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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Conflict of Interest disclosure slide for representative speakers or investigators

Research fund	■scientific research fund □contract □donation □other （ ） □N/A	Sponsor	This study was coordinated by Public Health Research Foundation with funding from AstraZeneca.

Name of lead presenter	Susumu Takeuchi	Institution or company/position	Tokyo Medical University

	No	If yes, please specify the name of company, organization, your status.
employee or adviser of company and/or profit-making organization	■	
profit of stock	■	
patent fee	■	
lecturer fee	□	AstraZeneca, Taiho, Ono, Nippon Kayaku, Kyowa Kirin, Eli Lilly and Company Japan, Bristol Myers Squibb, Novartis Japan, MSD and Chugai Pharmaceutical Company Ltd.
manuscript fee	■	
research expenses from company	■	
contributions or endowed chair	■	
fees of testimony, judgment, comment, etc.	■	
presents or other payment	■	
representative of organization for clinical study receiving research expenses from company	■	

Name of principal investigator	Hideo Kunitoh	Institution or company/position	Japanese Red Cross Medical Center

	No	If yes, please specify the name of company, organization, your status.
employee or adviser of company and/or profit-making organization	■	
profit of stock	■	
patent fee	■	
lecturer fee	□	AstraZeneca, Boehringer Ingelheim, Chugai, Daiichi-Sankyo, Johnson and Johnson
manuscript fee	■	
research expenses from company	■	
contributions or endowed chair	■	
fees of testimony, judgment, comment, etc.	■	
presents or other payment	■	
representative of organization for clinical study receiving research expenses from company	■	

Background

- Osimertinib is a third-generation, irreversible epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitor (TKI) that selectively inhibits both EGFR-TKI-sensitizing and EGFR-T790M-resistant mutations.

- In a phase III FLAURA trial for untreated EGFR-mutated advanced non-small cell lung cancer (NSCLC), osimertinib showed efficacy superior to that of first-generation gefitinib and erlotinib, with a similar safety profile and lower rates of serious adverse events.

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Background

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- 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 clinical practice have not been fully verified.

Objectives

We performed a multicentre, prospective cohort study to evaluate the activity of osimertinib treatment in clinical practice.

Inclusion Criteria

- EGFR mutation-positive
- Advanced or recurrent NSCLC patients
- Those receiving first-line osimertinib monotherapy were followed-up for clinical courses.

