Long-term outcomes of tepotinib in patients with *MET* exon 14 skipping NSCLC from the VISION study

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CONCLUSIONS

- **In long-term follow-up of the largest clinical trial targeting *MET*ex14 skipping, tepotinib continued to demonstrate robust and durable activity across treatment lines**
- **In the overall population, ORR was 51.4%, mDOR was 18.0 months, mPFS was 11.2 months, and mOS was 19.6 months, with clinically meaningful efficacy seen in both 1L and 2L+ patients**
- **Time-dependent endpoints appeared longest in 1L T+ patients, who had an ORR of 58.6%, with a mDOR of 46.4 months, mPFS of 15.9 months, and mOS of 29.7 months**
- **Overall HRQoL, dyspnea and chest pain remained stable during treatment, and there was a clinically meaningful improvement in cough**
- **Tepotinib demonstrated a manageable safety profile that was consistent with earlier observations, with no new safety signals**
- **This analysis of VISION supports global approvals of tepotinib, further defining its use in clinical practice**

INTRODUCTION

- *MET*ex14 skipping is reported in 3–4% of patients with NSCLC and these tumors are sensitive to MET inhibition[1–4]
- Tepotinib is an oral, once-daily, and highly selective MET TKI, approved in multiple countries for the treatment of advanced/metastatic *MET*ex14 skipping NSCLC[5,6]
- We previously reported robust and durable activity of tepotinib from the Phase II VISION study (data cut: February 20, 2022) with a median follow-up of 26.1 months[7]
- Here, we report long-term outcomes from VISION (data cut: November 20, 2022) with ≥35 months' follow-up from primary Cohort A and ≥18 months' follow-up from confirmatory Cohort C[8]
  - This data cut fulfills an FDA post-market requirement

These long-term results from VISION are also being published in *JAMA Oncology*[8] in parallel with this ASCO presentation

METHODS

- VISION (NCT02864992) is a single-arm, Phase II trial of tepotinib in patients with advanced NSCLC harboring *MET*ex14 skipping detected by TBx and/or LBx (**Figure S1**)
- Both treatment-naïve and pretreated patients were eligible (up to two lines of prior therapy was allowed)
- The primary endpoint was objective response by independent review using RECIST v1.1
- Secondary endpoints included DOR, PFS, OS, HRQoL (assessed using the EQ-5D-5L, EORTC QLQ-C30, and EORTC QLQ-LC13 questionnaires), and safety
- Predefined analyses included 1L, 2L+, and patients with *MET*ex14 skipping detected by TBx
- An MMRM analysis was used to evaluate longitudinal changes from baseline in EORTC QLQ-LC13 symptom scores

PLAIN LANGUAGE SUMMARY

Background

- **Tepotinib is a targeted anti-cancer drug taken by mouth**
- **VISION is a Phase II study that assessed the efficacy and safety of tepotinib in patients with *MET* exon 14 skipping NSCLC**
- **VISION included 313 patients**
- **In this poster, we present the long-term results from the VISION study**

Patient characteristics

- **Average age (years): 72**
- **50.8% female**
- **62.3% White**
- **47.6% smokers**

Key efficacy findings

- **51% of patients had a response (tumor disappeared or decreased in size by at least 30%) after receiving 500 mg once daily dose of tepotinib**
- **The responses observed lasted for an average of 18.0 months (duration of response)**
- **After taking tepotinib, participants lived for an average of 19.6 months (overall survival)**

Key safety findings

- **91.7% of participants reported a treatment-related adverse event but these were mostly mild to moderate**
- **The most common treatment-related adverse events were peripheral edema (swelling of the hands, arms, feet or legs), nausea (stomach discomfort), and hypoalbuminemia (low levels of protein albumin)**

RESULTS

Baseline characteristics

- Of 313 patients enrolled, median age was 72 years (range 41–94); the majority were T+ (**Table 1**)

