

363P- A multicenter, real-world observational study of efficacy and safety of first-line osimertinib treatment in patients with epidermal growth factor receptor (EGFR) activating mutation-positive advanced non-small cell lung cancer (Reiwa study)

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Comprehensive Support Project

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Background

- Osimertinib is a third-generation, irreversible EGFR-TKI that selectively inhibits both EGFR-TKI-sensitizing and EGFR-T790M (resistant) mutations.
- In a phase III trial (FLAURA), osimertinib showed efficacy superior to that of first-generation gefitinib and erlotinib, with a similar safety profile and lower rates of serious adverse events.
- Osimertinib is currently being used as the first-line treatment for patients with advanced EGFR mutation-positive NSCLC.
- However, the efficacy and safety of osimertinib treatment in real-world clinical practice have not been fully verified.

Methods

【Design】

- A multicenter, prospective cohort study in Japan

【Patients】

- EGFR mutation-positive
- Advanced or recurrent NSCLC patients
- Started EGFR-TKI treatment from September 2018 to August 2020 were enrolled
- Those receiving first-line osimertinib monotherapy were followed-up for clinical courses.

【Primary endpoint】

- Progression free survival (PFS) with osimertinib

EGFR mutation-positive NSCLC
From Sep 2018 to Aug 2020

Obtained consent (n=660)
→ Ineligible (n=1)

Osimertinib (n=583)

Other EGFR-TKI (n=76)