Primary Endpoint

・Progression free survival (PFS) with osimertinib

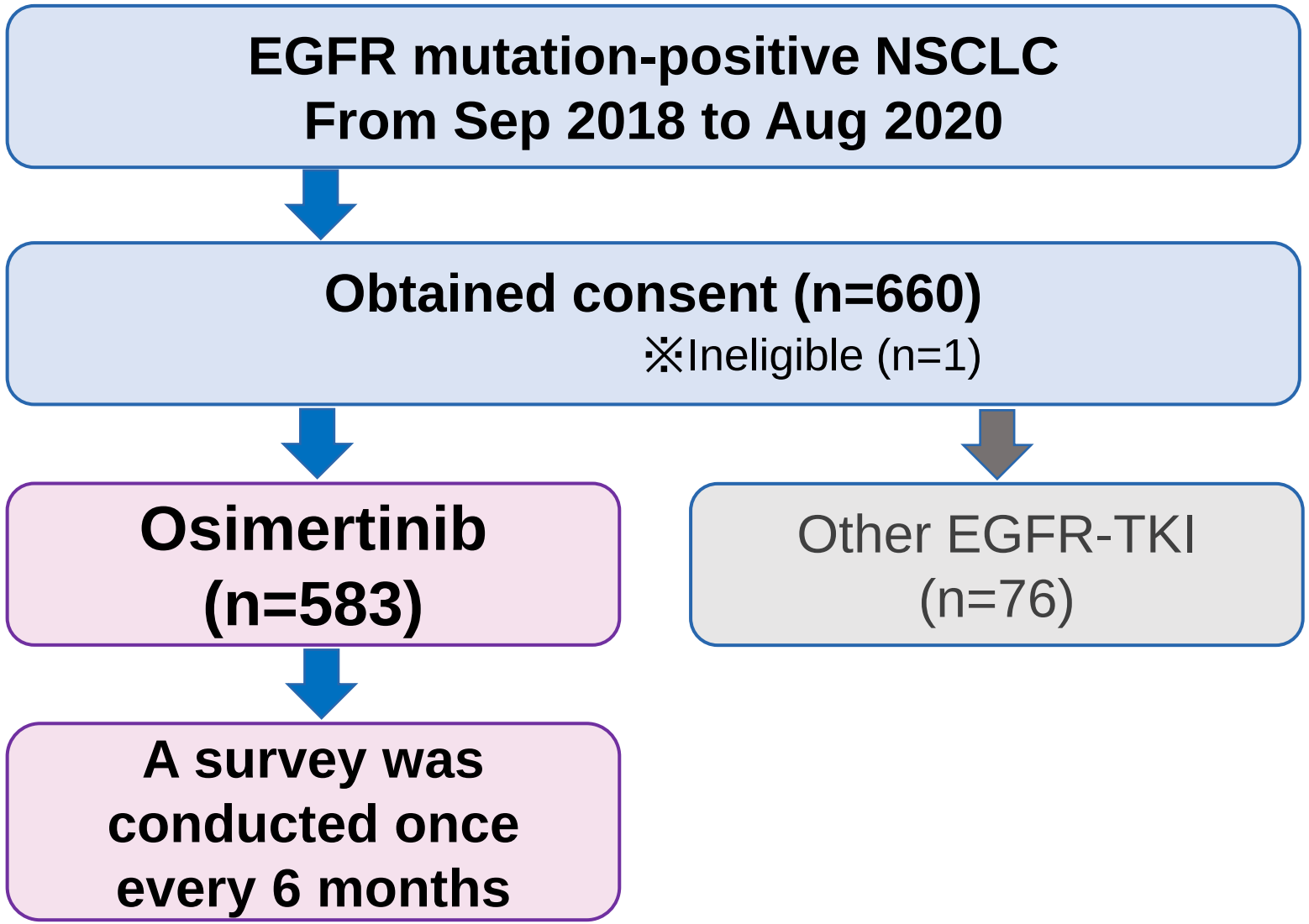
Secondary Endpoint

・Overall survival (OS)

・Objective Response Rate (ORR)

・Adverse events

Patient Flow Chart



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Patient Characteristics (n=583)

