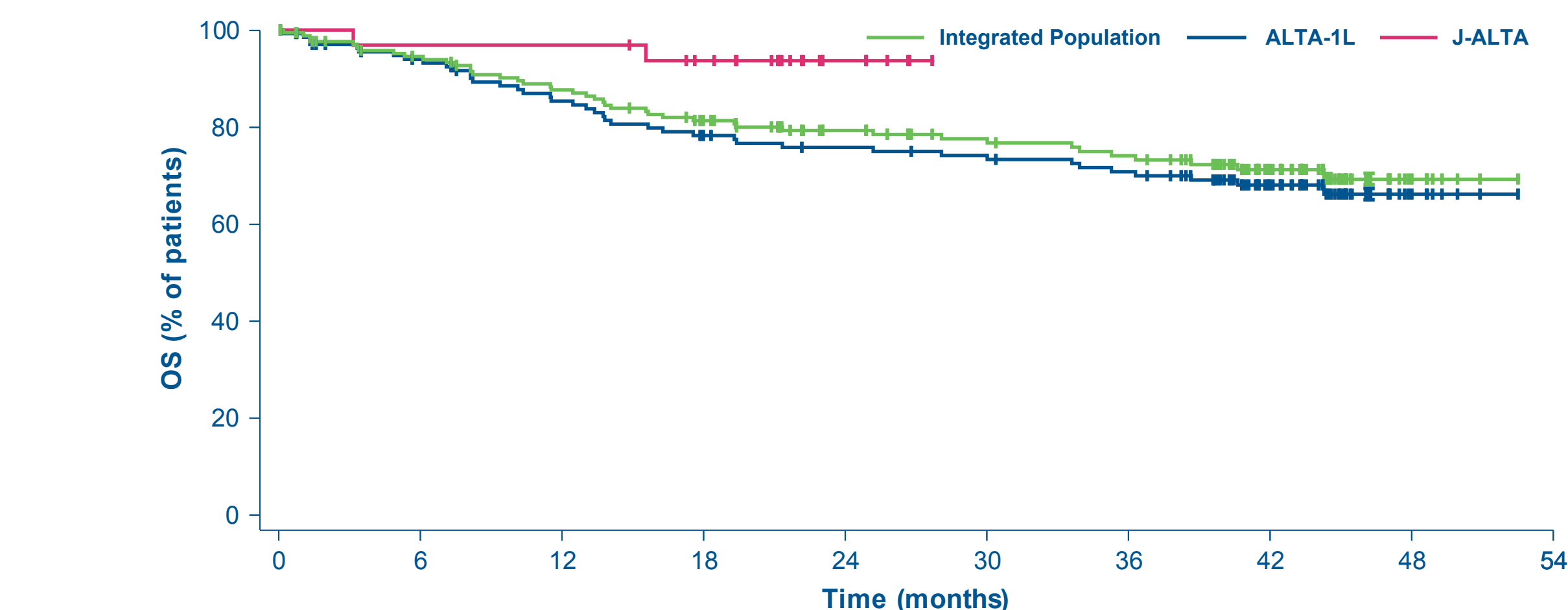
Figure 3: Duration of response



Patient population	Patients with events, n	Median DOR, months (95% CI)	Probability of maintaining response at 24 months, % (95% CI)
Integrated population (N=169)	133	38.1 (22.9–NE)	57 (48–66)
ALTA-1L (n=137)	102	33.2 (22.1–NE)	55 (44–64)
J-ALTA TKI-naïve cohort (n=32)	31	NE (19.4–NE)	70 (46–85)

- Median OS was not reached in the integrated population (Figure 4)