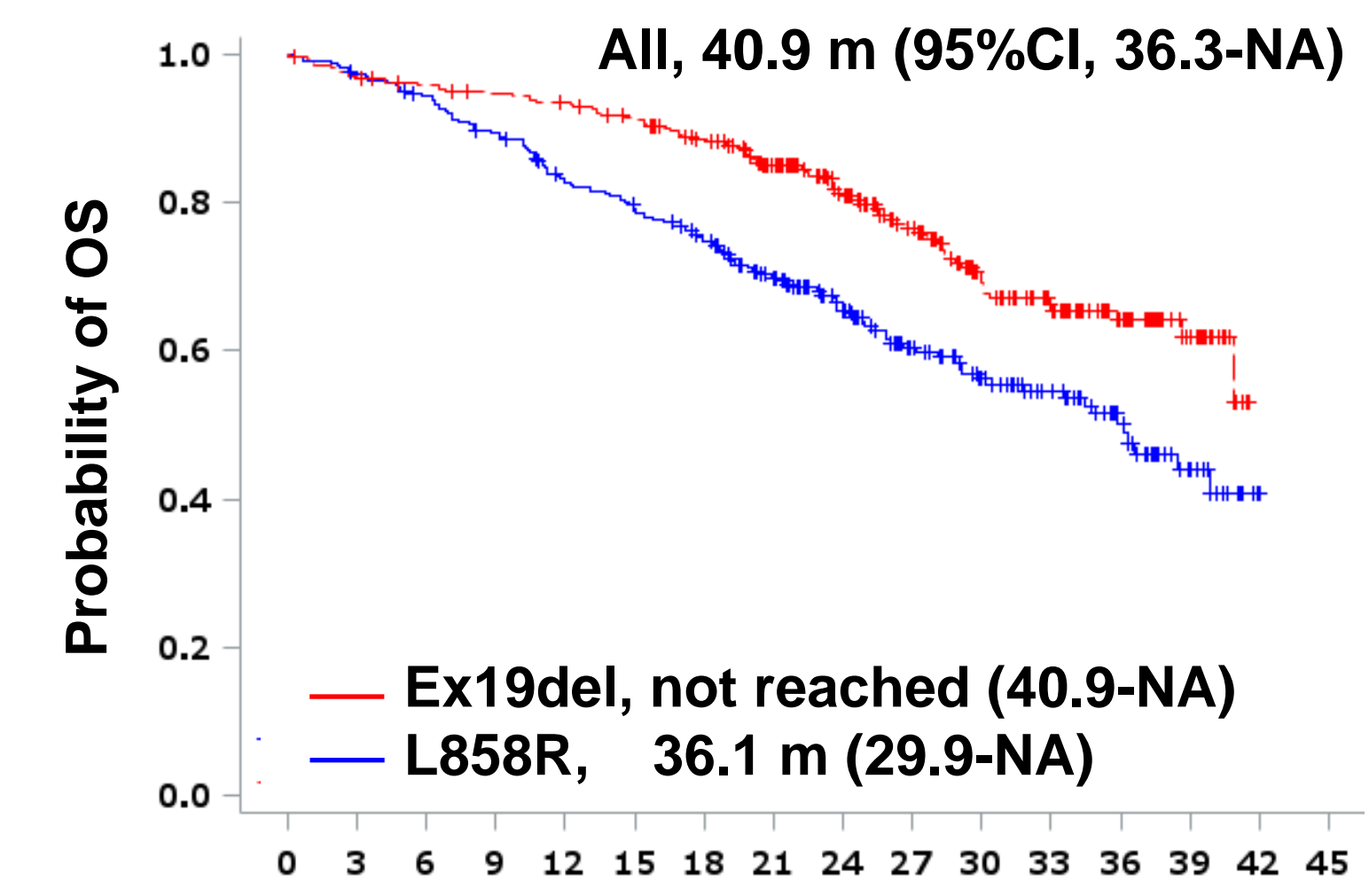
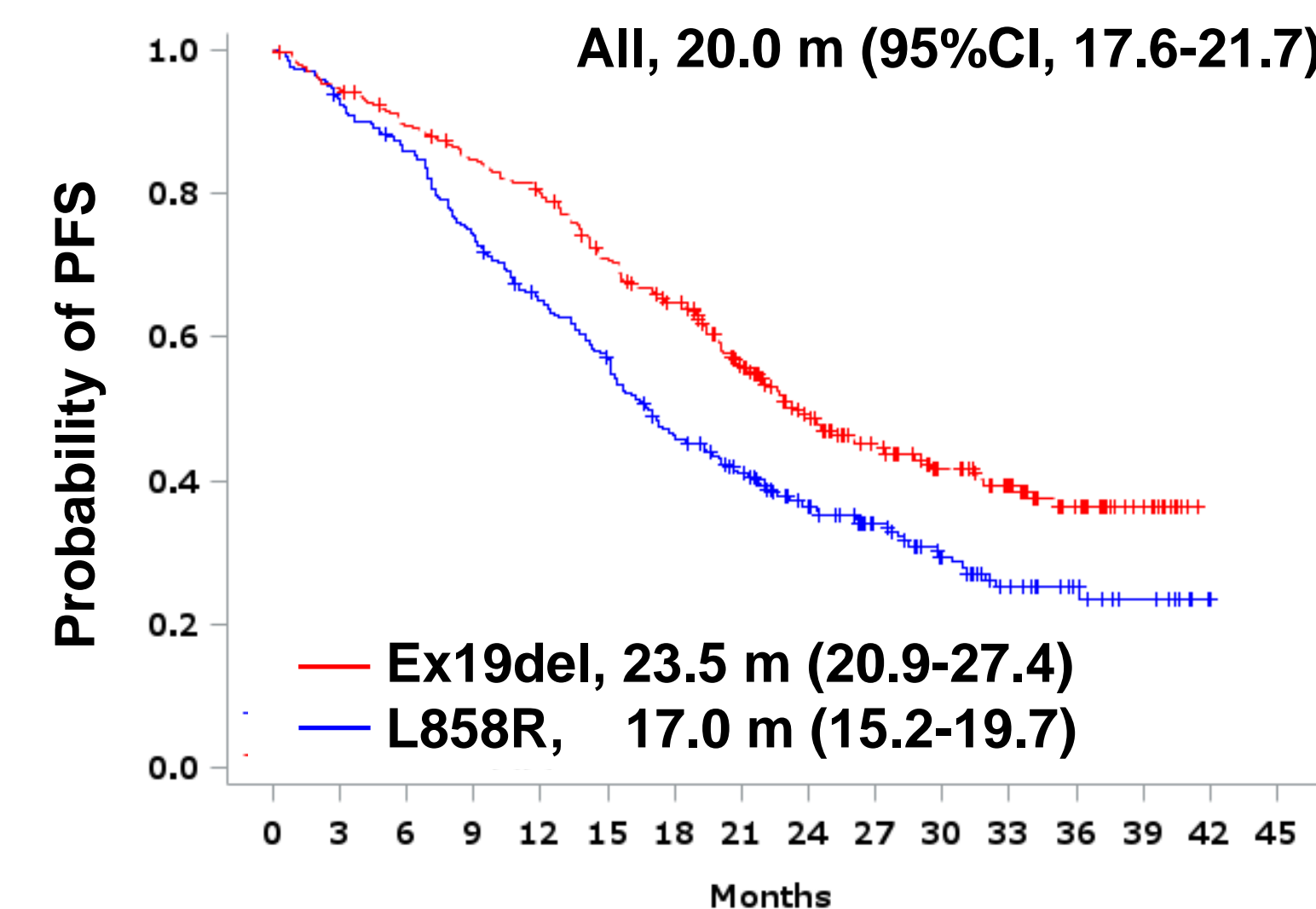
A survey was conducted once every six months

