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Updated Efficacy and Safety of Taletrectinib in Patients with ROS1+ Non–Small Cell Lung Cancer

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Declaration of Interests

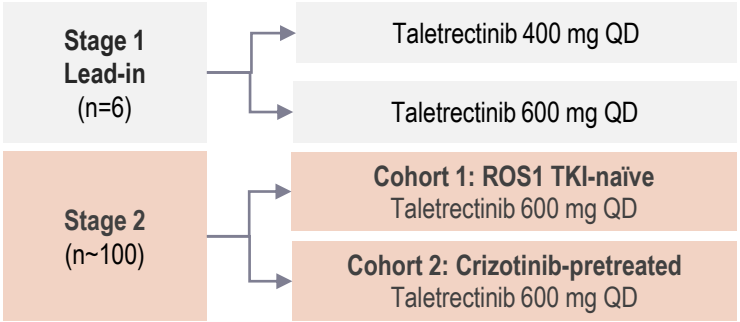
I have no conflict of interest to declare.

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

Key Eligibility Criteria

Inclusion Criteria:

- Locally advanced or metastatic NSCLC
- Age ≥18 years
- ECOG PS 0-1
- Evidence of ROS1 fusion in tumor tissue



Endpoints

Primary:
IRC-assessed cORR per RECIST 1.1

Secondary:

- DoR
- DCR
- IC-ORR
- PFS
- TTR (RECIST1.1)
- OS

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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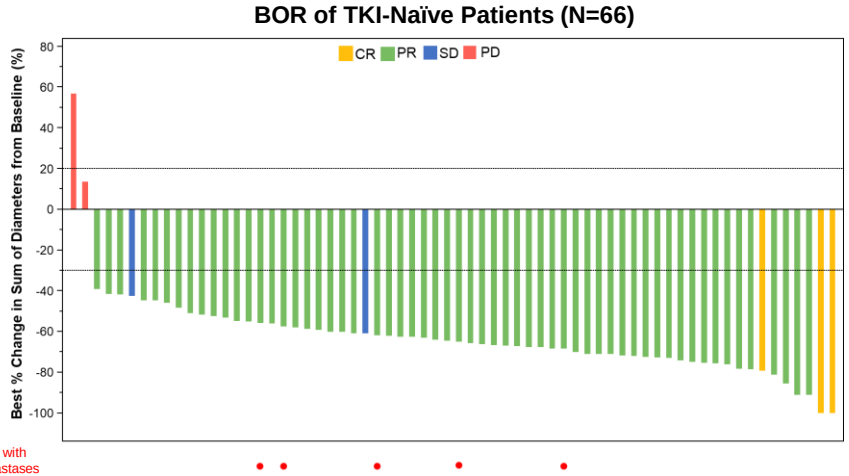
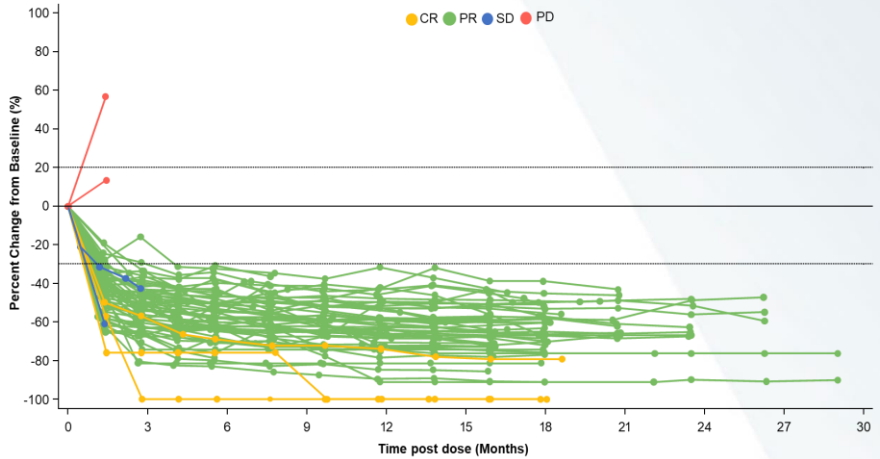
[a]Includes patients enrolled prior to Feb. 2022.
cORR, confirmed overall response rate; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, intra-cranial; IRC, independent review committee; NSCLC, non-small cell lung cancer; ORR, 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.

