Phase II study of brigatinib in ROS1 positive non-small cell lung cancer patients previously treated with crizotinib: Barossa cohort 2.

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IASLC 2021 World Conference on Lung Cancer
SEPTEMBER 8 - 14, 2021 I WORLDWIDE VIRTUAL EVENT

Presenter DISCLOSURES

Ineligible Company (formerly: Commercial Interest)	**Relationship(s)**
Eli Lilly	Research grant (institution)

Background

- The ROS1 protein is a proto-oncogene receptor tyrosine kinase involved in proliferation and differentiation of cells.
- ROS1 rearrangements occur in approximately 1% of patients with non-small cell lung cancer (NSCLC) and other solid tumors.
- Crizotinib is the first drug approved for the treatment of ROS1 fusion-positive NSCLC.
- Standard treatment for crizotinib-resistant ROS1-positive NSCLC is not established.
- Brigatinib is a next-generation tyrosine kinase inhibitor targeting ALK and ROS1.
- Barossa is a multicenter, phase II basket study of brigatinib in patients with ROS1-positive solid tumors.

Study design

- Advanced solid tumor
- ROS1 fusion-positive
- 20 years or older
- ECOG PS 0-2
- Measurable lesion according to RECIST1.1

Enroll

Brigatinib 180mg/day, once daily
(lead-in: 90mg/day for 7 days)
28 days cycle
Until PD or unacceptable toxicities

Cohort 1: Crizotinib-naïve ROS1+ NSCLC (n=28)

Cohort 2: Crizotinib-treated ROS1+ NSCLC (n=19)

Cohort 3: ROS1+ solid tumor other than lung cancer (n≤5)

Primary endpoint: Overall response rate (ORR) by independent review (RECIST 1.1)

Secondary endpoints: Overall survival (OS), progression-free survival (PFS), intracranial ORR, intracranial PFS, time to intracranial progression, safety

- The sample size was set at 19 subjects, with a one-sided alpha of 0.05, a beta of 0.2, and threshold and expected values for the primary endpoints of 20% and 50% in the cohort 2.
- Clinical trial information: JapicCTI-194851

Patient eligibility

Key inclusion criteria (cohort 2):

- **Advanced or recurrent NSCLC with ROS1 fusion which was determined by a validated RT/PCR or NGS using tissues or blood**
- **Prior treatment of crizotinib (other ROS1 inhibitors were not allowed)**
- **Age ≥ 20 years**
- **ECOG performance status (PS) of 0-2**
- **Adequate organ function**
- **Written informed consent**

Key exclusion criteria

- **ALK fusion gene positive**
- **Symptomatic brain metastases**
- **Interstitial fibrosis or interstitial lung disease**