Table 1. Baseline characteristics

Baseline characteristics		Cohorts A+C		
		Overall (N=313)	1L (n=164)	2L+ (n=149)
Median age, years (range)		72.0 (41–94)	74.0 (47–94)	70.8 (41–89)
Sex, n (%)	Male	154 (49.2)	83 (50.6)	71 (47.7)
	Female	159 (50.8)	81 (49.4)	78 (52.3)
Race*, n (%)	White	195 (62.3)	112 (68.3)	83 (55.7)
	Asian	106 (33.9)	50 (30.5)	56 (37.6)
ECOG PS†, n (%)	0	81 (25.9)	45 (27.4)	36 (24.2)
	1	231 (73.8)	118 (72.0)	113 (75.8)
Smoking history‡, n (%)	Yes	149 (47.6)	88 (53.7)	61 (40.9)
	No	154 (49.2)	75 (45.7)	79 (53.0)
Histology§, adenocarcinoma, n (%)		252 (80.5)	131 (79.9)	121 (81.2)
*MET*ex14 skipping detection, n (%)	TBx	208 (66.5)	111 (67.7)	97 (65.1)
	LBx	178 (56.9)	95 (57.9)	83 (55.7)

*Nine patients had race reported as 'other' or missing or not collected at the site'. †One patient had ECOG PS 2. ‡Smoking history was missing for 10 patients (one in 1L and nine in 2L+). §59 patients had histologies other than adenocarcinoma (32 in 1L and 27 in 2L+) and two had missing histology information (one each in 1L and 2L+).

Efficacy (IRC)

- Overall patients received tepotinib for a mean of 11.5 months (SD: 11.6); median follow-up was 32.6 months (range 0.3–71.9)
  - ORR was 51.4%, mDOR was 18.0 months, mPFS was 11.2 months, and mOS was 19.6 months (**Table 2, Table 3**)
  - ORR and mDOR were consistent irrespective of age, sex, smoking history, and ECOG PS (**Table S1, Figure S2**)
- 1L (n=164) patients received tepotinib for a mean of 12.4 months (SD: 12.2), with 27 patients (16.5%) still receiving treatment
  - ORR was 57.3%, mDOR was 46.4 months, mPFS was 12.6 months, and mOS was 21.3 months (**Table 2**, **Table 3**, **Figure 1, Figure S3**)
  - Among 111 1L T+ pts, ORR was 58.6%, mDOR was 46.4 months, mPFS was 15.9 months, and mOS was 29.7 months (**Table 2**, **Table 3**, **Figure S4**)
- 2L+ (n=149) patients received tepotinib for a mean of 10.5 months (SD: 11.0), with 10 patients (6.7%) still receiving treatment
  - ORR was 45.0% (95% CI: 36.8, 53.3), mDOR was 12.6 months (95% CI: 9.5, 18.5), mPFS was 11.0 months (95% CI: 8.2, 13.7), and mOS was 19.3 months (95% CI: 15.6, 22.3) (**Table S2**, **Figure 1**, **Figure S2**)

Table 2. ORR with tepotinib: Overall, 1L, 1L T+

	N	ORR* (95% CI)
Overall	313	51.4 (45.8, 57.1)
1L	164	57.3 (49.4, 65.0)
1L T+	111	58.6 (48.8, 67.8)

*One treatment-naïve patient had a complete response; all other objective responses were partial responses.

