Tepotinib in Asian patients with *MET* exon 14 skipping non-small cell lung cancer (NSCLC) in long-term follow-up from VISION

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CONCLUSIONS

- **VISION included the largest population of Asian patients with *MET*ex14 skipping NSCLC in a MET TKI trial**
- **In long-term follow-up in the Asian subgroup, tepotinib had robust and durable activity with an ORR of 56.6%, mDOR of 18.5 months, mPFS of 13.8 months, and mOS of 25.5 months**
- **Efficacy was greatest in 1L, with an ORR of 64.0%, mDOR of 20.7 months, mPFS of 16.5 months, and mOS of 32.7 months**
- **Efficacy in Asian patients was comparable to that seen in the overall population[1]**
- **Overall HRQoL and symptom scores in Asian patients remained stable during treatment**
- **Tepotinib demonstrated manageable safety in Asian patients, with no new safety signals**

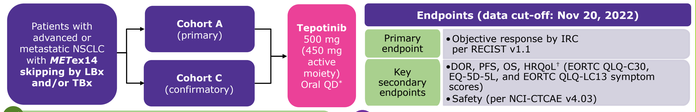
INTRODUCTION

- Tepotinib, a once-daily and highly selective MET TKI,[2] is approved for *MET*ex14 skipping NSCLC in many countries worldwide including several Asian countries[3,4]
- Tepotinib has been incorporated into clinical practice guidelines,[5,6] including the ATORG Expert Consensus,[4] which recommends tepotinib for treatment-naïve and previously treated patients with *MET*ex14 skipping NSCLC
- In the global VISION trial (N=313), tepotinib demonstrated durable clinical activity with an ORR of 51.4% and a median DOR of 18.0 months in long-term follow-up (median 32.6 months; data cut-off: November 20, 2022)[1]
- Here, we report long-term outcomes from VISION in the subgroup of Asian patients

METHODS

- VISION (NCT02864992) is a single-arm, Phase II trial of tepotinib in patients with advanced NSCLC harboring *MET*ex14 skipping (**Figure 1**)
- Subgroup analyses of patients of Asian race was preplanned

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



*Treatment continues until disease progression, intolerable toxicity, or withdrawal of consent. †Linear mixed model regression was performed to obtain the mean change from baseline for each of the PROs.

RESULTS

Baseline characteristics

- 106 Asian patients were enrolled: 100 in Asia (38 in Japan, 20 in South Korea, 12 in Taiwan, 30 in China) and six outside Asia
- Asian patients were predominantly elderly, most had adenocarcinoma, and a majority had ECOG PS 1 (**Table 1**)

Table 1. Baseline characteristics in Asian patients

Baseline characteristics		Asian patients (N=106)
Median age, years (range)		70.5 (52–89)
Sex, n (%)	Male	64 (60.4)
	Female	42 (39.6)
Smoking history, n (%)	Yes	43 (43.4)
Histology, n (%)	Adenocarcinoma	84 (79.2)
	Squamous	7 (6.6)
	Sarcomatoid	5 (4.7)
ECOG PS, n (%)	0	28 (26.4)
	1	78 (73.6)
Line of therapy, n (%)	1L	50 (47.2)
	2L+	56 (52.8)
*MET*ex14 skipping detection, n (%)	Liquid biopsy	48 (45.3)
	Tissue biopsy	83 (78.3)

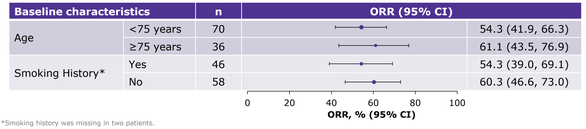
Efficacy

- In Asian patients overall, ORR was 56.6% (95% CI: 46.6, 66.2), mDOR was 18.5 months (95% CI: 10.4, ne), mPFS was 13.8 months (95% CI: 10.8, 22.0), and mOS was 25.5 months (95% CI: 19.3, 36.4) (**Table 2**)
- Patients in 1L had an ORR of 64.0% (95% CI: 49.2, 77.1) with an mDOR of 20.7 months (95% CI: 10.4, ne), mPFS of 16.5 months (95% CI: 9.6, 49.7), and mOS of 32.7 months (95% CI: 16.3, ne) (**Table 2**, **Figure 3**)
- Patients in 2L+ had an ORR of 50.0% (95% CI: 36.3, 63.7) with an mDOR of 10.8 months (95% CI: 5.6, 20.8), mPFS of 12.1 months (95% CI: 6.8, 19.9), and mOS of 23.7 months (95% CI: 17.1, 34.4) (**Table 2**, **Figure 3**)
- Overall in Asian patients, ORR was consistent irrespective of age, smoking history, and other baseline characteristics (**Figure 2, S1**)