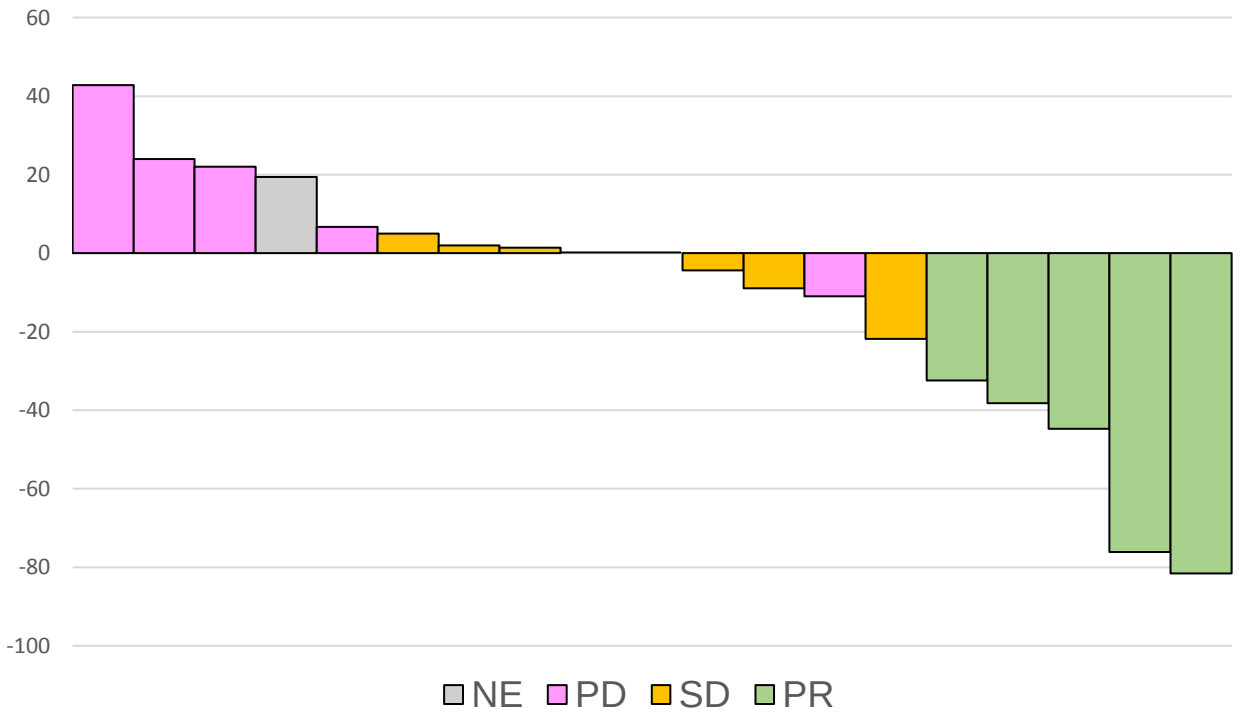
Patient characteristics (n=19)

		No.
Age (years)	Median (range)	60 (31-75)
Gender	Male	9
	Female	10
PS	0-1	18
	2	1
Histological type	Adenocarcinoma	18
	Squamous cell carcinoma	1
Brain metastasis		14
Prior cytotoxic chemotherapy		17
Prior PD-1/PD-L1 inhibitor		4
Prior crizotinib as the latest treatment		9

Treatment delivery (n=19)

Median duration of treatment (days) (range)	172 (13-479)
Dose reduction (n)	5
Treatment interruption (n)	14
Median duration of interruption (days) (range)	13.5 (1-75)

Response assessed by independent review

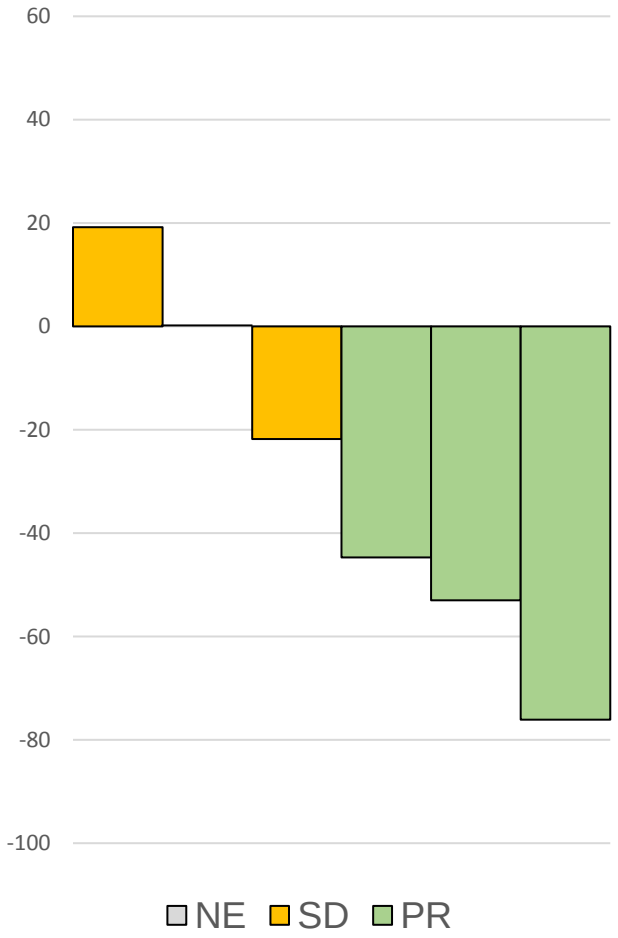


Overall Response	No.
PR	5
SD	6
PD	7
NE	1

ORR: 26.3% **(90%CI, 11.0-47.6)**
(95%CI, 9.1-51.2)
DCR: 57.9% **(95%CI, 33.5-79.7)**

Confirmed PR and SD are indicated.

