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Background

- Befotertinib is an oral, potent, CNS-active, third-generation EGFR-TKI targeting both EGFR-sensitizing mutations and the T790M resistance mutation in patients with advanced NSCLC.^{1,2}
- In the primary analysis of this phase III study (NCT04206072), befotertinib significantly prolonged IRC-assessed PFS compared with icotinib in patients with previously untreated, EGFR-mutated advanced NSCLC (22.1 vs 13.8 months; HR 0.49, 95% CI 0.36-0.68; p<0.0001).²
- Among first-line third-generation EGFR-TKI monotherapies, a statistically significant OS benefit has been reported only with osimertinib in FLAURA (38.6 vs 31.8 months; HR 0.80, 95.05% CI 0.64-1.00; p=0.046).³
- We report the final OS analysis, together with updated PFS and long-term safety outcomes, after extended follow-up in this phase III trial of befotertinib versus icotinib.

Methods

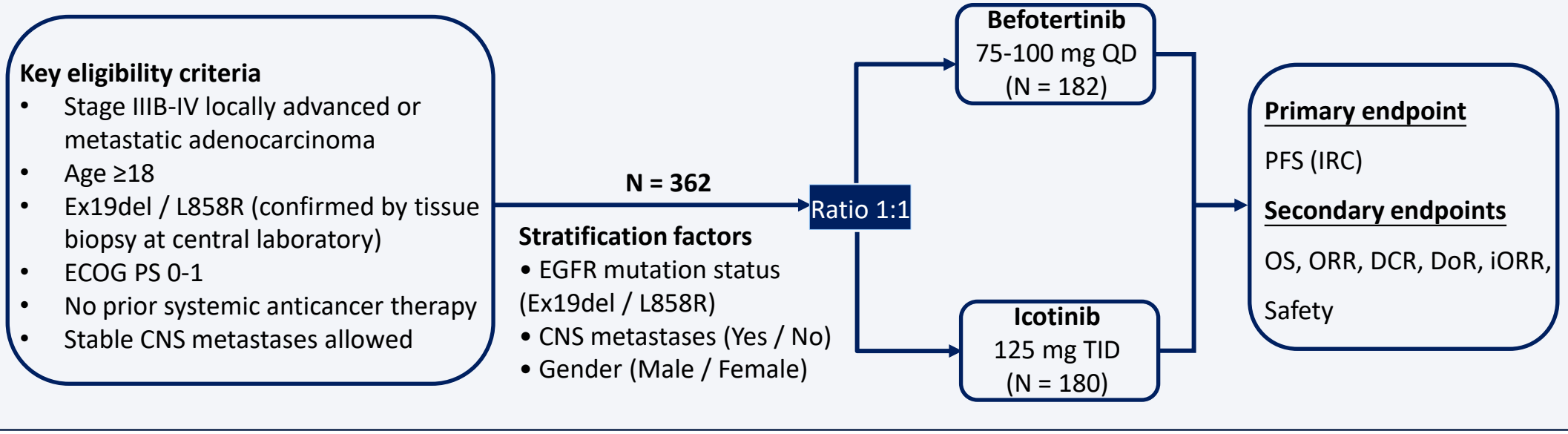
- This multicenter, open-label, randomized phase III trial enrolled patients with previously untreated, unresectable stage IIIB-IV NSCLC harboring an EGFR exon 19 deletion or exon 21 L858R mutation between December 24, 2019, and December 18, 2020, across 39 hospitals in China.
- Patients were randomly assigned 1:1 to receive befotertinib 75-100 mg orally once daily or icotinib 125 mg orally three times daily until disease progression, unacceptable toxicity, or withdrawal of consent. Patients in the icotinib group with acquired EGFR T790M mutation were permitted to cross over to befotertinib after progression.
- The primary endpoint was IRC-assessed progression-free survival (PFS). Secondary endpoints included overall survival (OS), objective response rate (ORR), disease control rate (DCR), duration of response (DoR), intracranial efficacy, and safety.
- The final OS analysis was conducted at the data cutoff of April 30, 2024. Efficacy was assessed in the intention-to-treat population, and safety was assessed in all patients who received at least one dose of study treatment.