Table 2. Efficacy outcomes in Asian patients, overall, and by line of therapy

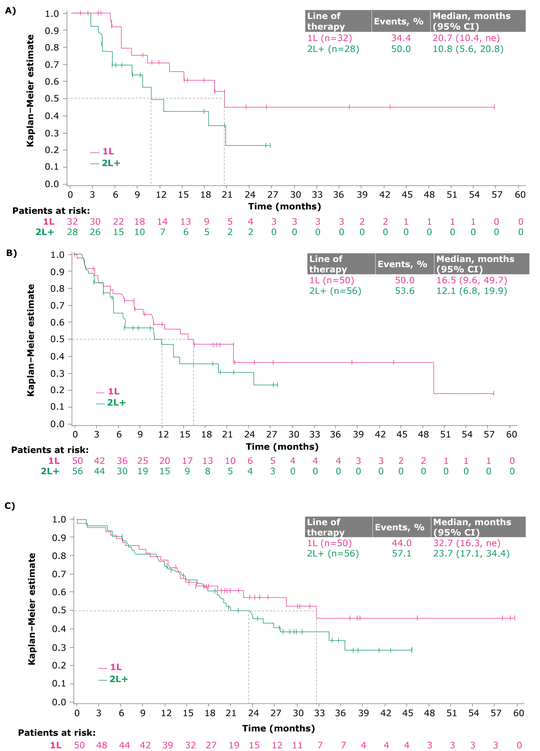
Efficacy outcomes		Overall (N=106)	1L (n=50)	2L+ (n=56)
ORR, n (%) [95% CI]		60 (56.6) [46.6, 66.2]	32 (64.0) [49.2, 77.1]	28 (50.0) [36.3, 63.7]
DOR	Median, months (95% CI)	18.5 (10.4, ne)	20.7 (10.4, ne)	10.8 (5.6, 20.8)
PFS	Median, months (95% CI)	13.8 (10.8, 22.0)	16.5 (9.6, 49.7)	12.1 (6.8, 19.9)
OS	Median, months (95% CI)	25.5 (19.3, 36.4)	32.7 (16.3, ne)	23.7 (17.1, 34.4)

Figure 2. ORR in subgroups according to age and smoking history



*Smoking history was missing in two patients.

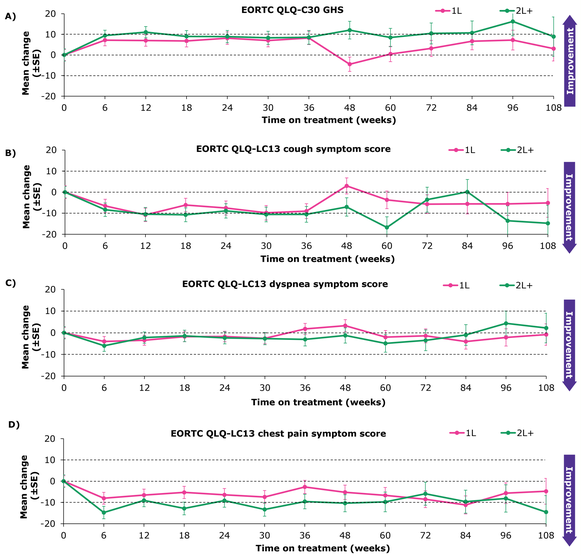
Figure 3. (A) DOR, (B) PFS, and (C) OS in Asian patients according to line of therapy



HRQoL

- Overall, HRQoL data were available from 99 Asian patients (1L, n=48; 2L+, n=51) with baseline and at least one post-baseline observation
- EORTC QLQ-C30 GHS and EQ-5D-5L VAS remained stable during treatment (**Figure 4, S2**)
- EORTC QLQ-LC13 symptom scores also showed stability in cough, dyspnea, and chest pain (**Figure 4**)

Figure 4. HRQoL scores* mean change from baseline in Asian patients by line of therapy (N=99; 1L=48, 2L+=51)† (A) EORTC QLQ-C30 GHS, **(B)** EORTC QLQ LC13 cough, **(C)** dyspnea, and **(D)** chest pain symptom scores, for treatment-naïve and previously treated patients



*EORTC QLQ-C30 GHS patient functioning scales – higher scores indicate greater function (scale 0–100). EORTC QLQ LC13 symptom score - lower scores indicate milder symptoms (scale 0–100). †Overall, 100 Asian patients across treatment completed the EORTC QLQ LC13 symptom score, EORTC QLQ-C30 GHS, and EQ-5D-5L VAS; however, there were no baseline PRO score observations for one patient. Dashed lines show minimal clinically important difference of +/- 10 points.

Safety

- The majority of patients had treatment-related AEs of Grade 1/2 (**Table 3**)
  - Grade ≥3 treatment-related AEs occurred in 39.6% of patients; 13.2% of patients discontinued treatment due to treatment-related AEs
  - Peripheral edema was the most common treatment-related AE; any grade treatment-related peripheral edema occurred in 62.3% of patients (Grade 3: 7.5%) (**Table S1**)

Table 3. Tepotinib safety profile in Asian patients (N=106)

AE, n (%)	All cause AEs	Treatment-related AEs
Any AE	105 (99.1)	101 (95.3)
Grade ≥3 AEs	65 (61.3)	42 (39.6)
AEs leading to dose reduction	35 (33.0)	32 (30.2)
AEs leading to treatment interruption	58 (54.7)	51 (48.1)
AEs leading to permanent discontinuation	21 (19.8)	14 (13.2)
AEs leading to death	10 (9.4)	1 (0.9)

Abbreviations: 1L, first line; 2L+, second or later line; AE, adverse event; ALK, anaplastic lymphoma kinase; ATORG, Asian Thoracic Oncology Research Group; CI, confidence interval; 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; LBx, liquid biopsy; m, median; MET, mesenchymal–epithelial transition factor; *MET*ex14, *MET* exon 14; 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 outcomes; 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; SE, standard error; TBx, tissue biopsy; TKI, tyrosine kinase inhibitor; VAS, visual analogue scale.

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