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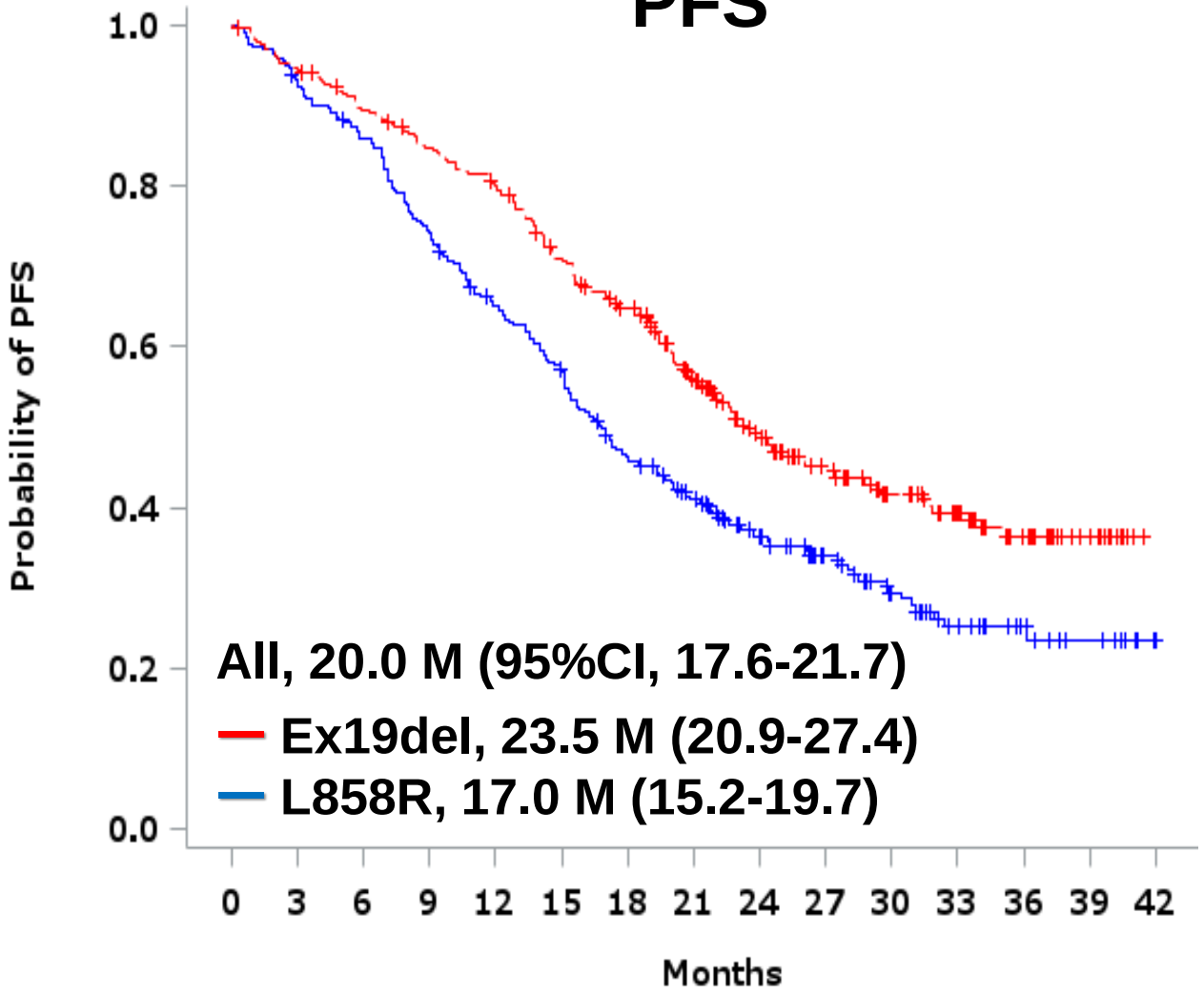
	n (%)
Age, years	
median (range)	72 (30-95)
Gender	
male	224 (38.4)
female	359 (61.6)
ECOG PS	
0	216 (37.1)
1	281 (48.2)
2	60 (10.3)
3	20 (3.4)
4	2 (0.3)
missing	4 (0.7)
Smoking status	
never	325 (55.8)
former	224 (38.4)
current	34 (5.8)
Histology	
adeno	571 (97.9)
squamous	9 (1.5)
NOS	2 (0.3)
LCNEC	1 (0.1)

	n (%)
Mutation type*	
Ex19del	285 (48.9)
L858R	266 (45.6)
others	33 (5.5)
Stage	
locally advanced	9 (1.5)
metastatic	384 (65.9)
recurrence	190 (32.6)
Brain metastases	
yes	169 (29.0)
no	414 (71.0)

