Treatment (Tx) sequencing with tepotinib in previously treated patients (pts) with *MET* exon 14 (*MET*ex14) skipping NSCLC in the VISION trial

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CONCLUSIONS

- **Tepotinib demonstrated clinically meaningful efficacy in patients treated in 2L+, including 2L and 3L+**
  - **Earlier use of tepotinib in the treatment sequence may help maximize the number of patients receiving METi therapy[1]**
- **In VISION, patients treated in 2L+ had a median age of 70.8 years; approximately half (50.4%) received subsequent treatment**
  - **This proportion was higher than the 20–30% reported for 1L CT or IO in the IPSOS trial in elderly patients (median age 75 years)[2]**
- **After discontinuation of tepotinib, a proportion of 2L+ patients received METi including tepotinib again with clinical benefit**

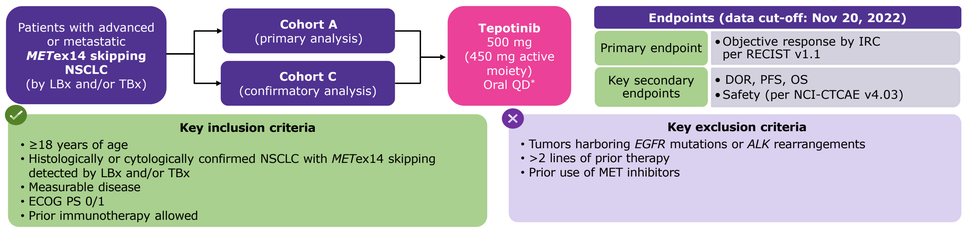
INTRODUCTION

- *MET*ex14 skipping is reported in 3–4% of patients with NSCLC and sensitizes the tumor to MET inhibition[3–6]
- Tepotinib, a METi, is approved for treatment of advanced/metastatic *MET*ex14 skipping NSCLC, after immunotherapy and/or platinum-based chemotherapy in the EU, and regardless of prior treatment in other countries including the UK and Switzerland[7–9]
- In the VISION trial, tepotinib showed durable activity regardless of prior treatment[9]
  - In 1L, ORR was 57.3% (95% CI: 49.4, 65.0), mDOR was 46.4 months (95% CI: 13.8, ne), and mPFS was 12.6 months (95% CI: 9.7, 17.7)
- **We report long-term efficacy in previously treated patients according to number of prior treatment lines (2L/3L+), and outcomes with prior and post-tepotinib treatment (data cut-off: November 20, 2022)**

METHODS

- VISION (NCT02864992) is a single-arm, Phase II trial of tepotinib in patients with advanced NSCLC harboring *MET*ex14 skipping (**Figure 1**)
- Predefined subgroup analyses evaluated patients treated with tepotinib in 2L, 2L+, and 3L+
- Prior or post tepotinib treatment was investigator's choice and the outcomes were reported as per investigator
- Regimens evaluated: Platinum-based CT without IO, IO monotherapy, IO + platinum-based CT, and METi (subsequent treatment only)

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



*Treatment continues until disease progression, intolerable toxicity, or withdrawal of consent.

RESULTS

Baseline characteristics

- Of 313 patients enrolled, 149 were previously treated (median age 70.8 years)
  - 92 (61.7%) received tepotinib in 2L
  - 57 (38.3%) received tepotinib in 3L+ (n=54 in 3L; n=3 in 4L) (**Table 1**)
- 1L regimens prior to enrolling in VISION were platinum-based CT without IO (n=99, 66.4%), IO monotherapy (n=59, 39.6%), and IO + platinum-based CT (n=22, 14.8%)

Table 1. Baseline characteristics

Baseline characteristics		Previously treated patients		
		All 2L+ (n=149)	2L (n=92)	3L+ (n=57)
Median age, years (range)		70.8 (41–89)	70.4 (41–89)	71.9 (52–88)
Sex, %	Male	47.7	50.0	43.9
	Female	52.3	50.0	56.1
Race*, %	White	55.7	55.4	56.1
	Asian	37.6	39.1	35.1
ECOG PS, %	0	24.2	25.0	22.8
	1	75.8	75.0	77.2
Smoking history†, %	Yes	40.9	39.1	43.9
	No	53.0	54.3	50.9

*Race was missing/not collected at the study site for eight patients, two patients were Black/African American, and one patient was recorded as 'other'. †Smoking history was missing in nine patients.