Follow-up period median 24.6 months (range, 0.1-42.0)

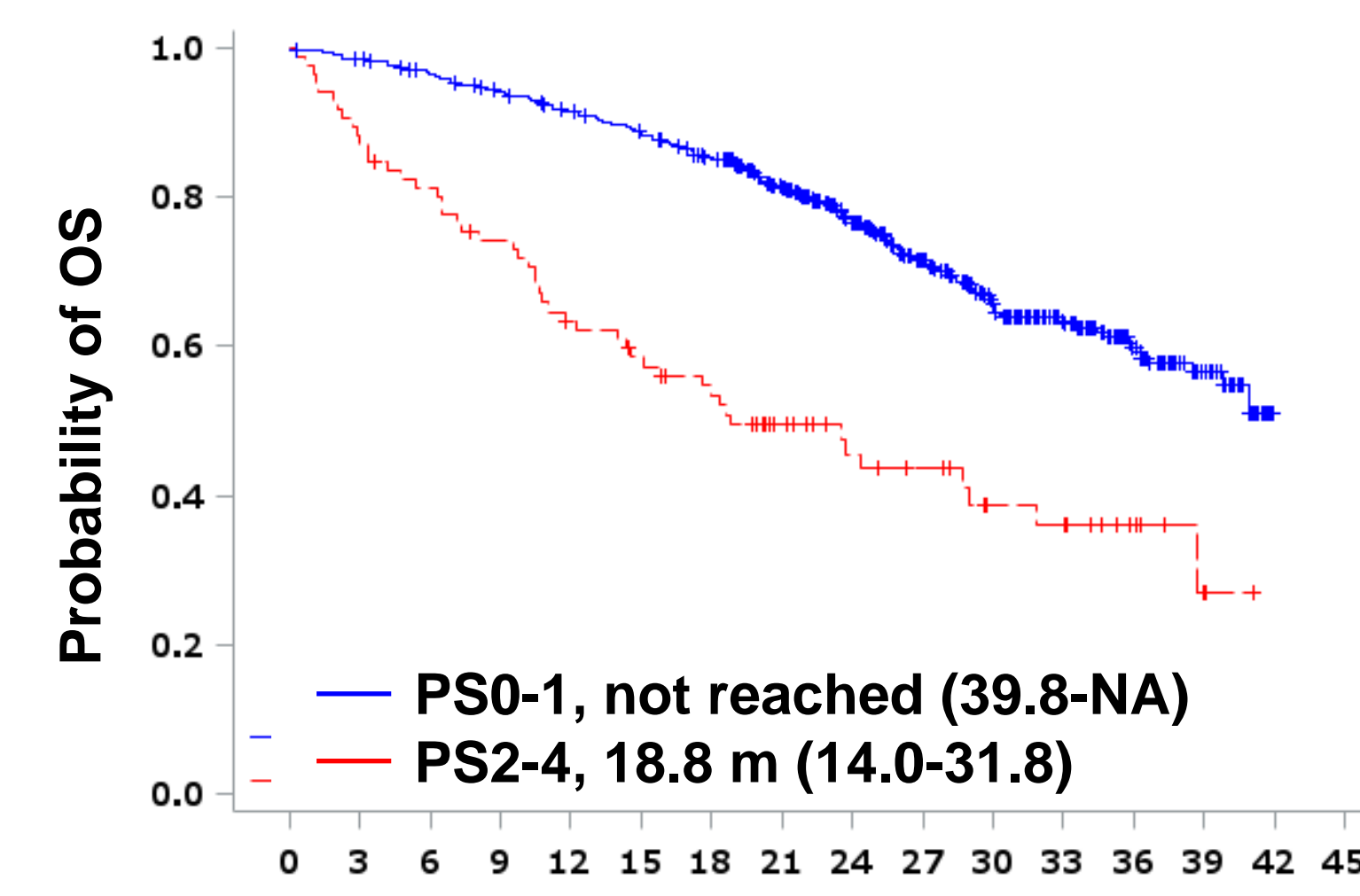