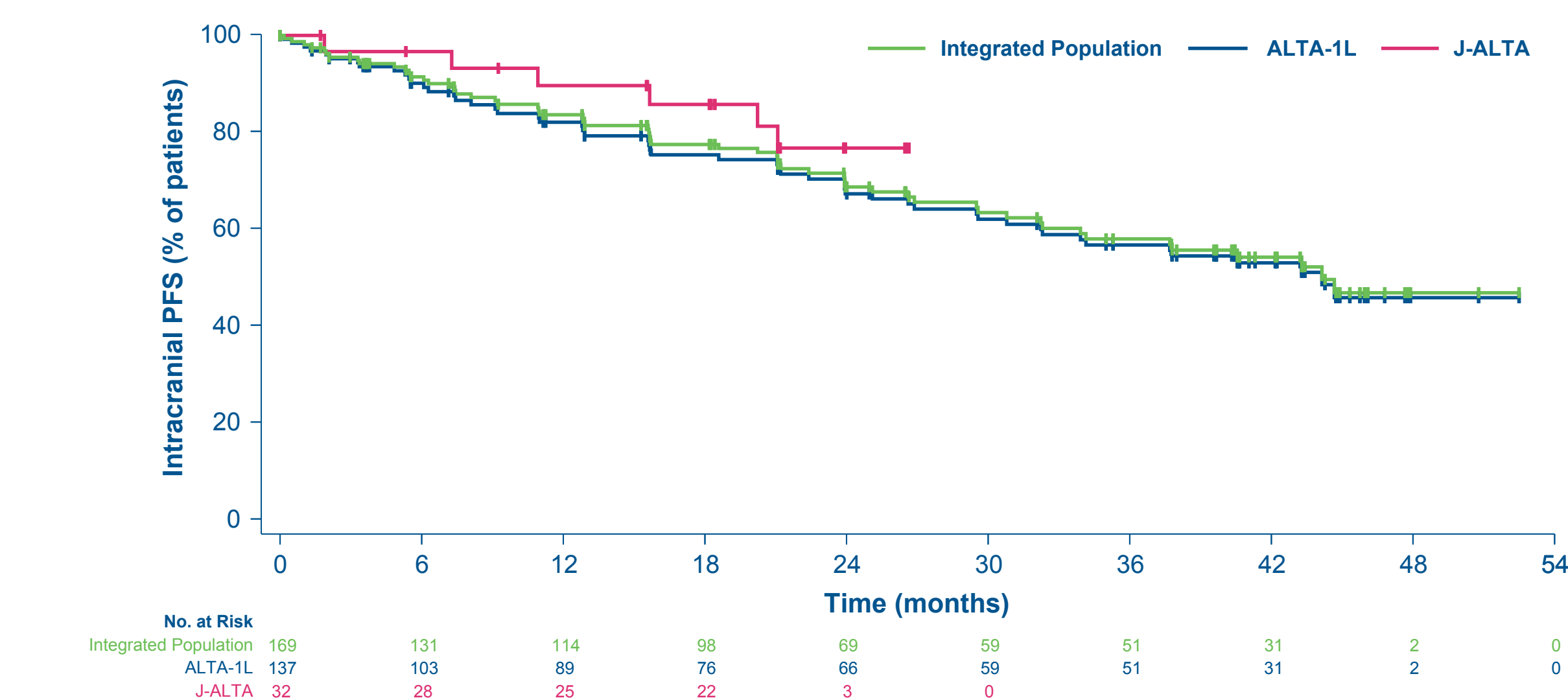
Figure 4: Overall survival



Patient population	Median OS, months	2-year OS, % (95% CI)	3-year OS, % (95% CI)
Integrated population (N=169)	NE (NE–NE)	79 (72–85)	74 (66–80)
ALTA-1L (n=137)	NE (NE–NE)	76 (67–82)	71 (62–78)
J-ALTA TKI-naïve cohort (n=32)	NE (NE–NE)	94 (77–98)	NE (NE–NE)

- Median intracranial PFS in the integrated population was 44.1 months (Figure 5)

Figure 5: Intracranial progression-free survival



Patient population	Patients with events, n	Median IPFS, months (95% CI)	2-year IPFS, % (95% CI)
Integrated population (N=169)	58	44.1 (33.9–NE)	69 (60–76)
ALTA-1L (n=137)	52	44.1 (32.2–NE)	67 (57–75)
J-ALTA TKI-naïve cohort (n=32)	6	NE (NE–NE)	77 (55–89)