*One patient had both Ex19del and L858R mutations

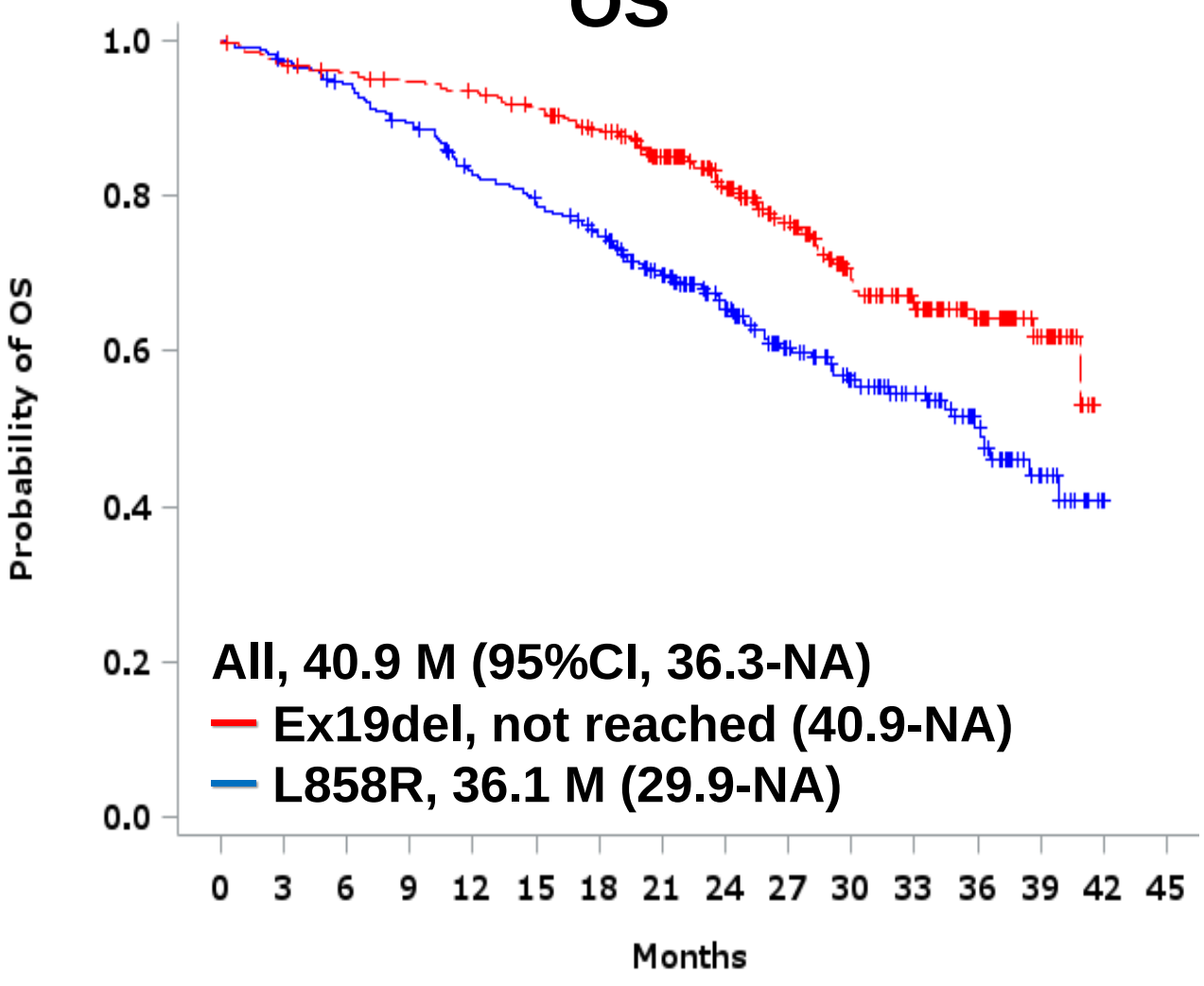
PFS and OS by EGFR mutation type

PFS



Ex 21 L858R	265	244	226	195	168	147	117	97	72	54	38	24	16	10	0
Exon 19 del	285	268	251	236	222	194	172	135	103	81	61	46	28	13	0

