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The Phase II Study of Unecritinib (TQ- B3101) monotherapy in the first line treatment in patients with *ROS1* positive non-small cell lung cancer (NCT03972189)

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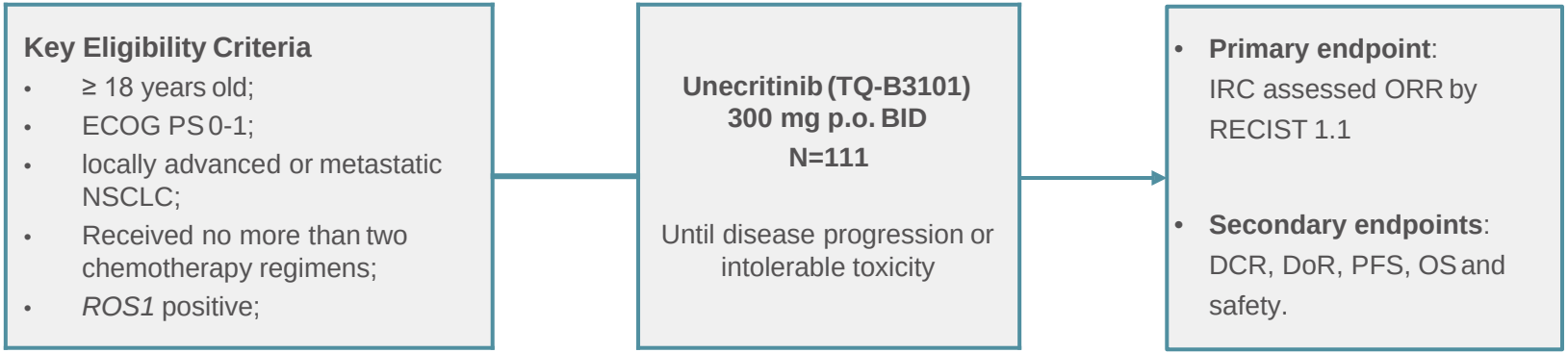
Introduction and Study Design

- At present, Crizotinib and Entrectinib are the standard first-line treatment for *ROS1* positive advanced NSCLC, with ORR of 71.7% and 67.1% and mPFS of 15.9 months and 15.7 months, respectively[1,2].
- Unecritinib (TQ-B3101) is a novel compound, which deacetylated metabolite targets to receptor tyrosine kinases including ALK, ROS1 and MET.
- As reported in ASCO 2019, previous phase I study showed that Unecritinib (TQ-B3101) twice daily showed good clinically efficacy with tolerable side effects in *ALK*, *ROS1* positive and *MET* amplification patients, who failed to standard therapy[3].
  - Phase I study (n=30): ORR was 62.5% in all cohorts, 87.5% in 350 mg BID cohort. G3 AEs were 40.0% in 350 mg BID cohort and 16.7% in 300 mg BID cohort.



- The ORR assessed by investigator (RECIST 1.1) is for sensitivity analysis.
- A sample size of 111 patients achieving >85% power to detect a difference of 0.15 (P0=0.50, P1=0.65) using an 2 sided binomial test with a significance level of 0.05.
- A total 111 Chinese patients entered the study from 29 sites in China between Nov, 2019 to Jan, 2021.

ClinicalTrials.gov Identifier: NCT03972189

1. Yi-Long Wu, et al. J Clin Oncol. 2018 May 10;36(14):1405-1411.
2. Rafal Dziadziuszko et al. J Clin Oncol. 2021 Apr 10;39(11):1253-1263.
3. Yong Fang, et al. J Clin Oncol 38: 2020 (suppl; abstract e21705).