IPFS, intracranial progression-free survival

- All patients experienced treatment-emergent adverse events (TEAEs; Table 3)

Table 3: Summary of TEAEs

TEAEs, n (%)	Integrated population (N=168)	ALTA-1L (n=136)	J-ALTA TKI-naïve cohort (n=32)
Any TEAE	168 (100)	136 (100)	32 (100)
Grade 3–4 TEAEs	124 (74)	95 (70)	29 (91)
TEAEs leading to treatment discontinuation	18 (11)	18 (13)	0
TEAEs leading to dose interruption	128 (76)	98 (72)	30 (94)
TEAEs leading to dose reduction	82 (49)	60 (44)	22 (69)
Grade 5 TEAEs	11 (7)	11 (8)	0
Treatment-related grade 5 TEAEs	0	0	0

- TEAEs led to treatment discontinuation in 11% of patients
  - In the ALTA-1L brigatinib arm, TEAEs leading to treatment discontinuation occurring in >1 patient were pneumonia (n=3), pneumonitis (n=3), bradycardia (n=2), and interstitial lung disease (n=2)
- Grade 3–4 TEAEs were reported in 74% of patients and were mainly due to asymptomatic elevations in blood chemistry (Table 4)

Table 4: Any grade TEAEs reported in >20% of all patients and grade ≥3 TEAEs reported in >5% of patients in the integrated population

TEAEs, n (%)	Integrated population (N=168)		ALTA-1L (n=136)		J-ALTA TKI-naïve cohort (n=32)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Diarrhea	96 (57)	3 (2)	79 (58)	3 (2)	17 (53)	0
Increased blood CPK	95 (57)	52 (31)	68 (50)	36 (26)	27 (84)	16 (50)
Hypertension	63 (38)	30 (18)	44 (32)	19 (14)	19 (59)	11 (34)
Cough	52 (31)	0	49 (36)	0	3 (9)	0
Increased AST	50 (30)	8 (5)	35 (26)	6 (4)	15 (47)	2 (6)
Nausea	51 (30)	3 (2)	45 (33)	3 (2)	6 (19)	0
Increased lipase	45 (27)	27 (16)	32 (24)	21 (15)	13 (41)	6 (19)
Increased ALT	42 (25)	10 (6)	31 (23)	6 (4)	11 (34)	4 (13)
Back pain	38 (23)	1 (<1)	35 (26)	1 (<1)	3 (9)	0
Increased amylase	38 (23)	12 (7)	35 (26)	8 (6)	13 (41)	4 (13)
Arthralgia	37 (22)	1 (<1)	35 (26)	1 (<1)	2 (6)	0
Constipation	36 (21)	1 (<1)	27 (19)	1 (<1)	9 (28)	0
Headache	35 (21)	3 (2)	32 (24)	3 (2)	3 (9)	0

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase

- Any grade interstitial lung disease/pneumonitis was reported in 12 (7.1%) of patients

## Summary

- Brigatinib treatment demonstrated clinically meaningful systemic and intracranial efficacy in this integrated analysis of patients with ALK TKI-naïve advanced or metastatic *ALK*+ NSCLC in the ALTA-1L and J-ALTA trials
  - Median PFS was 29.3 months, and the 2-year PFS rate was 55%
  - Median OS was not reached, and the 3-year OS rate was 74%
  - Confirmed ORR was 79%, with 36 patients achieving a complete response
  - Patients with CNS metastases had a median intracranial PFS of 44.1 months and a 2-year intracranial PFS rate of 69%
- Safety results were consistent with the known profile for brigatinib, with no new safety findings
- This integrated analysis shows brigatinib efficacy and safety in a larger ALK TKI-naïve *ALK*+ NSCLC patient population with similar baseline characteristics
  - One confounder is that the J-ALTA study only enrolled an Asian population

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