



European Lung
Cancer Congress 2023

Updated Efficacy and Safety of Taletrektinib in Patients with ROS1⁺ Non-Small Cell Lung Cancer

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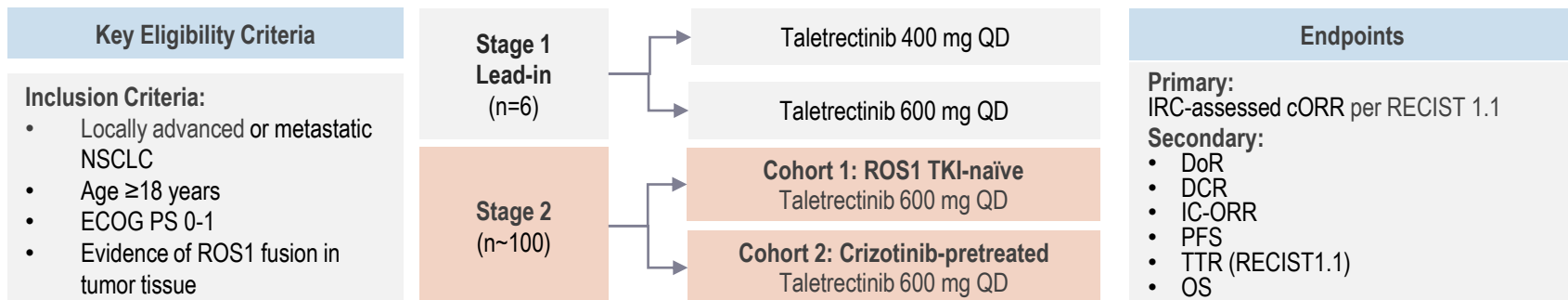
Declaration of Interests

I have no conflict of interest to declare.



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TRUST-I (NCT04395677): Phase II Trial of Talretrectinib in ROS1⁺ NSCLC



Key Demographics	TKI-Naïve N=67 (%)	Crizotinib-Pretreated N=42 (%)	Total ^a N=109 (%)
Male, n (%)	28 (41.8)	16 (38.1)	44 (40.4)
Age, median (range)	54 (26, 75)	52 (31, 77)	54 (26, 77)
ECOG PS 0/1, n (%)	11 (16.4)/ 56 (83.6)	17 (40.5)/ 25 (59.5)	28 (25.7)/ 81 (74.3)
Adenocarcinoma, n (%)	64 (95.5)	38 (90.5)	102 (93.5)
Prior chemotherapy, n (%)	15 (22.4)	14 (33.3)	29 (26.6)
Non-smoker/current smoker, n (%)	62 (92.5)/ 5 (7.5)	42 (100.0)/0	104 (95.4)/ 5 (4.6)
Brain Metastasis, n (%)	8 (11.9)	16 (38.1)	24 (22.0)