References & Acknowledgements

- References:**
 - Lu S, et al. *J Thorac Oncol.* 2022, 17(10): 1192-1204.
 - Lu S, et al. *Lancet Respir Med.* 2023, 11(10): 905-915.
 - Ramalingam SS, et al. *N Engl J Med.* 2020, 382(1): 41-50.
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Trial Design

- Data cut-off: April 30th, 2024
- Median Follow-up Duration: for PFS: 37.2 vs 23.5 months; for OS: 43.2 vs 44.0 months



Baseline Characteristics

- Baseline characteristics were balanced between the two groups.

Baseline Characteristic	Data are n (%) or median (range)	Befotertinib (N = 182)	icotinib (N = 180)
Age, years	Median (range)	60 (38-81)	58 (28-84)
Gender			
Male		72 (39.6%)	72 (40.0%)
Female		110 (60.4%)	108 (60.0%)
ECOG PS*			
0		35 (19.2%)	39 (21.7%)
1		146 (80.2%)	141 (78.3%)
Smoking history			
Yes		61 (33.5%)	55 (30.6%)
No		121 (66.5%)	125 (69.4%)
Tumor stage			
IIIB		17 (9.3%)	6 (3.3%)
IV		165 (90.7%)	174 (96.7%)
EGFR mutation status			
exon 19 deletion		117 (64.3%)	117 (65.0%)
exon 21 Leu858Arg		65 (35.7%)	63 (35.0%)
CNS metastases*			
Yes		47 (25.8%)	45 (25.0%)
No		135 (74.2%)	135 (75.0%)

Note: *One patient tested ECOG PS of 1 after first dose of treatment in the befotertinib group, which was treated as missing data for baseline characteristics. *CNS metastasis status based on the assessment by investigators. Brain metastasis at baseline occurred in 36 patients (30.8%) in the befotertinib arm and in 56 (31.1%) patients in the icotinib arm per IRC assessment, respectively.

Efficacy

- At the data cutoff of April 30, 2024, 196 deaths had occurred (OS maturity, 54.1%): 95/182 (52.2%) with befotertinib and 101/180 (56.1%) with icotinib.
- Median OS was 40.0 vs 37.5 months (HR 0.96, 95% CI 0.72-1.27; p=0.76; **Figure 1**), with no significant OS difference across prespecified subgroups (**Figure 2**).
- Subsequent anticancer therapy was more common with icotinib than befotertinib (82.2% vs 62.6%), including greater use of third-generation EGFR-TKIs (67.2% vs 37.9%; 33 patients (18.3%) in the icotinib arm crossed over to befotertinib (**Table 1**).
- Median OS was 40.0 (95% CI 34.1-NE) months for befotertinib, versus 41.6 (34.2-NE) and 24.5 (15.2-37.7) months for icotinib patients with and without subsequent third-generation EGFR-TKIs, respectively (**Figure 3A/B**).
- Befotertinib significantly prolonged median PFS versus icotinib (22.0 vs 13.8 months; HR 0.52, 95% CI 0.39-0.69; p<0.0001; **Figure 4**).
- ORR and DCR were comparable between groups, while median DoR was longer with befotertinib (24.9 vs 12.4 months); intracranial ORR also numerically favored befotertinib (92.3% vs 55.6%; **Table 2**).

