Tepotinib in Asian patients with advanced NSCLC with *MET* exon 14 (*MET*ex14) skipping

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CONCLUSIONS

- **Tepotinib demonstrated robust and durable clinical activity in Asian patients with *MET*ex14 skipping NSCLC, irrespective of investigated baseline characteristics (sex, age, histology, smoking history, ECOG PS), treatment line, and *MET*ex14 skipping detection method**
- **HRQoL remained stable during treatment with tepotinib in Asian patients; this is the first presentation of HRQoL in Asian patients with *MET*ex14 skipping NSCLC treated with a MET inhibitor**
- **Tepotinib had a manageable safety profile with few discontinuations**

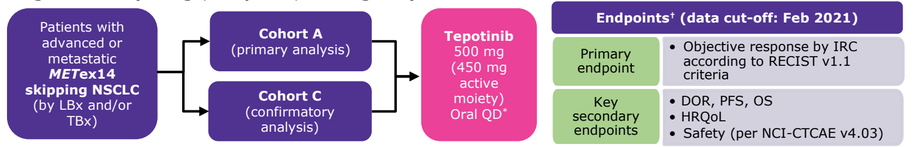
INTRODUCTION

- *MET*ex14 skipping is reported in 3–4% of patients with NSCLC, including 1–4% of Asian patients with lung adenocarcinoma, and is sensitive to MET inhibition[1–8]
- Tepotinib is an oral, once daily, highly selective, potent MET inhibitor that has shown clinical activity in MET-driven tumors[9,10] and is approved in many countries in North America, Europe, South America and Asia, including Hong Kong, Japan, Singapore, South Korea, Taiwan, and it is available in Hainan, China for treating advanced/metastatic *MET*ex14 skipping NSCLC
- **Here, we report outcomes in Asian patients from the VISION study including HRQoL**
- Efficacy of tepotinib according to line of therapy in Asian patients enrolled in the VISION study has been presented at the European Lung Cancer Congress (ELCC) 2022 by Yang J, et al. [Poster number 25P] (scan QR code to view poster)

METHODS

- VISION (NCT02864992) is a single-arm, Phase II trial of tepotinib in patients with NSCLC harboring *MET*ex14 skipping (Cohorts A and C) (**Figure 1**)

Figure 1. Study design, endpoints, and eligibility criteria of VISION



Key inclusion criteria
- ≥18 years of age
- Histologically or cytologically confirmed NSCLC with *MET*ex14 skipping detected by LBx and/or TBx
- Measurable disease
- ECOG PS 0/1
- Prior immunotherapy allowed

Key exclusion criteria
- Tumors harboring *EGFR* mutations or *ALK* rearrangements
- >2 lines of prior therapy
- Prior use of MET inhibitors

*Treatment continues until disease progression, intolerable toxicity, or withdrawal of consent.
†Efficacy was assessed in patients with more than 3 months' follow-up, and safety was analyzed in all patients having received at least one dose of tepotinib by the data cut-off.

HRQoL assessment

- Here, we report HRQoL analysis conducted in patients enrolled in Asia
- Change from baseline was calculated for each observation of EORTC QLQ-C30 GHS, EORTC QLQ-LC13 symptom scores (cough, dyspnea, chest pain), and EQ-5D-5L VAS recorded in the VISION trial
- Linear mixed model regression, including a covariate for response status (IRC defined), were performed to obtain the mean change from baseline for each of the PROs

RESULTS

Asian patients were mostly male and almost half had smoking history

- VISION enrolled 106 Asian patients (including patients enrolled after cut-off): 38 in Japan, 20 in South Korea, 12 in Taiwan, 30 in China, and 6 outside Asia
- At the data cut-off (Feb 1, 2021), enrollment was ongoing; 79 Asian patients had ≥3 months' follow-up, of which 73 patients were enrolled in Asia (**Table 1**)

Table 1. Baseline characteristics

Baseline characteristics		Asian population (n=79)
Median age, years (range)		71 (52–89)
Age, %	≥75 years	35
Sex, %	Male	62
Smoking history, %	Yes	42
Histology, %	Adenocarcinoma/squamous	77/9
ECOG PS, %	0/1	32/68
Presence of BM at baseline*, %	Yes	16
Line of therapy, %	Treatment-naïve/previously treated	34/66
*MET*ex14 skipping detection, %	T+/L+	72/47

*BM at baseline as identified by IRC or investigator assessment.