Intracranial response assessed by independent review



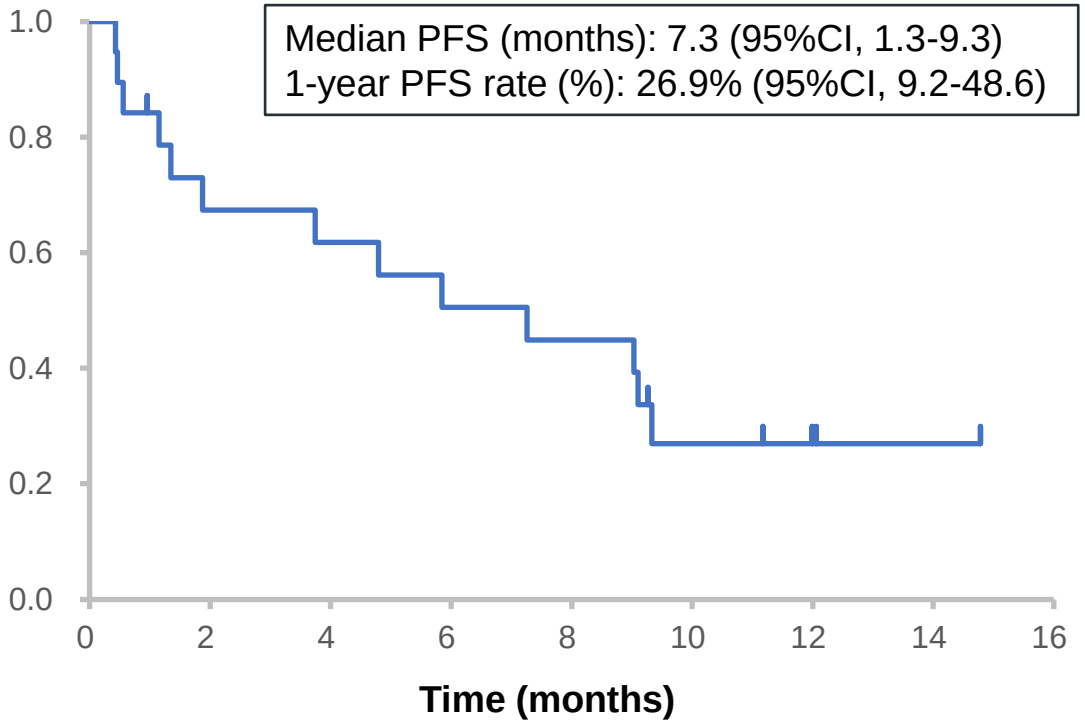
Intracranial Response	No.
PR	3
SD	2
PD	0
NE	1

iORR: 50.0% (95%CI, 11.8-88.2)
iDCR: 83.3% (95%CI, 35.9-99.6)