Efficacy outcomes with prior treatments and tepotinib

- Across all treatments prior to tepotinib, ORR was 28.9%, mDOR was 6.0 months (IQR: 4.0, 12.0), and mPFS was 5.0 months (IQR: 2.0, 11.0) (**Table 2**)
- Outcomes were similar across prior regimens, including platinum-based CT without IO (n=99), IO monotherapy (n=59), and IO + platinum-based CT (n=22)
- Compared with prior regimens, outcomes with tepotinib were greatly improved, with an ORR of 45.0% (95% CI: 36.8, 53.3), mDOR of 12.6 months (95% CI: 9.5, 18.5), and mPFS of 11.0 months (95% CI: 8.2, 13.7) in 2L+[9]
  - Tepotinib outcomes were similar between patients treated in 2L and 3L+

Table 2. Outcomes with all prior treatments and tepotinib

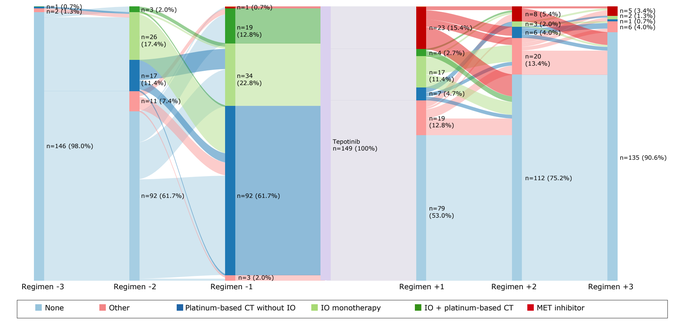
Efficacy outcomes	Patients, n	ORR, % (95% CI)*	mDOR†, months (IQR or 95% CI)‡	mPFS†, months (IQR or 95% CI)‡
All treatments prior to tepotinib by investigator assessment				
All prior regimens	149	28.9	6.0 (4.0, 12.0)	5.0 (2.0, 11.0)
Platinum-based CT without IO	99	29.3	5.0 (3.0, 12.0)	4.0 (2.0, 11.0)
IO monotherapy	59	22.0	6.0 (5.0, 9.0)	4.0 (2.0, 8.0)
IO + platinum-based CT	22	22.7	5.0 (1.0, 8.0)	5.0 (2.0, 7.0)
Tepotinib by IRC				
2L+[9]	149	45.0 (36.8, 53.3)	12.6 (9.5, 18.5)	11.0 (8.2, 13.7)
2L[9]	92	45.7 (35.2, 56.4)	12.6 (8.3, 18.5)	10.9 (8.2, 13.8)
3L+	57	43.9 (30.7, 57.6)	10.8 (8.3, 33.6)	11.0 (5.7, 14.7)

*95% confidence intervals for ORR calculated only for tepotinib. †For treatment prior to tepotinib, mDOR and mPFS as well as corresponding IQRs were based on a descriptive analysis and not on a survival analysis. ‡95% confidence intervals for efficacy outcomes with tepotinib and IQR for other treatments.

Subsequent treatments

- Overall, 139 (93.3%) 2L+ patients had discontinued tepotinib, of whom 70/139 (50.4%) had started subsequent treatment (**Figure 2**)
  - Considering the older age and poor prognosis of patients with *MET*ex14 skipping NSCLC, and receipt of treatment prior to tepotinib, the percentage of patients receiving subsequent treatment was high
- 16 patients received platinum-based CT without IO, 22 received IO monotherapy, and four received IO + platinum-based CT

Figure 2. Sankey plot for prior and subsequent therapies in previously treated patients who received tepotinib (N=149*)



*Treatment with tepotinib was ongoing in 10 patients at the data cut-off (November 20, 2022).