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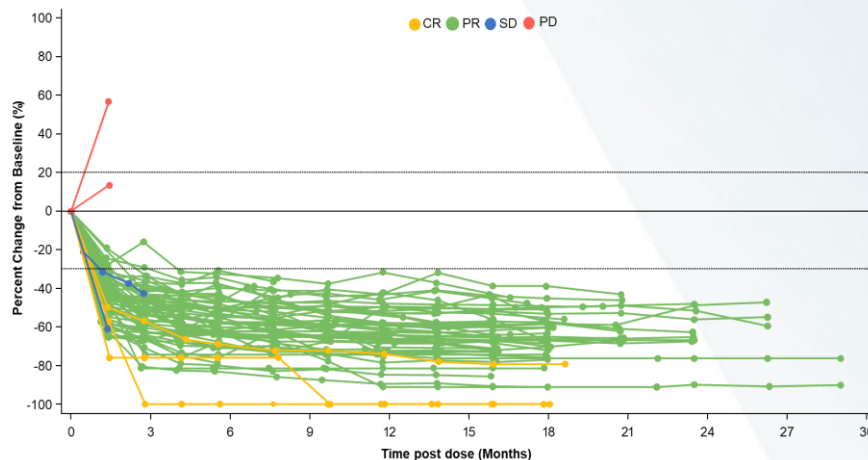
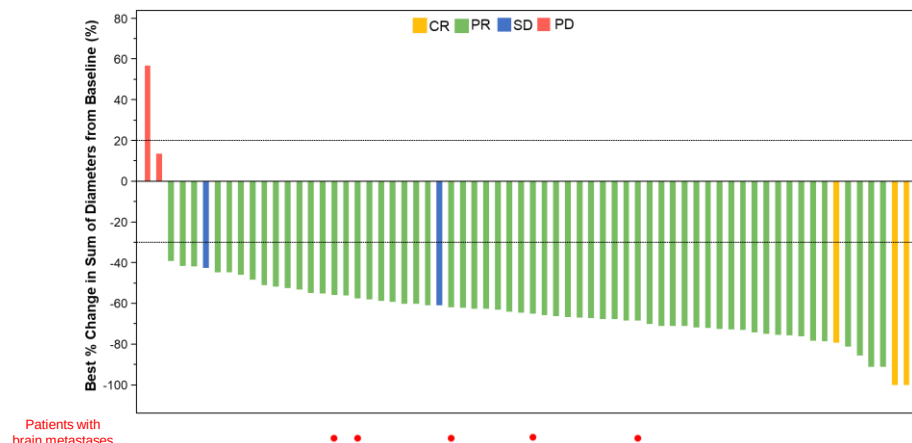
^aIncludes patients enrolled prior to Feb. 2022.

cORR, confirmed overall response rate; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, intra-cranial; IRC, independent review committee; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression free survival; QD, daily; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TKI, tyrosine kinase inhibitor; TTR, time to response.

Taletrectinib Efficacy in ROS1⁺ TKI-Naïve NSCLC^a

Responses	Taletrectinib efficacy (n=67)
IRC-assessed cORR, % (95% CI)	92.5 (83.4 – 97.5)
DCR, % (95% CI)	95.5 (87.5 – 99.1)
Median TTR, months (Range)	1.4 (1.2, 4.2)
mDoR, months (min, max)	NR (1.3 – 27.6)
mPFS, months (min, max)	NR (0.0 – 29.0)

BOR of TKI-Naïve Patients (N=66)



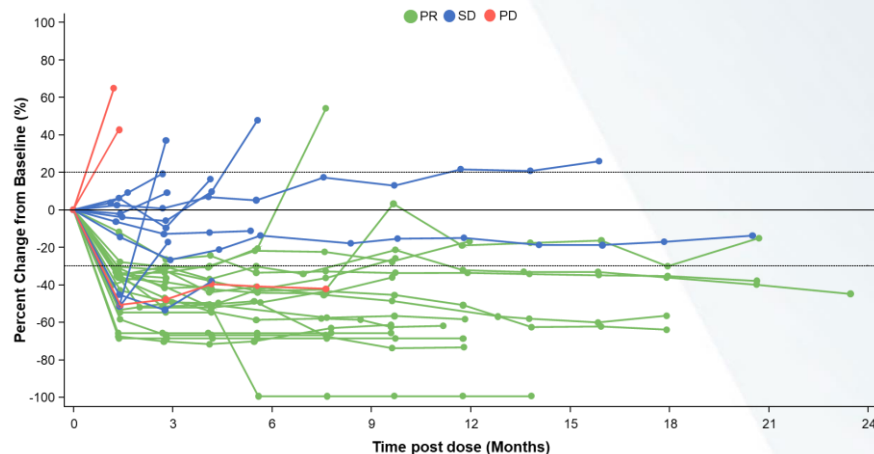
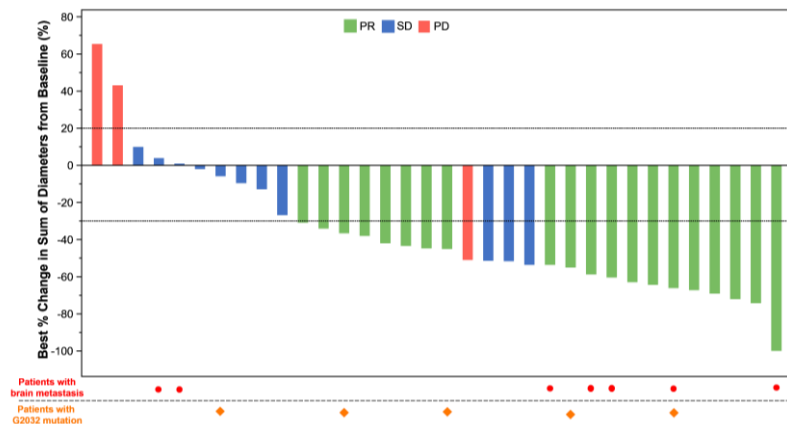
^aOne patient did not have post-treatment tumor assessment and was not included in the waterfall and spider plots.