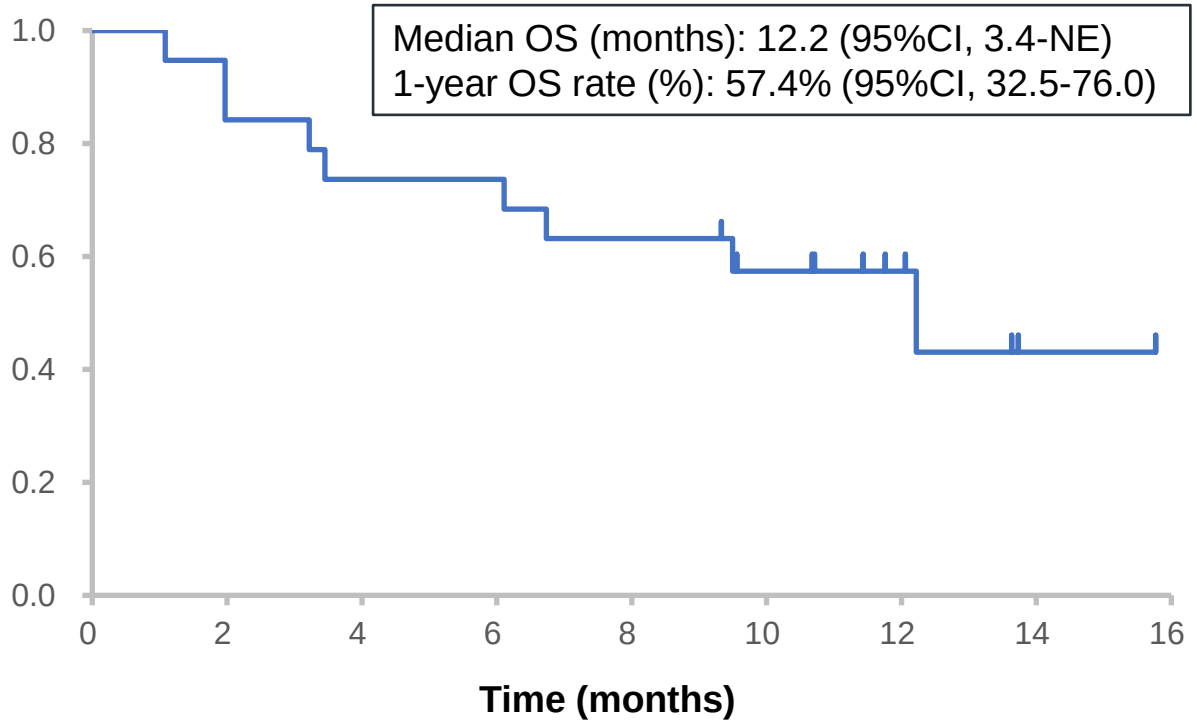
Six patients had measurable brain metastases.

PFS and OS

PFS assessed by independent review



OS



Data cut-off: 30 Oct 2020, median follow-up time: 12.0 months

Post-study treatment

	No.
Study treatment ongoing	10
Study treatment termination	9
Post-study treatment received	9
Cytotoxic chemotherapy	4
PD-1 inhibitor	2
Entrectinib	1
Crizotinib	1
Whole brain irradiation	1

Treatment-related adverse events

Grade	1	2	3	≥ 3 (%)
Hypertension	1	3	1	5.3
Diarrhea	6	0	0	0
Constipation	3	1	0	0
Mucositis oral	2	0	0	0
Headache	2	0	0	0
Anorexia	1	0	1	5.3
Erythema	0	0	1	5.3
Photosensitivity	1	1	0	0
Facial edema	1	1	0	0
Infection	0	0	1	5.3
Hypoxia	0	0	1	5.3
Pneumonitis	0	1	0	0
CPK increased	2	3	4	21.1
Amylase increased	4	2	0	0
AST increased	5	1	0	0
ALT increased	3	1	0	0
Lipase increased	0	5	0	0
ALP increased	2	0	0	0

- **No grade 4 or 5 treatment-related adverse event was observed.**

Take home messages

- **Brigatinib has modest activity for ROS1-positive NSCLC patients previously treated with crizotinib, although the primary endpoint was not met.**
- **Intracranial activity of brigatinib was promising.**
- **The safety profile of brigatinib was consistent with previous studies.**
- **Enrollment of the cohort 1 for ROS1 inhibitor-naïve NSCLC patients has been completed, and the data will be presented at a future congress.**

Acknowledgements and disclosure

- We would like to thank all the patients, the investigators and the institutes that participated in this trial.
- This study is supported by grants from the Practical Research for Innovation Cancer Control from the Japan Agency for Medical Research and Development, AMED (21ck0106655h0001).
- Brigatinib was provided by Takeda Pharmaceutical Company Limited.