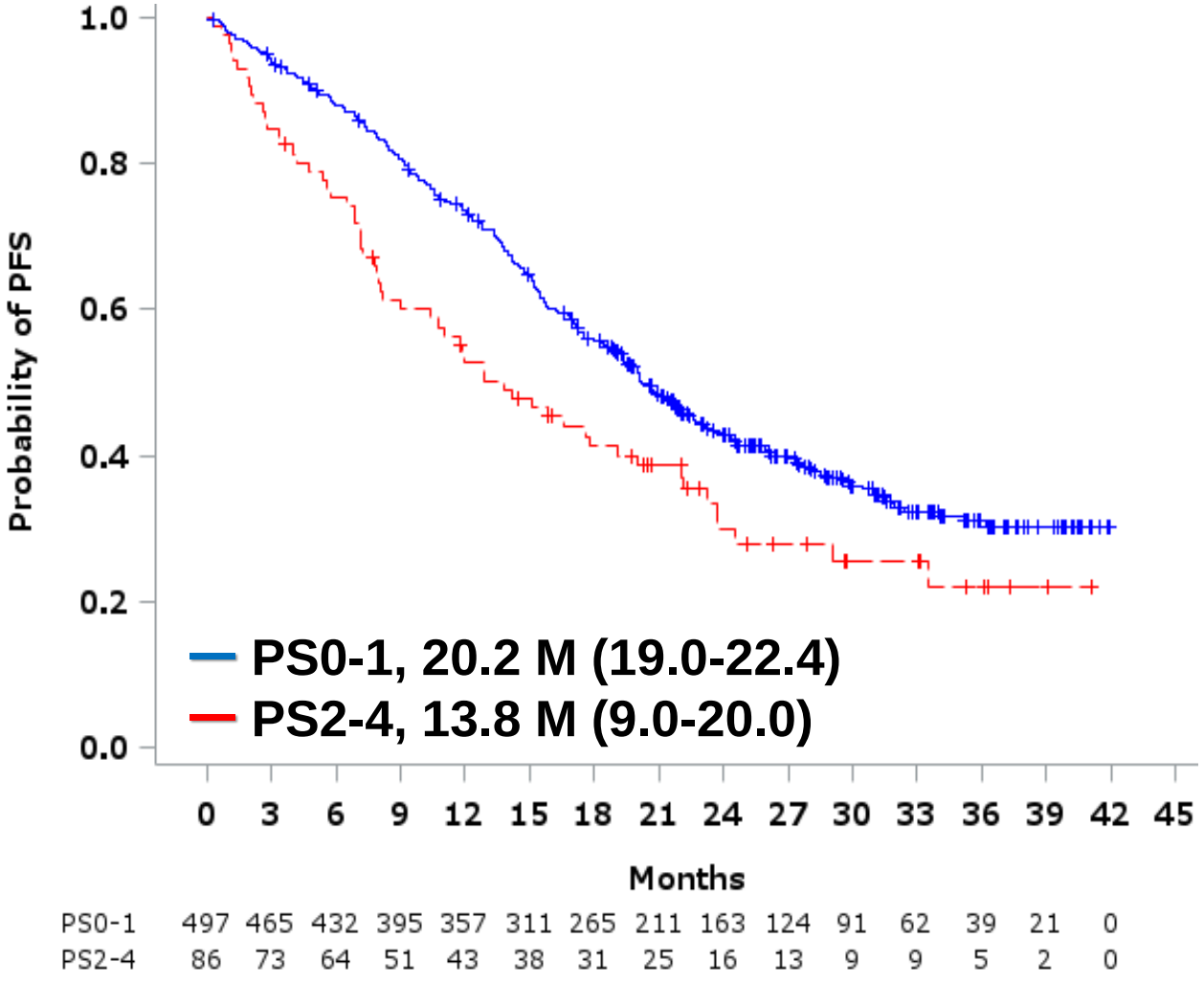
OS



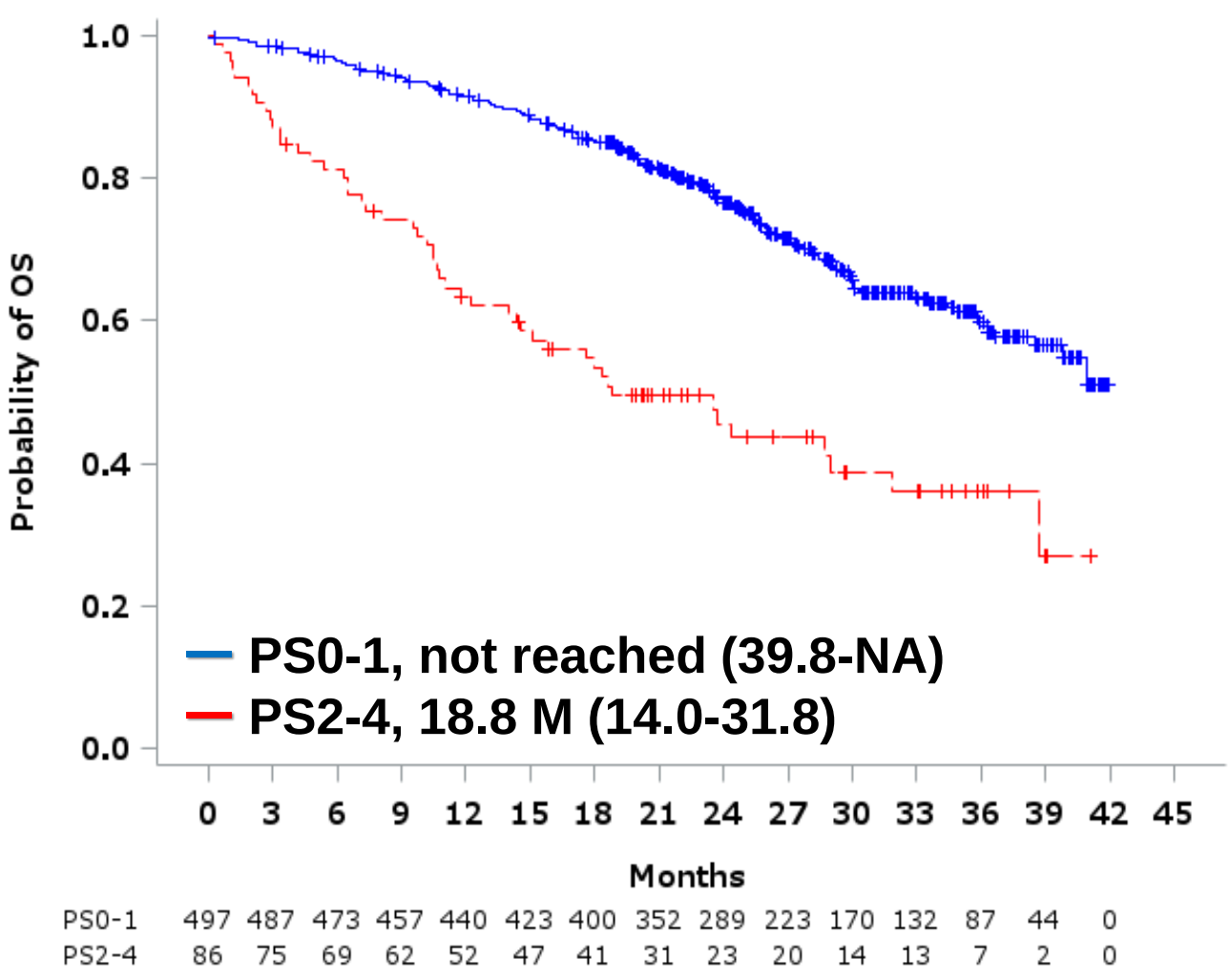
Ex 21 L858R	265	257	247	233	212	202	187	160	129	95	76	59	39	19	0
Exon 19 del	285	275	269	264	260	250	236	208	171	139	100	78	51	24	0

PFS and OS by ECOG PS

PFS



OS



Objective Response Rate (ORR)

Overall response rate：68% (95%CI, 63.8-71.5)

Disease control rate：87% (95%CI, 83.7-89.4)

Response to the therapy	n (%)
Complete response (CR)	17 (2.9)
Partial response (PR)	378 (64.8)
Stable Disease (SD)	111 (19.1)
Progressive disease (PD)	46 (7.9)
Not evaluable (NE)	28 (4.8)