BOR, best overall response; CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; DCR, disease control rate; IRC, independent review committee; mDoR, median duration of response; max: maximum; min, minimum; mPFS, median progression free survival; NE, not evaluable; NR, not reached; PD, progressive disease; PR, partial response; SD, stable disease; TKI, tyrosine kinase inhibitor; TTR, time to response.

Taletrectinib Efficacy in ROS1⁺ Crizotinib-Pretreated Patients^a

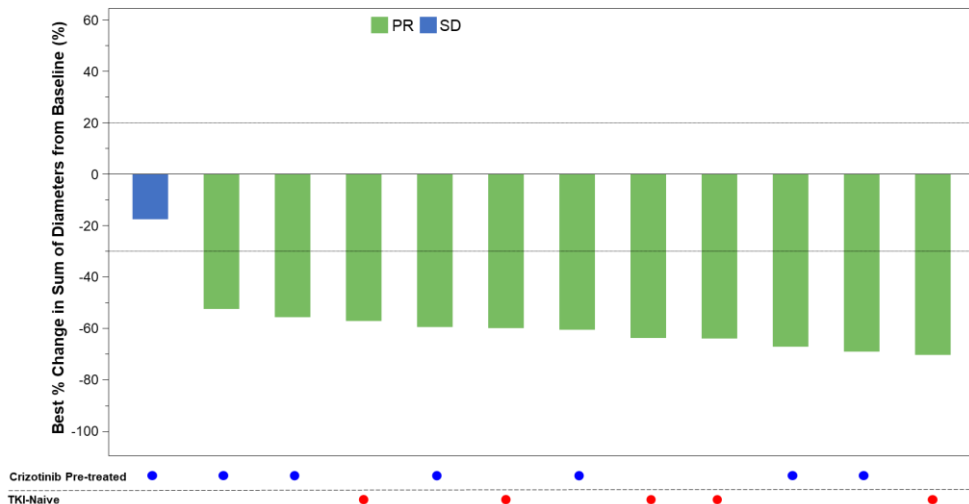
Responses	Taletrectinib Efficacy (n=38)
IRC-assessed cORR, % (95% CI)	52.6 (35.8 – 69.0)
DCR, % (95% CI)	81.6 (65.7 – 92.3)
Median TTR, months (Range)	1.4 (1.2 – 4.1)
mDoR, months (min, max)	NR (1.4 – 22.2)
mPFS, months (min, max)	9.8 (0.0 – 23.5)
G2032R ORR, ^b %, n/N	80.0 (4/5)

BOR of Crizotinib Pretreated Patients (n=34)

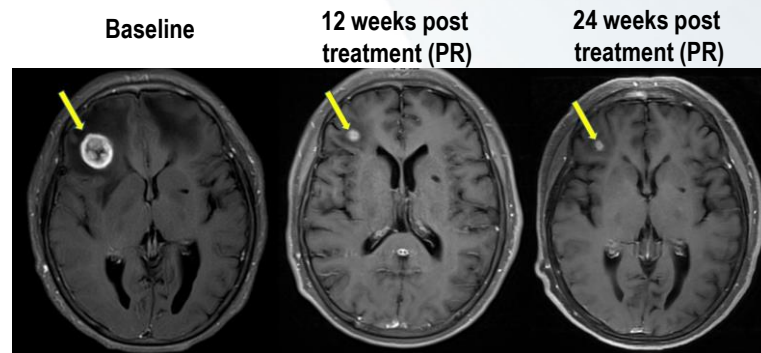


Taletrectinib Efficacy in Patients with Measurable Brain Metastases^a

Patients with Measurable Brain Metastases (n=12)