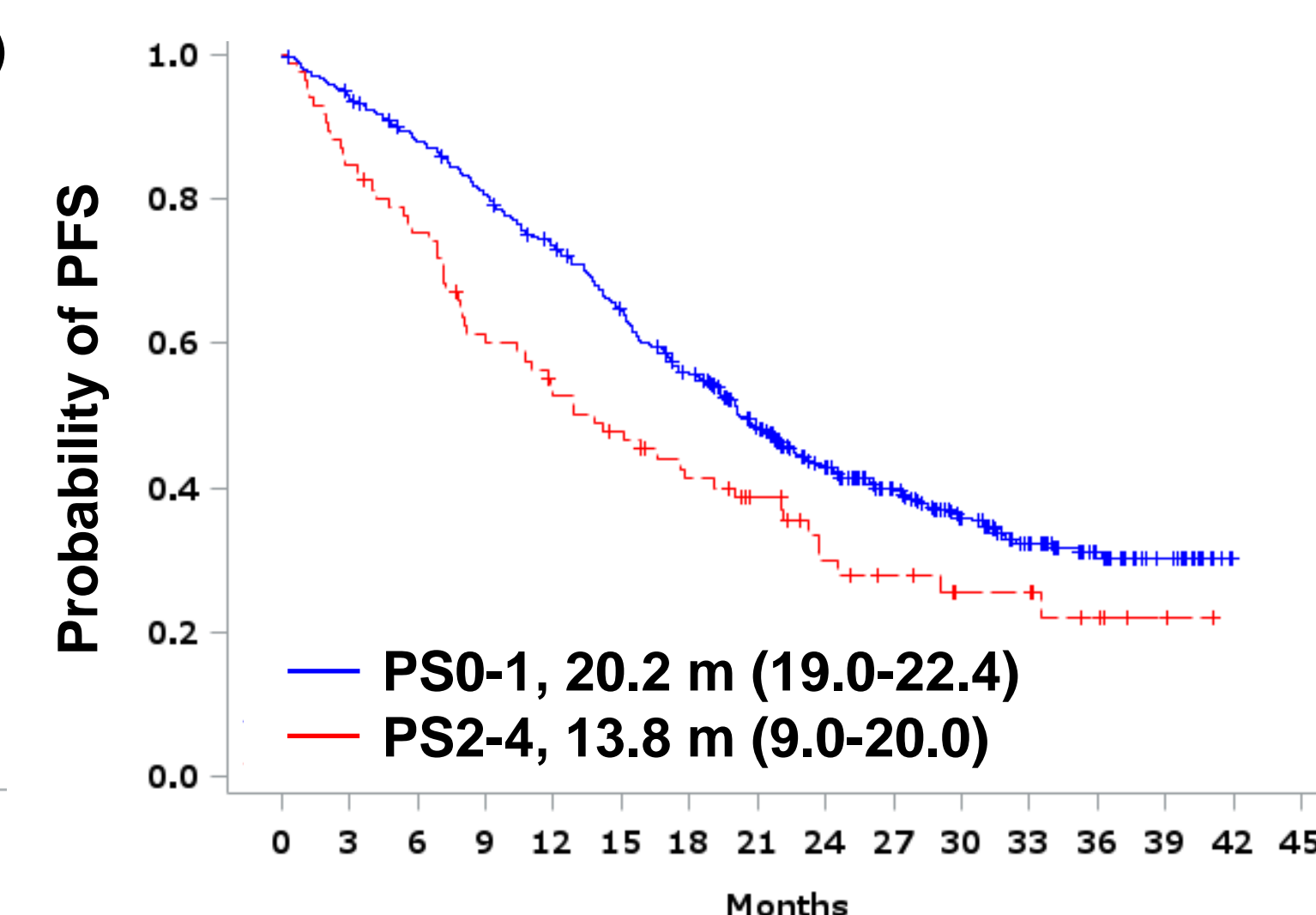
Patient Characteristics (n=583)