Data cut-off: Dec 31, 2022

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)





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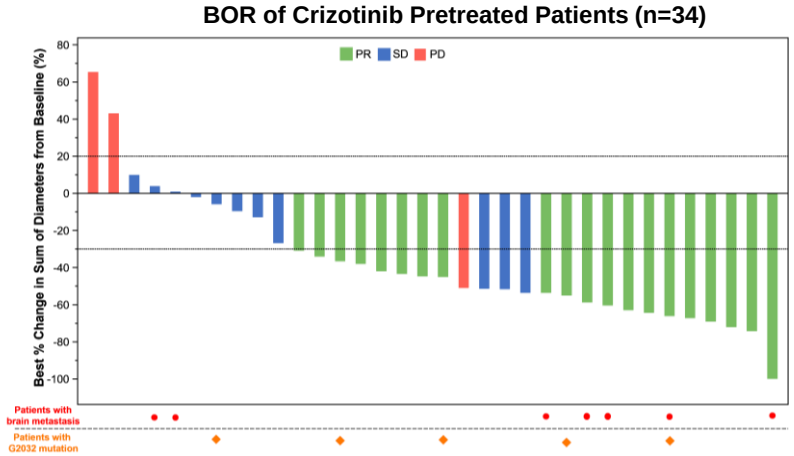
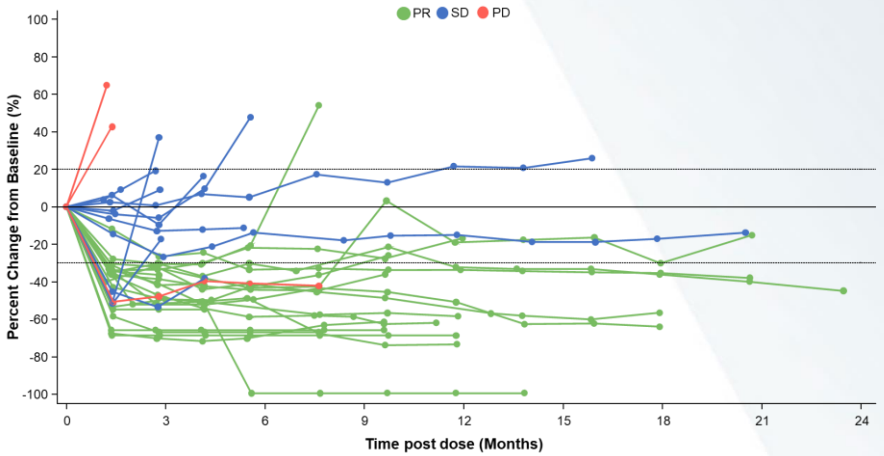
[a]One patient did not have post-treatment tumor assessment and was not included in the waterfall and spider plots.
BOR, best overall response; CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; DCR, disease control rate; IRC, independent review committee; mDoR, 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.

Data cut-off: Dec 31, 2022

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)





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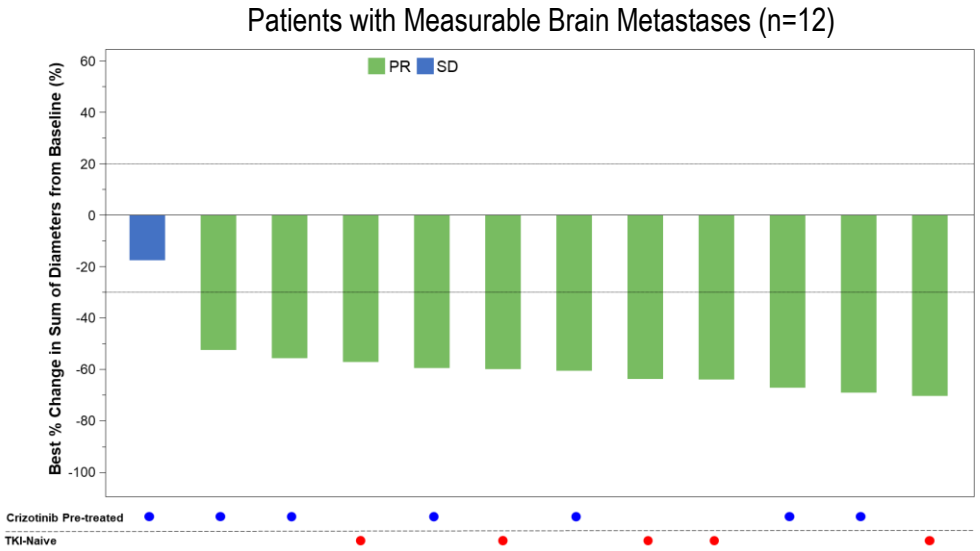
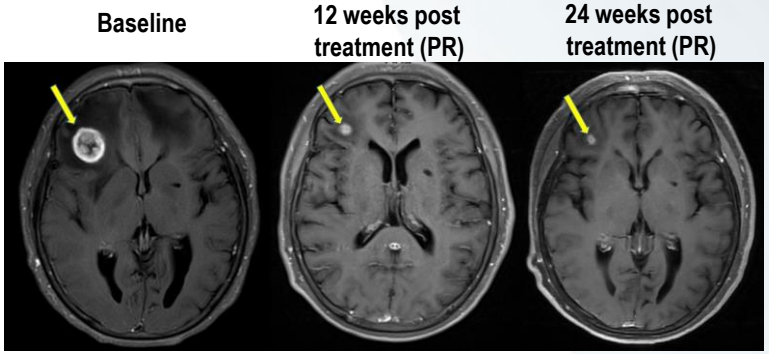
[a]Four patients did not have post-treatment tumor assessment and was not included in the waterfall and spider plots. [b]Tested by next-generation sequencing of tumor rebiopsy samples. BOR, best overall response; CI, confidence interval; cORR, confirmed objective response rate; DCR, disease control rate; IRC, independent review committee; mDoR, median duration of response; mPFS, median progression free survival; NR, not reached; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; TTR, time to response.