Efficacy (N=12)	
IC-ORR, % (n/N)	91.7 (11/12)
[95% CI]	[61.5% – 99.8%]
IC-DCR, % (n/N)	100 (12/12)
[95% CI]	[73.5% – 100.0%]



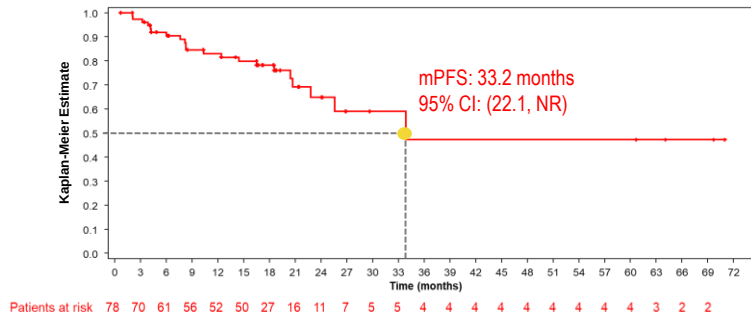
- ROS1⁺ NSCLC, crizotinib pre-treated, measurable brain lesions
- Treated at 600 mg QD
- PR at Week 12 and continued PR at Week 24

Taletrectinib Efficacy: Phase 1 and 2 Pooled data

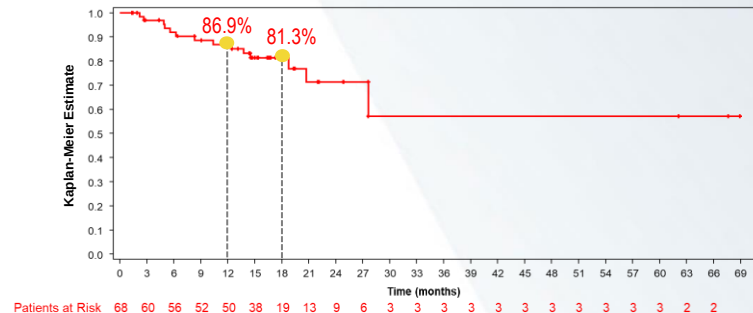
- Median follow-up for PFS among TKI-naïve patients was 18.0 months; median follow-up for PFS among crizotinib-pretreated patients was 15.9 months

Progression Free Survival

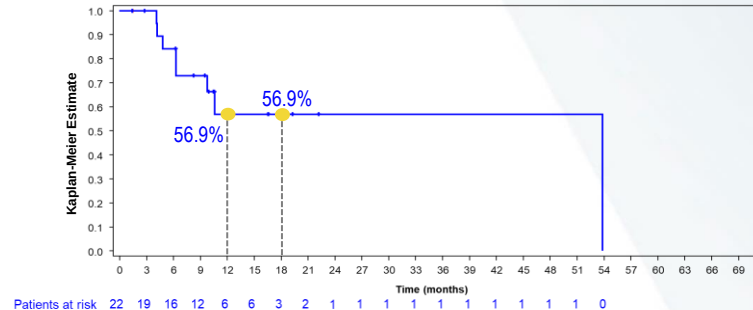
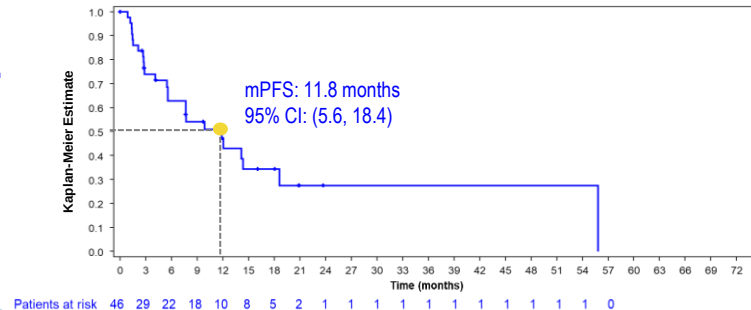
TKI-naïve