Efficacy

Figure 1. Kaplan-Meier curve for Overall Survival

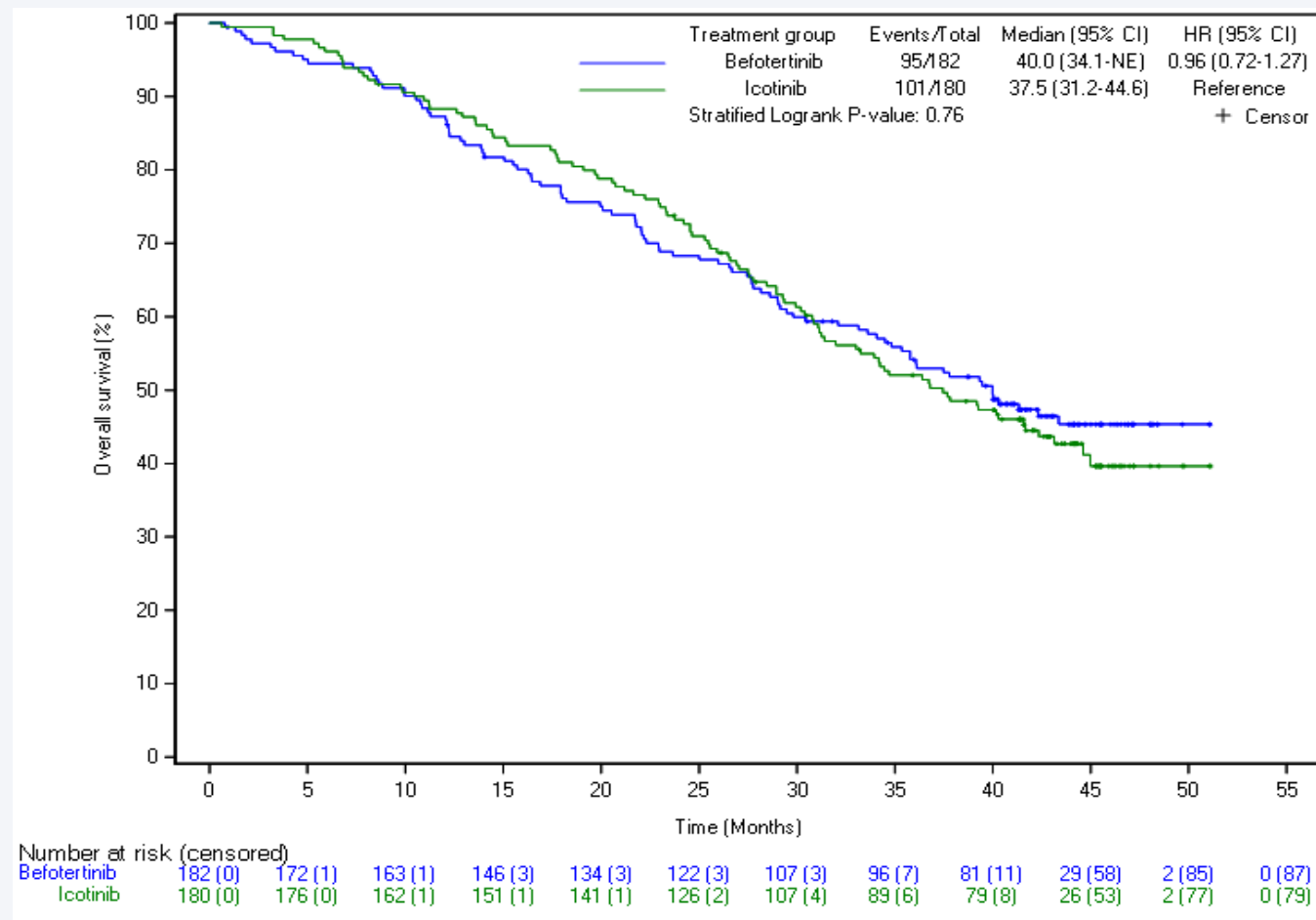


Figure 2. Overall survival in prespecified subgroups