Data cut-off: Dec 31, 2022

Taletrectinib Efficacy in Patients with Measurable Brain Metastases[a]



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

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[a]Includes both TKI-naïve and TKI-pretreated patients. Assessed per RANO-BM criteria.
BOR, best overall response; CI, confidence interval; DoR, duration of response; IC, intracranial; DCR, disease control rate; DoR, Duration of response, NR, not reached; PFS, progression-free survival; ORR, objective response rate; PR, partial response; RANO-BM, response assessment in neuro-oncology brain metastases; SD, stable disease; TKI, tyrosine kinase inhibitor.

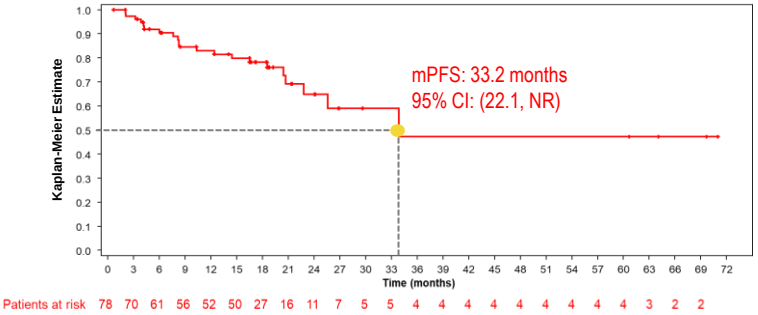
Data cut-off: Dec 31, 2022

Taletrectinib Efficacy: Phase 1 and 2 Pooled data

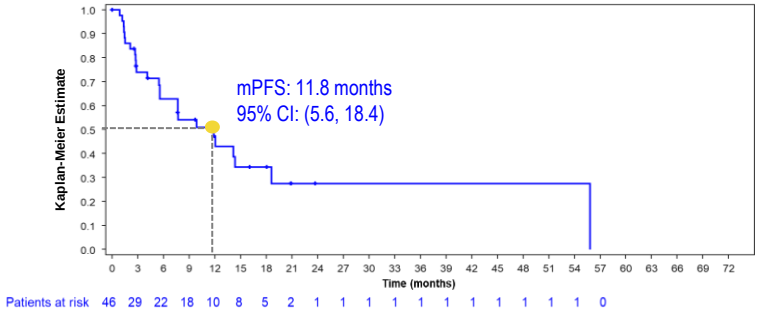
- Median follow-up for PFS among TKI-naïve patients was 18.0 months; median follow-up for PFS among crizotinib-pretreated patients was 15.9 months

Progression Free Survival

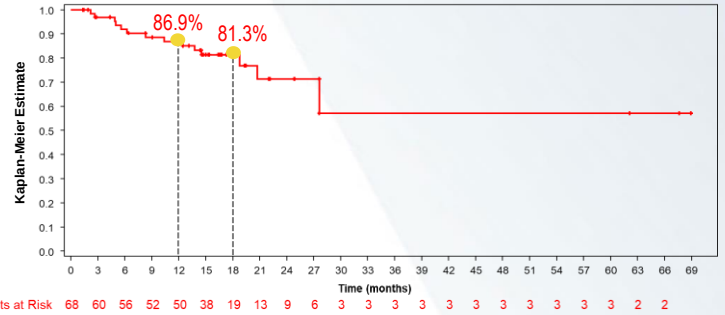
TKI-naïve

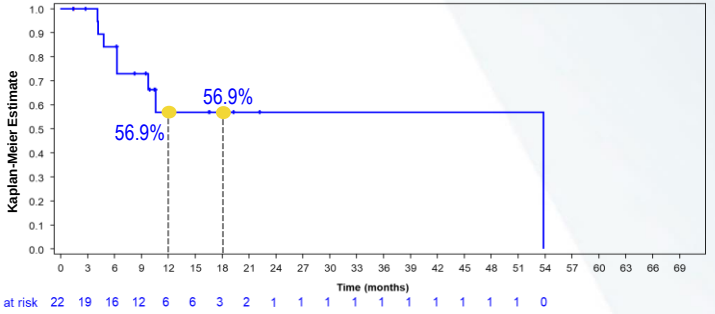


Crizotinib-pretreated



Duration of Response





mPFS, median PFS; CI, confidence interval; NR, not reached; TKI, tyrosine kinase inhibitor.

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

[a]Worst grade per patient is reported.
[b]Two 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 ongoing[1]

[1]Nagasaka M et al. *Future Oncol.* 2023.

Acknowledgements

On behalf of all the authors, we would like to thank the patients, study investigators, and site personnel for their participation in this study

This study was sponsored by AnHeart Therapeutics, Inc.

Medical writing and editorial assistance was provided by Peloton Advantage, LLC, an OPEN Health company, and funded by AnHeart Therapeutics, Inc.