Tepotinib demonstrated robust and durable clinical activity

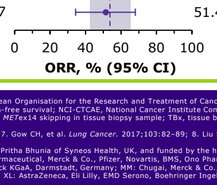
- In all Asian patients who were evaluable for efficacy (n=79), ORR was 54.4%, mDOR was 18.5 months, mPFS was 12.1 months, and mOS was 20.4 months (**Table 2; Figure 2**)
- ORR was 66.7% in treatment-naïve and 48.1% in previously treated patients (**Table 2; Figure 2**)
- In the T+ population, ORR was 70.0% in treatment-naïve and 51.4% in previously treated patients (**Table 2**)

Table 2. Efficacy of tepotinib in Asian patients

Efficacy (IRC)		Overall Asian patients			T+ Asian patients	
		Combined (n=79)	Treatment-naïve (n=27)	Previously treated (n=52)	Treatment-naïve (n=20)	Previously treated (n=37)
ORR, % (95% CI)		54.4 (42.8, 65.7)	66.7 (46.0, 83.5)	48.1 (34.0, 62.4)	70.0 (45.7, 88.1)	51.4 (34.4, 68.1)
DCR, % (95% CI)		77.2 (66.4, 85.9)	77.8 (57.7, 91.4)	76.9 (63.2, 87.5)	85.0 (62.1, 96.8)	81.1 (64.8, 92.0)
DOR	Median, months (95% CI)	18.5 (8.3, ne)	ne (6.9, ne)	9.7 (5.6, ne)	ne (8.3, ne)	8.3 (4.3, ne)
	12-month rate, % (95% CI)	53 (29, 72)	79 (38, 94)	29 (5, 60)	83 (27, 97)	24 (1, 62)
PFS	Median, months (95% CI)	12.1 (6.9, ne)	ne (8.3, ne)	11.0 (5.6, 19.9)	ne (9.6, ne)	11.1 (5.6, ne)
	12-month rate, % (95% CI)	51 (37, 64)	66 (40, 83)	44 (26, 61)	74 (43, 90)	42 (20, 63)
OS	Median, months (95% CI)	20.4 (19.1, ne)	ne (16.3, ne)	20.4 (14.3, ne)	ne (19.1, ne)	26.8 (14.3, ne)
	12-month rate, % (95% CI)	80 (69, 88)	84 (63, 94)	78 (63, 88)	89 (64, 97)	83 (64, 93)

Figure 2. Objective response rate in subgroups according to baseline characteristics

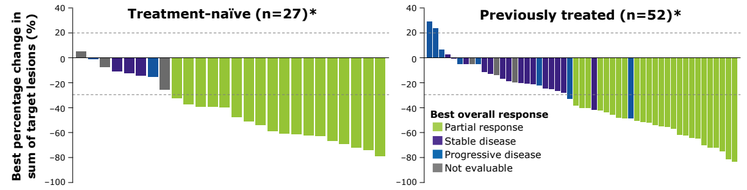
Subgroup		n	ORR (95% CI)
Overall		79	54.4 (42.8, 65.7)
Sex	Male	49	51.0 (36.3, 65.6)
	Female	30	60.0 (40.6, 77.3)
Age	<75 years	51	51.0 (36.6, 65.2)
	≥75 years	28	60.7 (40.6, 78.5)
Histology	Adenocarcinoma	61	55.7 (42.4, 68.5)
	Squamous	7	57.1 (18.4, 90.1)
Smoking history	Yes	33	54.5 (36.4, 71.9)
	No	44	56.8 (41.0, 71.7)
ECOG PS	0	25	56.0 (34.9, 75.6)
	1	54	53.7 (39.6, 67.4)
Presence of BM at baseline*	Yes	13	61.5 (31.6, 86.1)
	No	66	53.0 (40.3, 65.4)
Previous treatment	Treatment-naïve	27	66.7 (46.0, 83.5)
	Previously treated	52	48.1 (34.0, 62.4)
*MET*ex14 skipping detection†	T+	57	57.9 (44.1, 70.9)
	L+	37	51.4 (34.4, 68.1)



*BM at baseline as identified by IRC or investigator assessment – efficacy data for subgroups are systemic ORR per RECIST v1.1 and accounts for both intra- and extra-cranial lesions. †Patients with *MET*ex14 skipping detected by both liquid and tissue biopsy are included in both L+ and T+ groups.