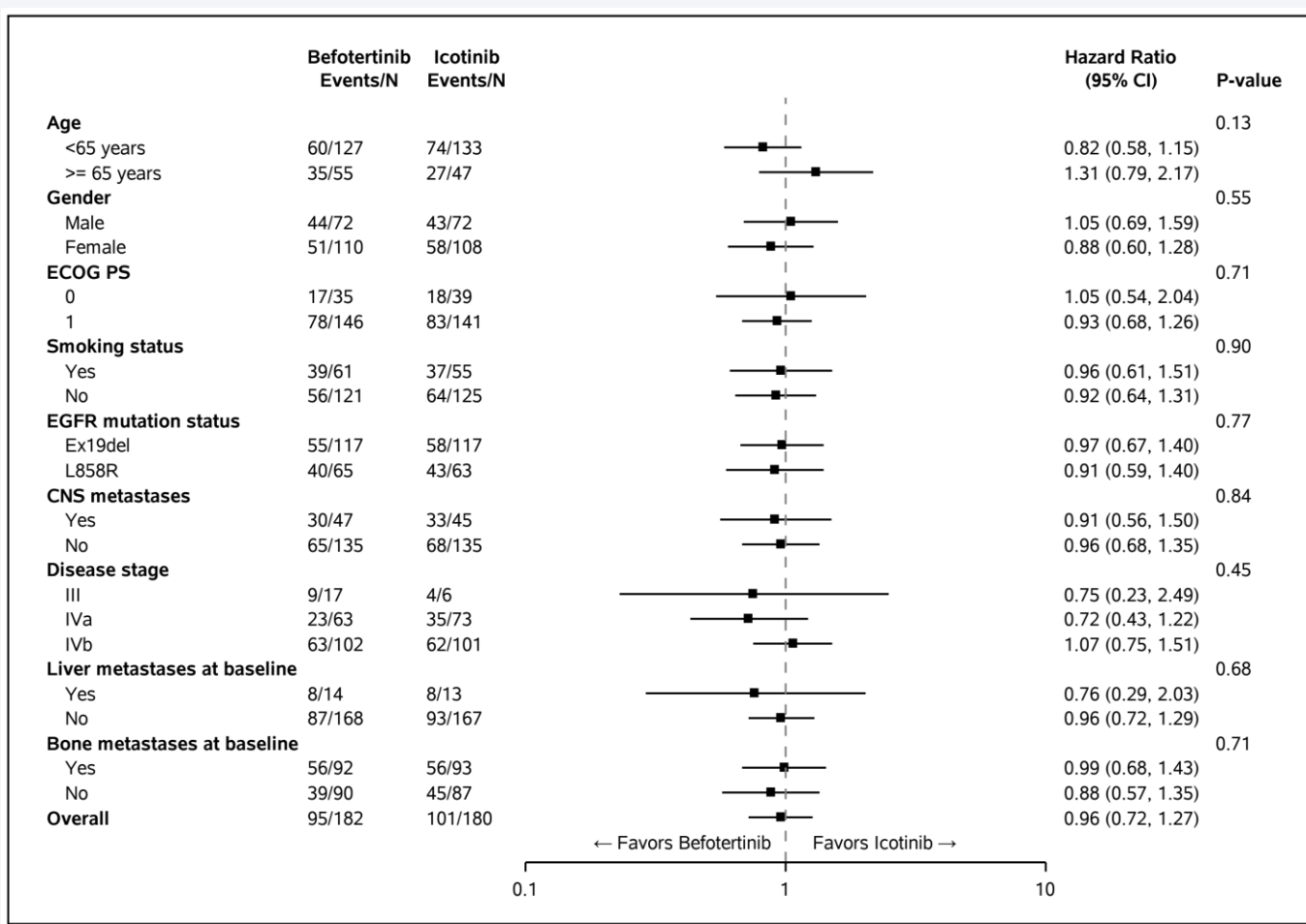


Figure 3. Overall survival with befotertinib versus icotinib with (A) or without (B) subsequent third-generation EGFR-TKI