Figure 1. Efficacy of tepotinib in Cohorts A+C patients A. PFS, B. OS

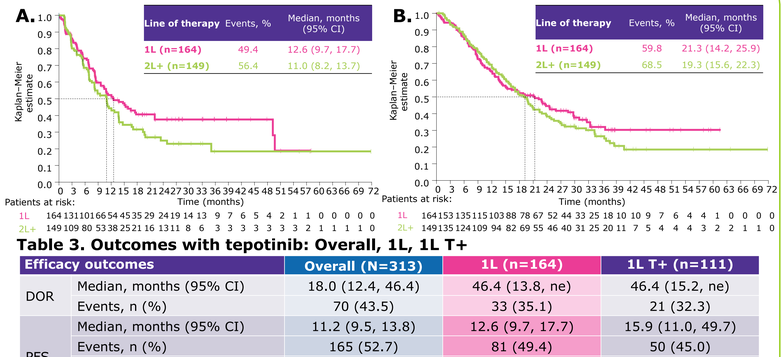

Table 3. Outcomes with tepotinib: Overall, 1L, 1L T+

Efficacy outcomes		Overall (N=313)	1L (n=164)	1L T+ (n=111)
DOR	Median, months (95% CI)	18.0 (12.4, 46.4)	46.4 (13.8, ne)	46.4 (15.2, ne)
	Events, n (%)	70 (43.5)	33 (35.1)	21 (32.3)
PFS	Median, months (95% CI)	11.2 (9.5, 13.8)	12.6 (9.7, 17.7)	15.9 (11.0, 49.7)
	Events, n (%)	165 (52.7)	81 (49.4)	50 (45.0)
	12-month rate, % (95% CI)	49 (42.0, 55.0)	52 (43.0, 60.0)	59 (48.0, 69.0)
	24-month rate, % (95% CI)	32 (25.0, 39.0)	38 (29.0, 47.0)	42 (30.0, 53.0)
OS	Median, months (95% CI)	19.6 (16.2, 22.9)	21.3 (14.2, 25.9)	29.7 (18.8, ne)
	Events, n (%)	200 (63.9)	98 (59.8)	55 (49.5)

HRQoL

- EQ-5D-5L VAS and EORTC QLQ-C30 GHS responses showed stability in overall HRQoL over time (**Figure S5**)
- For EORTC QLQ-LC13 symptom scores, dyspnea and chest pain remained stable, while there was a clinically meaningful improvement in cough (**Figure S6**)

Safety

- Most treatment-related AEs were Grade 1/2; Grade ≥3 occurred in 34.8% of patients (**Table 4**)
- Peripheral edema was the most common AE and was mostly Grade 1/2; treatment-related any grade: 67.1%, Grade ≥3: 11.2% (**Table S3**)
- Patients requiring treatment interruptions or dose reductions were able to continue to benefit from tepotinib (**Figure S7**)

Table 4. Tepotinib safety profile in Cohorts A+C

AE, n (%)	Overall (N=313)	
	All cause AEs	Treatment-related AEs
Any AE	310 (99.0)	287 (91.7)
Serious AEs	159 (50.8)	49 (15.7)
Grade ≥3 AEs	203 (64.9)	109 (34.8)
Grade ≥4 AEs	57 (18.2)	12 (3.8)
AEs leading to dose reduction	113 (36.1)	105 (33.5)
AEs leading to treatment interruption	165 (52.7)	135 (43.1)
AEs leading to permanent discontinuation	78 (24.9)	46 (14.7)
AEs leading to death	41 (13.1)	3* (1.0)

*Of the three patients with treatment-related AEs leading to death, two patients were already detailed in Le X, et al. *Clin Cancer Res*. 2022;28(6):1117–1126, and the third patient had progressive disease or a lung cancer-related condition leading to multiple organ failure, which was considered treatment-related due to a missing causality report.

Abbreviations: 1L, first line; 2L+, second or later line; AE, adverse event; CI, confidence interval; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC, European Organisation for Research and Treatment of Cancer; EQ-5D-5L, EuroQol Five-Dimension Five-Level scale; GHS, global health status; 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; MMRM, mixed-effect model repeated measures; ne, not estimable; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-LC13, Quality of Life Questionnaire Lung Cancer 13; RECIST, Response Evaluation Criteria in Solid Tumors; SD, standard deviation; T+, positive detection of *MET*ex14 skipping in tissue biopsy sample; TBx, tissue biopsy; VAS, visual analog scale.

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Supplementary materials

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