- Median longest PFS with subsequent platinum-based CT without IO, IO monotherapy, or IO + platinum-based CT was poorer than that attained with prior tepotinib (**Table 3**)

Table 3. Subsequent treatment outcomes with platinum-based CT without IO, IO monotherapy, or IO + platinum-based CT

Efficacy outcomes	Patients, n	mPFS*, months (IQR)
Overall		
Platinum-based CT without IO	35	2.0 (2.0, 2.0)
IO monotherapy	48	3.0 (2.0, 7.0)
IO + platinum-based CT	17	5.5 (3.5, 7.5)
2L+		
Platinum-based CT without IO	16	2.0 (2.0, 2.0)
IO monotherapy	22	3.5 (2.0, 8.0)
IO + platinum-based CT	4	3.0 (3.0, 3.0)
2L		
Platinum-based CT without IO	12	2.0 (2.0, 7.0)
IO monotherapy	19	5.0 (2.0, 8.0)
IO + platinum-based CT	3	3.0 (3.0, 3.0)
3L+		
Platinum-based CT without IO	4	2.0 (0, 2.0)
IO monotherapy	3	1.0 (1.0, 1.0)
IO + platinum-based CT	1	ne (ne, ne)

*mPFS as well as corresponding IQRs were based on a descriptive analysis and not on a survival analysis.

METi rechallenge

- 34 patients received subsequent METi (12 crizotinib, 13 capmatinib, 3 tepotinib, 3 cabozantinib, 2 amivantamab, 2 SYM 015, and 1 elzovantinib) after tepotinib in 2L+
  - 22 patients received subsequent METi after 2L (6 crizotinib, 12 capmatinib, 2 tepotinib, and 2 SYM 015, 1 cabozantinib), while 12 patients received subsequent METi after 3L+ (6 crizotinib, 2 amivantamab, 2 cabozantinib, 1 capmatinib, 1 tepotinib, and 1 elzovantinib)
  - 23 patients received METi as next subsequent treatment after tepotinib
- In 34 patients who received subsequent METi after 2L+ tepotinib, best response was PR in two and SD in 10 patients, and the median (IQR) longest PFS was 6.0 months (2.0, 11.0) (**Table S1**)
  - Of the two patients with PRs, both discontinued tepotinib due to PD; subsequent METi were given as the first subsequent therapy in one patient, and after initiation of subsequent chemotherapy in the other
- In 22 patients who received subsequent METi after 2L tepotinib, best response was PR in two and SD in seven patients, while in 12 patients who received subsequent METi after 3L+ tepotinib, best response was SD in three patients
  - The median (IQR) longest PFS was 10 months (5.5, 11.0) in patients who received subsequent METi after 2L tepotinib, while it was 4.0 months (2.0, 6.0) in patients who received subsequent METi after 3L+ tepotinib (**Table S1**)

Abbreviations: 1L, first line; 2L, second line; 2L+, second or later line; 3L+, third or later line; 4L, fourth line; ALK, anaplastic lymphoma kinase; CI, confidence interval; CT, chemotherapy; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; IO, immunotherapy; IPSOS, a Phase III, global, multicenter, open-label, randomized, controlled study examining the efficacy, safety and patient-reported outcomes with atezolizumab versus single agent chemotherapy in patients who were considered unsuitable for 1L platinum-doublet chemotherapy; IQR, interquartile range; IRC, independent review committee; LBx, liquid biopsy; m, median; MET, mesenchymal–epithelial transition factor; *MET*ex14, *MET* exon 14; METi, MET inhibitors; 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; PD, progressive disease; PFS, progression-free survival; PR, partial response, QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TBx, tissue biopsy.

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Supplementary materials
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SUPPLEMENTARY RESULTS

Table S1. Subsequent treatment outcomes with MET inhibitors

Efficacy outcomes	Patients, n	DCR,* %	mPFS†, months (IQR)
2L+	34	35.3	6.0 (2.0, 11.0)
2L	22	40.9	10.0 (5.5, 11.0)
3L+	12	25.0	4.0 (2.0, 6.0)

*DCR was calculated based upon the no. of patients who had CR, PR, and SD. †mPFS, and the corresponding IQRs were based on a descriptive analysis and not on a survival analysis.

Abbreviations: 2L, second line; 2L+, second or later line; 3L+, third or later line; CR, complete response; DCR, disease control rate; IQR, inter quartile range; m, median; ne, not estimable; PFS, progression-free survival; PR, partial response; SD, stable disease.

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