	n (%)
Age, years median (range)	72 (30-95)
Gender male female	224 (38.4) 359 (61.6)
ECOG PS 0 1 2 3 4 missing	216 (37.1) 281 (48.2) 60 (10.3) 20 (3.4) 2 (0.3) 4 (0.7)
Smoking status never former current	325 (55.8) 224 (38.4) 34 (5.8)
Histology adeno squamous NOS LCNEC	571 (97.9) 9 (1.5) 2 (0.3) 1 (0.1)
Mutation type* Ex19del L858R others	285 (48.9) 266 (45.6) 33 (5.7)
*One patient had both Ex19del and L858R mutations	
Stage locally advanced metastatic recurrence	9 (1.5) 384 (65.9) 190 (32.6)
Brain metastases yes no	169 (29.0) 414 (71.0)

Survival by mutation type



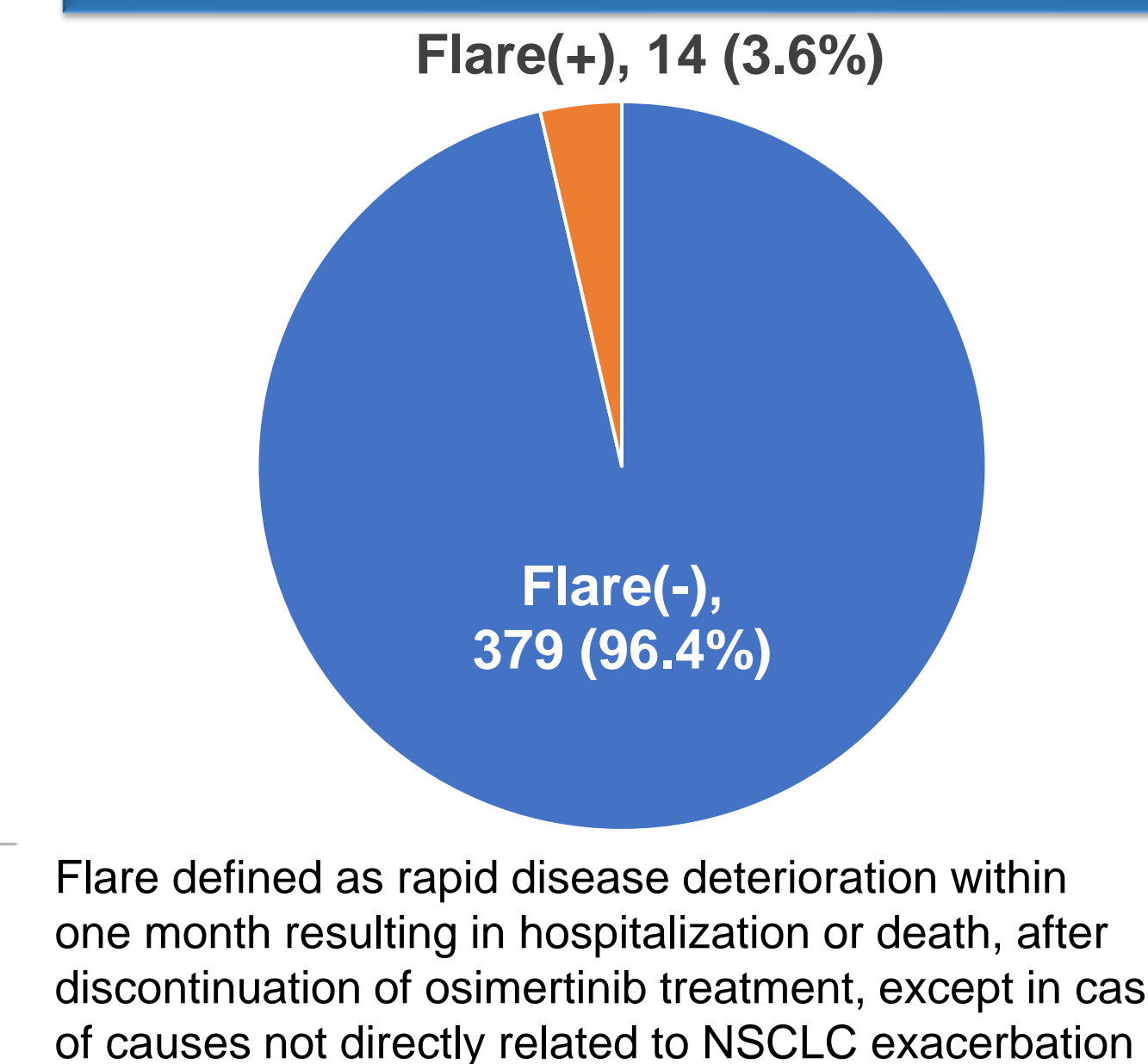
Survival by ECOG PS



Adverse events

Pneumonitis, n (%)	PS 0-1	PS 2-4
Any grade	67 (13.4)	8 (9.3)
Grade 1	19 (3.8)	2 (2.3)
Grade 2	34 (6.8)	2 (2.3)
Grade 3	10 (2.0)	2 (2.3)
Grade 4	4 (0.8)	2 (2.3)
Grade 5	0	0

Disease flare



Exacerbation pattern

n (%)	Asymptomatic and no clinical exacerbation	Symptomatic and no clinical exacerbation	Clinical exacerbation	total
CNS metastasis	15 (4.8)	4 (1.3)	17 (5.4)	36 (11.4)
Single organ other than CNS (up to 3 per organ)	94 (30.0)	28 (8.9)	16 (5.1)	138 (43.7)
Multiple organs	66 (20.9)	37 (11.7)	39 (12.3)	142 (44.9)
Total	175 (55.4)	69 (21.8)	72 (22.8)	316 (100)

AE ≥ Grade 3, n (%)	PS 0-1	PS 2-4
All events	105 (21.3)	27 (31.4)
Pneumonitis	14 (2.8)	4 (4.7)
Rash	14 (2.8)	3 (3.5)
AST/ALT increased	10 (2.0)	3 (3.5)
Neutropenia	9 (1.8)	1 (1.2)
Paronychia	9 (1.8)	0 (0)
Anorexia	8 (1.6)	3 (3.5)
Anemia	7 (1.4)	3 (3.5)
Diarrhea	4 (0.8)	2 (2.3)
Thrombocytopenia	4 (0.8)	1 (1.2)
Leukopenia	3 (0.6)	1 (1.2)
Prolonged QT interval	2 (0.4)	2 (2.3)

AE leading to discontinuation, n (%)	PS 0-1	PS 2-4
All events	95 (19.1)	21 (24.4)
Pneumonitis	48 (9.7)	5 (5.8)
Hematotoxicity	6 (1.2)	1 (1.2)
Rash	6 (1.2)	5 (5.8)
Paronychia	6 (1.2)	0 (0)
AST/ALT increased	3 (0.6)	2 (2.3)
Prolonged QT interval	1 (0.2)	2 (2.3)

Conclusion

- Osimertinib showed activity with a manageable safety profile in clinical practice, consist with results of previous clinical trials.
- Efficacy was different according to mutation type.
- More evidence is needed for patients with poor PS.

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