Exacerbation pattern

n (%)	Asymptomatic and no clinical exacerbation	Symptomatic and no clinical exacerbation	Clinical exacerbation	Total
CNS-only metastasis	15 (4.8)	4 (1.3)	17 (5.4)	**36 (11.4)**
Single organ other than CNS (up to 3 lesions)	94 (29.7)	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)**

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Adverse events

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AE ≧ Grade 3, n (%)	Total	PS 0-1	PS 2-4
All events	**132 (22.6)**	**105 (21.3)**	**27 (31.4)**
Pneumonitis	**18 (3.1)**	14 (2.8)	4 (4.7)
Rash	**17 (2.9)**	14 (2.8)	3 (3.5)
AST/ALT increased	**13 (2.2)**	10 (2.0)	3 (3.5)
Neutropenia	**10 (1.7)**	9 (1.8)	1 (1.2)
Paronychia	**9 (1.5)**	9 (1.8)	0 (0)
Anorexia	**11 (1.9)**	8 (1.6)	3 (3.5)
Anemia	**10 (1.7)**	7 (1.4)	3 (3.5)
Diarrhea	**6 (1.0)**	4 (0.8)	2 (2.3)
Thrombocytopenia	**5 (0.9)**	4 (0.8)	1 (1.2)
Prolonged QT interval	**4 (0.7)**	2 (0.4)	2 (2.3)

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Adverse events leading to discontinuation

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AE leading to discontinuation, n (%)	Total	PS 0-1	PS 2-4
All events	**116 (20.0)**	**95 (19.1)**	**21 (24.4)**
Pneumonitis	**53 (9.1)**	48 (9.7)	5 (5.8)
Hematological toxicity	**7 (1.2)**	6 (1.2)	1 (1.2)
Rash	**11 (1.9)**	6 (1.2)	5 (5.8)
Paronychia	**16 (1.0)**	6 (1.2)	0 (0)
AST/ALT increased	**5 (0.9)**	3 (0.6)	2 (2.3)
Prolonged QT interval	**3 (0.5)**	1 (0.2)	2 (2.3)

Pneumonitis

n (%)	Total	PS 0-1	PS 2-4
All grade	**75 (12.9)**	**67 (13.4)**	**8 (9.3)**
Grade 1	**21 (3.6)**	19 (3.8)	2 (2.3)
Grade 2	**36 (6.2)**	34 (6.8)	2 (2.3)
Grade 3	**12 (2)**	10 (2.0)	2 (2.3)
Grade 4	**6 (1.0)**	4 (0.8)	2 (2.3)
Grade 5	**0**	0	0

Conclusion

This study reproduced the efficacy and safety results of osimertinib in FLAURA trial in real-world Japanese patients.

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List of Investigator Sites

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KKR Sapporo Medical Center	Kyorin University Hospital	Fujisawa City Hospital
Hokkaido University Hospital	Japanese Red Cross Medical Center	Kanagawa Cancer Center
Iwate Prefectural Central Hospital	National Center for Global Health and Medicine	Showa University Northern Yokohama Hospital
Tohoku University Hospital	Showa University Hospital	Niigata Cancer Center Hospital
Japanese Red Cross Akita Hospital	Tokyo Medical University Hospital	Kanazawa University Hospital
Ibaraki Prefectural Central Hospital	Tokyo Saiseikai Central Hospita	Shinshu University Hospital
Gunma University Hospital	Toho University Omori Medical Center	Hamamatsu University Hospital
Kasukabe Medical center	Mitsui Memorial Hospital	Osaka Medical and Pharmaceutical University Hospital
National Cancer Center Hospital East	Juntendo University Hospital	Hyogo Prefectural Amagasaki General Medical Center
NTT Medical Center Tokyo	Tokyo Metropolitan Police Hospital	Okayama University Hospital
Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital	Kitasato University Hospital	Ehime University Hospital
	Yokohama Municipal Citizen's Hospital	Okinawa National Hospital