ORR, objective response rate; DCR, disease control rate; DoR, duration of response; PFS, progression free survival; OS, overall survival; IRC, independent review committee; RECIST 1.1, Response Evaluation Criteria in Solid Tumors

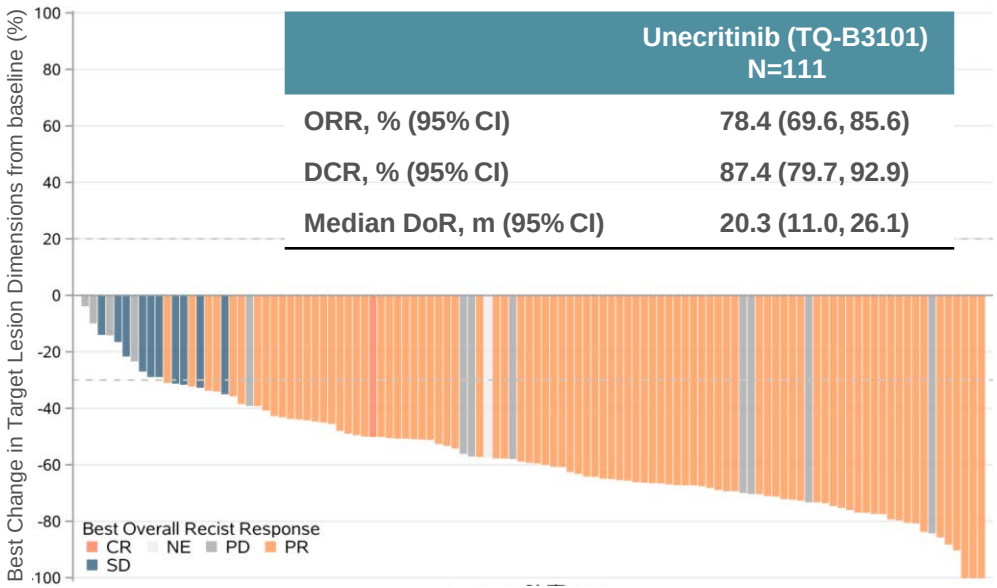
Demographics and Baseline Characteristics

n (%)	Unecritinib (TQ-B3101) N=111
Age, median (range), years	52.0 (44.0, 59.0)
Sex	
Male	43 (38.7)
Female	68 (61.3)
ECOG	
0	32 (28.8)
1	79 (71.2)
Smoking history	
Never	80 (72.1)
Ever	28 (25.2)
Current	3 (2.7)

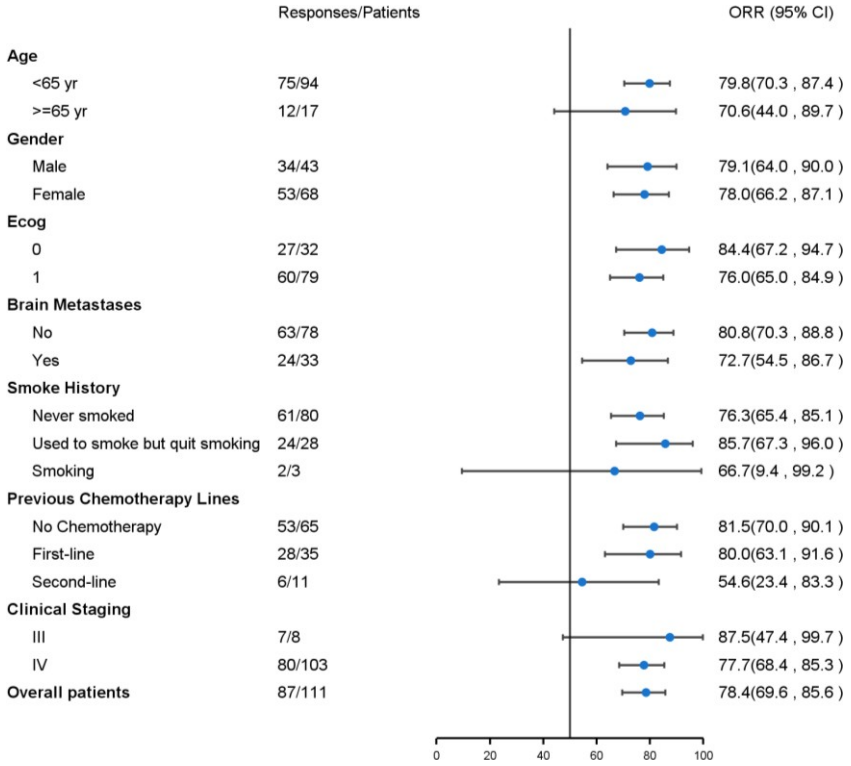
n (%)	Unecritinib (TQ-B3101) N=111
Pathology	
Adenocarcinoma	110 (99.1)
Unknown	1 (0.9)
Stage	
III	8 (7.2)
IV	103 (92.8)
Brain Metastatic	
Yes	33 (29.7)
No	78 (70.3)
Number of previous chemotherapy lines	
0	65 (58.6)
1	35 (31.5)
2	11 (9.9)