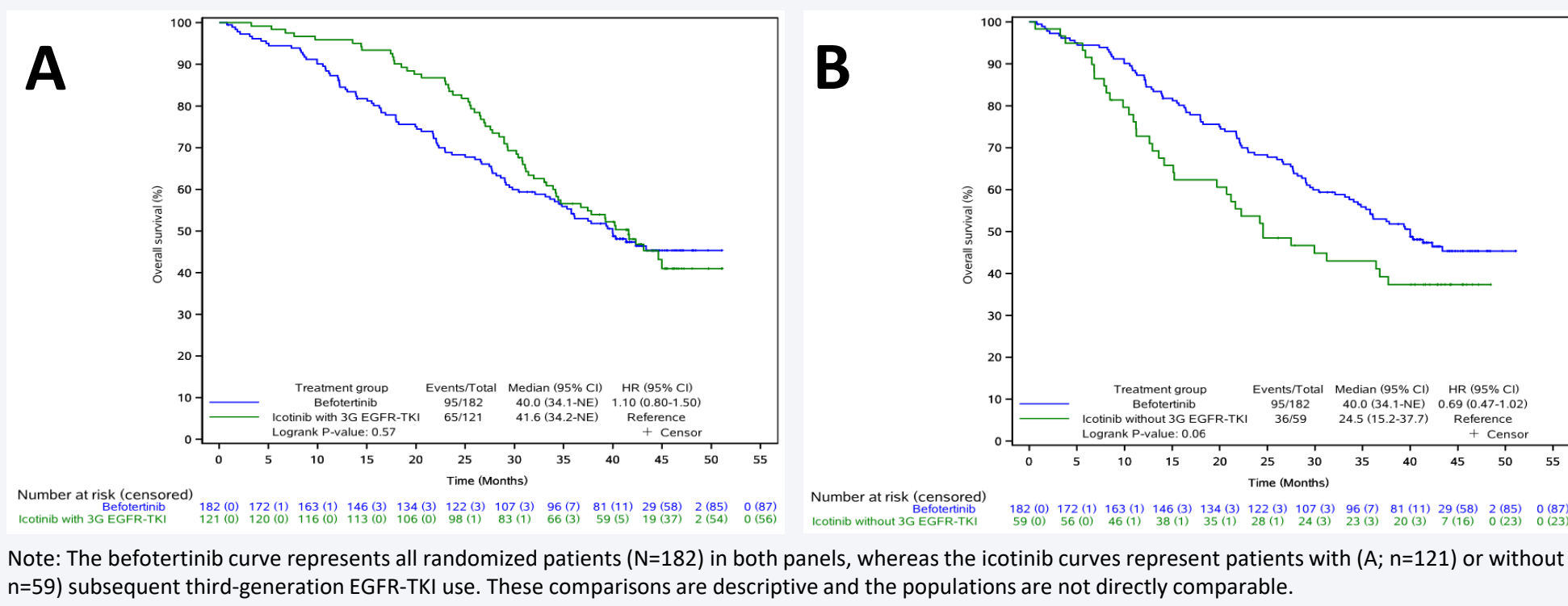


Figure 4. Kaplan-Meier curve for IRC-assessed Progression-free survival

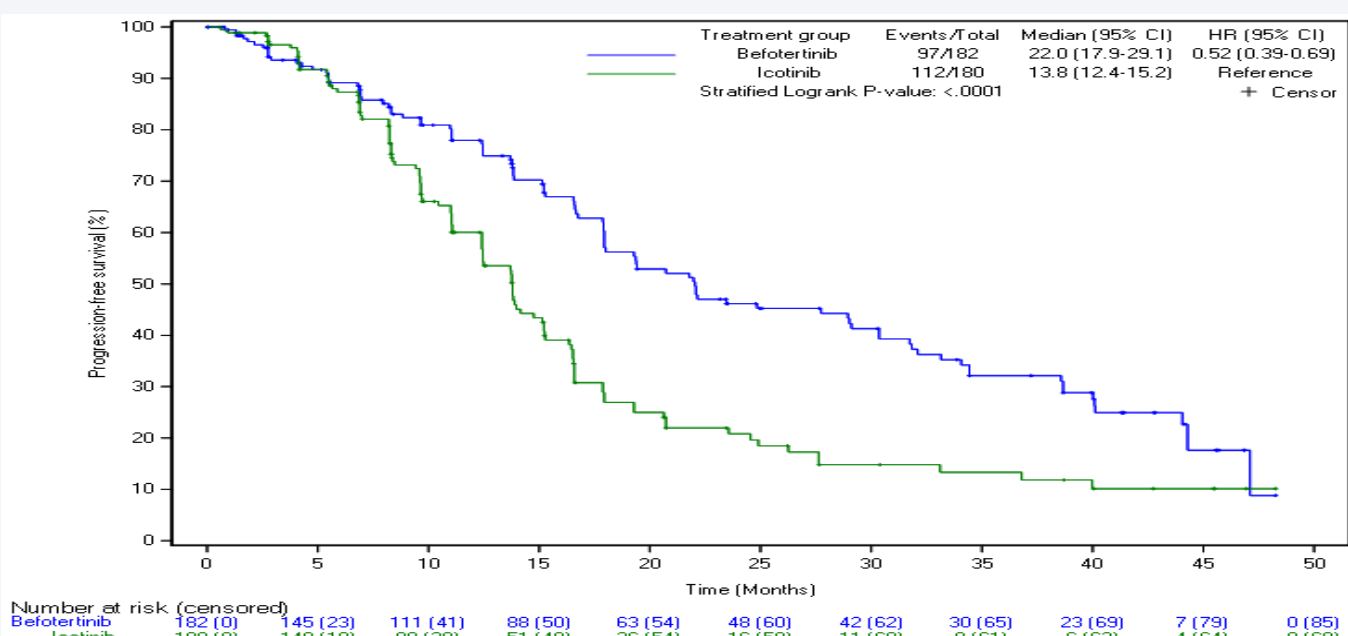


Table 1. Subsequent antitumor therapies

Subsequent therapy	Befotertinib (N = 182)	icotinib (N = 180)
Any subsequent therapy	114 (62.6%)	148 (82.2%)
Third-generation EGFR-TKI	69 (37.9%)	121 (67.2%)
Second-generation EGFR-TKI	10 (5.5%)	2 (1.1%)
First-generation EGFR-TKI	27 (14.8%)	5 (2.8%)
Chemotherapy	61 (33.5%)	79 (43.9%)
Immunotherapy	18 (9.9%)	33 (18.3%)
Antiangiogenic therapy	51 (28.0%)	65 (36.1%)
	7 (3.8%)	14 (7.8%)