Duration of Response



Crizotinib-pretreated



Taletrectinib Safety: Phase 1 and 2 Pooled data^a

Patients with TEAEs (≥15%): Taletrectinib 600mg Safety Population (N=178)

	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 ^b n (%)	Any Grade N (%)
AST increased	86 (48.3)	28 (15.7)	12 (6.7)	0	0	126 (70.8)
ALT increased	69 (38.8)	32 (18.0)	13 (7.3)	0	0	114 (64.0)
Diarrhea	81 (45.5)	22 (12.4)	6 (3.4)	0	0	109 (61.2)
Vomiting	56 (31.5)	18 (10.1)	3 (1.7)	0	0	77 (43.3)
Nausea	65 (36.5)	8 (4.5)	2 (1.1)	0	0	75 (42.1)
Anemia	39 (21.9)	20 (11.2)	4 (2.2)	0	0	63 (35.4)
WBC count decreased	24 (13.5)	12 (6.7)	4 (2.2)	0	0	40 (22.5)
Neutrophil count decreased	18 (10.1)	8 (4.5)	8 (4.5)	4 (2.2)	0	38 (21.3)
Hepatic function abnormal	20 (11.2)	5 (2.8)	12 (6.7)	0	0	37 (20.8)
Dizziness	34 (19.1)	2 (1.1)	1 (0.6)	0	0	37 (20.8)
Blood bilirubin increased	28 (15.7)	3 (1.7)	0	1 (0.6)	0	32 (18.0)
Decreased appetite	28 (15.7)	4 (2.2)	0	0	0	32 (18.0)
Constipation	26 (14.6)	3 (1.7)	0	0	0	29 (16.3)
Hyperuricemia	28 (15.7)	1 (0.6)	1 (0.6)	0	0	30 (16.9)
Blood creatinine increased	26 (14.6)	2 (1.1)	0	0	0	28 (15.7)

- Median duration of exposure: 7.6 months (range 0.2-64.1)
- Any patient with a TEAE leading to dose reduction: 36 (20.2%)
- Any patient with a TEAE leading to treatment discontinuation: 9 (5.1%)
- Most TEAEs were of Grade 1–2, transient and reversible
- Neurological TEAEs were low, majority were Grade 1

^aWorst grade per patient is reported.

^bTwo Grade 5 TEAEs, rated Possibly Related, were reported and both are pending final confirmation: 1 Hepatic Failure & 1 Infections & Infestations.

AST, aspartate aminotransferase; ALT, alanine aminotransferase; CPK, creatine phosphokinase; SD, standard deviation; TEAE, treatment emergent adverse events; WBC, white blood cell.

Summary and Conclusions

- Taletrectinib, a potent, next-generation ROS1 TKI, continued to demonstrate meaningful efficacy outcomes in both ROS1-TKI-naïve and crizotinib-pretreated NSCLC patients
 - High and durable ORR was observed in TKI-naïve and crizotinib-pretreated patients
 - High intracranial ORR regardless of line of therapy
 - Prolonged PFS in TKI-naïve and crizotinib-pretreated patients
 - Activity against secondary resistance mutations, including G2032R
- Taletrectinib demonstrated tolerable safety in ROS1-TKI-naïve and crizotinib-pretreated NSCLC patients
 - TEAEs were mostly of grades 1–2
 - Low incidence of neurological adverse events, most of which were grade 1
 - Treatment discontinuations and dose reductions due to TEAEs were low
- Pivotal global Phase 2 (TRUST-II; NCT04919811) of taletrectinib in ROS1-positive non-small-cell lung cancer and other solid tumors is ongoing¹

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