Data cut-off: October 15, 2021

Efficacy: ORR and DCR by IRC



Unecritinib (TQ-B3101) N=111	
ORR, % (95% CI)	78.4 (69.6, 85.6)
DCR, % (95% CI)	87.4 (79.7, 92.9)
Median DoR, m (95% CI)	20.3 (11.0, 26.1)

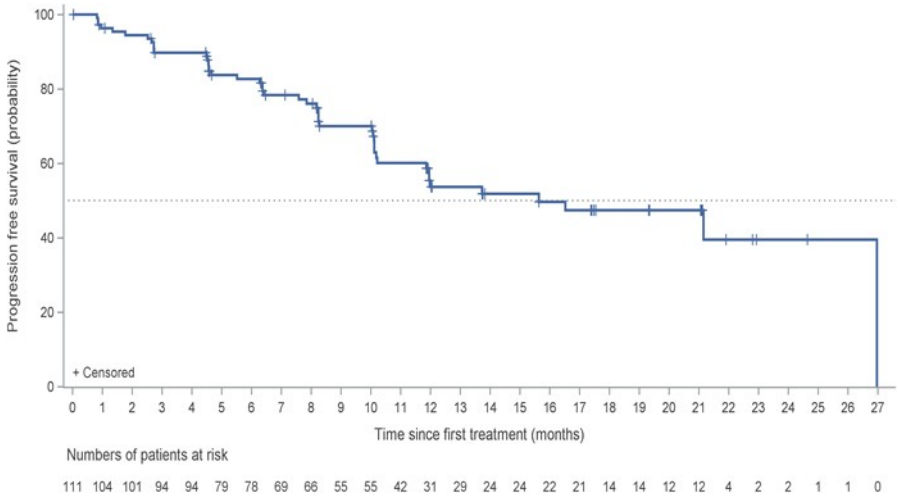


- Analysis of ORR by IRC was consistent with the investigator-based analysis.
- At time of data cut-off, the median duration of follow up was 12.1 months (95% CI 11.9, 17.4).

Data cut-off: October 15, 2021

Efficacy: PFS by IRC and OS

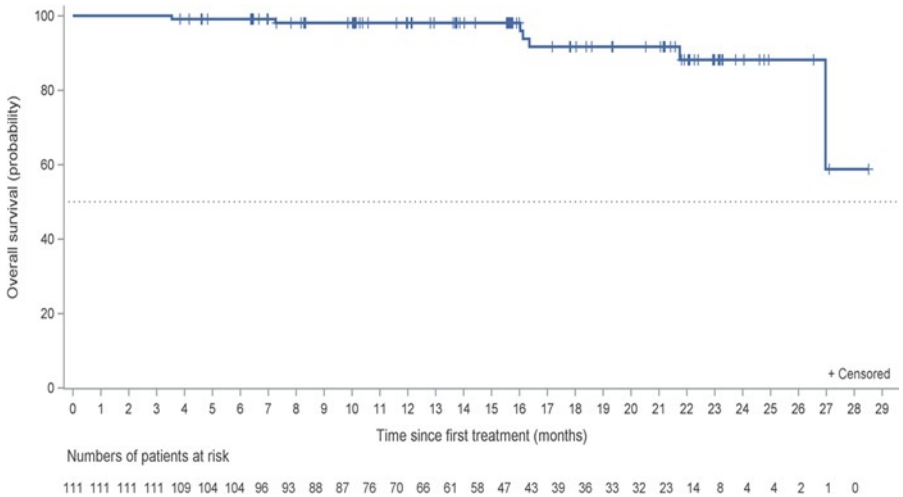
PFS by IRC



PFS	Unecritinib (TQ-B3101) N=111
Events, n (%)	45 (40.5)
Median, m (95% CI)*	**15.6 (10.2, 27.0)**
3-month rate, % (95% CI)	89.7 (82.2, 94.2)
6-month rate, % (95% CI)	82.7 (73.9, 88.7)
12-month rate, % (95% CI)	53.7 (42.0, 64.0)