- In treatment-naïve and previously treated patients, >90% of patients had tumor shrinkage (**Figure 3**)

Figure 3. Tumor response according to line of therapy

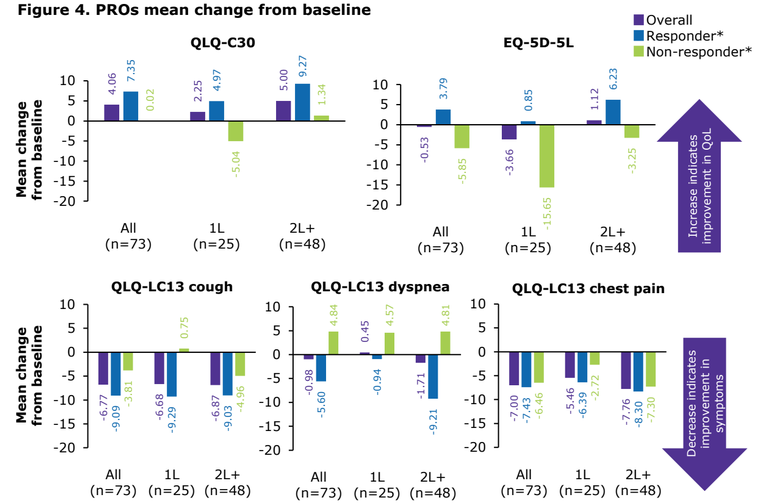


*One treatment-naive patient and one previously treated patient are not shown due to baseline/on-treatment measurements not being available.

HRQoL remained stable during treatment in Asian patients

- In patients analyzed for HRQoL (n=73), mean change from baseline for EORTC QLQ-C30 GHS was 4.06, EQ-5D-5L VAS was -0.53, EORTC QLQ-LC13 symptom scores for cough was -6.77, dyspnea was -0.98, and chest pain was -7.00 (**Figure 4**)
- Overall, patients with tumor responses (responders) had more pronounced symptom improvements, compared with patients without responses (non-responders) (**Figure 4**)

Figure 4. PROs mean change from baseline



*Overall, 39 patients were considered responders and 34 non-responders; in 1L, 17 were responders and 8 were non-responders; in 2L+, 22 were responders and 26 were non-responders.

Tepotinib was generally well tolerated, with mostly mild to moderate TRAEs

- Grade ≥3 TRAEs occurred in 29.5% of patients, with no fatal TRAEs and a low proportion (14.8%) of patients discontinued due to TRAEs (**Table 4**)

Table 4. Tepotinib safety profile in Asian patients

AEs in Asian patients (n=88)	All-cause AEs, n (%)	TRAEs, n (%)
Any grade	86 (97.7)	82 (93.2)
Grade ≥3	48 (54.5)	26 (29.5)
Leading to dose reduction	30 (34.1)	26 (29.5)
Leading to permanent discontinuation	19 (21.6)	13 (14.8)
Leading to death	8 (9.1)	0
All-cause AEs (any grade) occurring in ≥15% of Asian patients, n (%)		
Peripheral edema	46 (52.3)	
Blood creatinine increase	34 (38.6)	
Diarrhea	32 (36.4)	
Hypoalbuminemia	30 (34.1)	
ALT increased	19 (21.6)	
Decreased appetite	15 (17.0)	

Abbreviations: 1L, first-line; 2L+, second-or-later line; AE, adverse event; ALK, anaplastic lymphoma kinase; ALT, alanine transaminase; BM, brain metastases; CI, confidence interval; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; EORTC, European Organisation for the Research and Treatment of Cancer; EQ-5D-5L, European Quality of Life five-dimension five-level; GHS, global health score; HRQoL, health-related quality of life; IRC, independent review committee; L+, positive detection of *MET*ex14 skipping in liquid biopsy sample; LBx, liquid biopsy; mDOR, median duration of response; MET, mesenchymal–epithelial transition factor; *MET*ex14, *MET* exon 14; mOS, median overall survival; mPFS, median progression-free survival; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; ne, not estimable; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PRO, patient-reported outcome; QD, once daily; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-LC13, Quality of Life Questionnaire Lung Cancer 13; RECIST, Response Evaluation Criteria in Solid Tumors; T+, positive detection of *MET*ex14 skipping in tissue biopsy sample; TBx, tissue biopsy; TRAE, treatment-related adverse event; VAS, visual analogue scale.

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