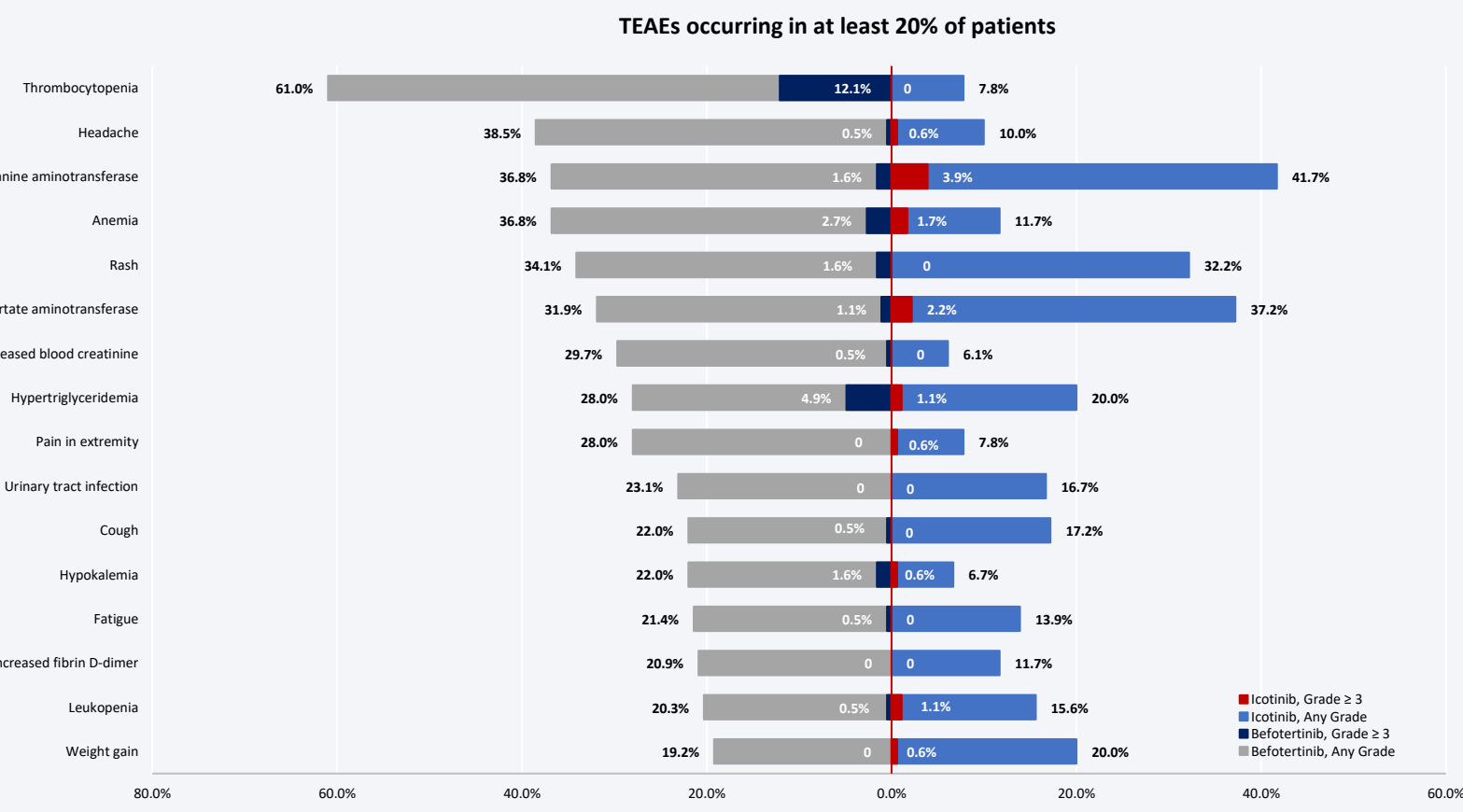
Table 2. Tumor Response

Endpoint	Befotertinib (N = 182)	icotinib (N = 180)	OR/HR	P-value
ORR (95% CI)	75.8% (68.9-81.9)	78.3% (71.6-84.1)	0.87 (0.53-1.43)	0.5753
DCR (95% CI)	94.5% (90.1-97.3)	98.3% (95.2-99.7)	0.29 (0.08-1.07)	0.0621
Median DoR, months (95% CI)	24.9 (19.1-31.8)	12.4 (11.0-13.8)	0.44 (0.32-0.60)	< 0.0001
iORR (95% CI)*	92.3% (64.0-99.8)	55.6% (30.8-78.5)	9.60 (1.02-90.34)	0.0480

Note: All efficacy endpoints were assessed by the independent review committee (IRC). *Evaluation of intracranial ORR based on 31 patients (13 patients with befotertinib and 18 patients with icotinib) who had evaluable target lesion at baseline assessed by IRC.

Safety

- Grade ≥3 TEAEs occurred in 52.7% of patients receiving befotertinib and 31.1% receiving icotinib.
- The most common grade ≥3 TEAE with befotertinib was thrombocytopenia (12.1%).
- Treatment-related deaths occurred in 1.1% and 0.6%, respectively, and no new safety signals were identified.



Conclusions

- Befotertinib provided a sustained and clinically meaningful PFS benefit versus icotinib as first-line treatment for EGFR-mutated advanced NSCLC.
- Final OS was not significantly different between treatment arms. Subsequent third-generation EGFR-TKI use was more frequent in the icotinib arm than in the befotertinib arm (67.2% vs 37.9%), including protocol-permitted crossover to befotertinib; however, the impact of subsequent therapy on OS cannot be definitively determined from this post-randomization analysis and warrants further evaluation.
- The safety profile of befotertinib remained consistent with previous analyses, with no new safety signals identified.