* Estimated using the Kaplan-Meier method

OS



OS	Unecritinib (TQ-B3101) N=111
Events, n (%)	7 (6.3)
Median, m (95% CI)*	**NR (27.0, NR)**
12-month rate, % (95% CI)	98.1 (92.5, 99.5)
24-month rate, % (95% CI)	88.1 (73.7, 94.9)

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Data cut-off: October 15, 2021

Safety Overview

Safety summary

AEs, n (%)	Unecritinib (TQ-B3101) N=111
Any TEAEs	111 (100.0)
TQ-B3101 TRAEs	110 (99.1)
≥ grade 3 TEAEs	59 (53.2)
≥ grade 3 TQ-B3101 TRAEs	50 (45.1)
SAEs	16 (14.4)
TQ-B3101 treatment-ralated SAEs	4 (3.6)
TQ-B3101 TRAEs leading to dose adjustment	18 (16.2)
TQ-B3101 TRAEs leading to dose disruption	39 (35.1)
TQ-B3101 TRAEs leading to discontinuation	18 (16.2)

AEs, adverse events; TEAEs, treatment emergent adverse events; SAEs, serious adverse events; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Treatment-related AEs (TRAEs) in ≥ 25% of

TRAEs, n (%)	Unecritinib (TQ-B3101) N=111	
	Any grade	≥ Grade 3
Increased AST	82 (73.9)	4 (3.6)
Increased ALT	80 (72.1)	8 (7.2)
Vomiting	70 (63.1)	0 (0.0)
Neutrophil count decreased	63 (56.8)	28 (25.2)
Leukocyte count decreased	58 (52.3)	8 (7.2)
Sinus bradycardia	58 (52.3)	0 (0.0)
Diarrhea	48 (43.2)	0 (0.0)
Elevated serum creatine phosphokinase	47 (42.3)	3 (2.7)
Nausea	42 (37.8)	0 (0.0)
Elevated blood lactate dehydrogenase	41 (36.9)	0 (0.0)
Constipation	34 (30.6)	0 (0.0)
Hypoalbuminemia	33 (29.7)	1 (0.9)
Anemia	30 (27.0)	2 (1.8)
Elevated serum creatinine	28 (25.2)	0 (0.0)

TRAEs of interest, n (%)	Any grade	≥ Grade 3
Ocular organ diseases*	**29 (26.1)**	**0 (0.0)**

* This item comprised a cluster of TRAEs that may represent similar clinical symptoms or syndromes, including visual impairment and vision blurred occurred in 8 patients, respectively; cataract and diplopia occurred in 3 patients, respectively; arteriosclerotic retinopathy, dry eye, high intraocular pressure, flash hallucination, visual fatigue, ocular cholesterosis, orbital edema, eye pain, ocular degenerative disease and eyelid edema, occurred in only 1 patient, respectively.

Data cut-off: October 15, 2021

Conclusion

- **For the first line treatment of *ROS1* positive locally advanced or metastatic NSCLC patients, Unecritinib (TQ-B3101) showed the promising efficacy with a manageable safety profile, offering a new first-line therapeutic strategy.**
  - ORR by IRC: 78.4%, DCR by IRC: 87.4%,
  - mPFS by IRC: 15.6ms, mDoR: 20.3ms,
  - 12- and 24-month OS rates were 98.1% and 88.1% respectively,
  - ≥ grade 3 TRAEs: 45.1%, Treatment-related SAEs: 3.6%,
  - Safety of ocular organ was good.