Efficacy and safety of tepotinib in patients with advanced age: VISION subgroup analysis of patients with *MET* exon 14 skipping NSCLC

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CONCLUSIONS

- ***MET*ex14 skipping is an oncogenic driver that occurs in patients with NSCLC of advanced age**
- **Tepotinib demonstrated robust and durable clinical activity with a favorable safety profile in patients with *MET*ex14 skipping NSCLC across all ages, including the elderly**
- **Given the vulnerability of patients of advanced age, prioritization of effective and convenient targeted therapies is warranted in this population**

INTRODUCTION

- Patients with *MET*ex14 skipping are typically older than patients harboring other oncogenic drivers, and patients who received immunotherapy in key clinical trials;[1,2]
  - *KRAS*-mutant NSCLC median age: 65 years[1]
  - *EGFR*-mutant NSCLC median age: 61 years[1]
  - Key immunotherapy trials median ages: ≤65 years[2]

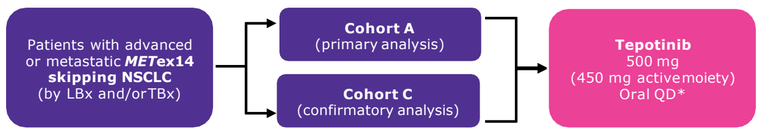
***MET*ex14 skipping NSCLC median age: 72.5 years[1]**

- Patients with such advanced age may be challenging to treat due to comorbidities[3]
- Tepotinib is an oral, once daily, highly selective, potent MET TKI, with established clinical activity in patients with *MET*ex14 skipping NSCLC, as reported in the VISION study[4,5]
- Here, we report updated results (data cut-off: February 1, 2021) and the outcomes according to age

METHODS

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

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



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

Endpoints† (data cut-off: Feb 1, 2021)

- Primary endpoint: Objective response by IRC according to RECIST v1.1 criteria
- Secondary endpoints include: DOR, PFS, OS; HRQoL; Safety (AEs were assessed using NCI-CTCAE v4.03)
- Analyses according to age were predefined

†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.

Key inclusion criteria
- ≥18 years of age
- Histologically or cytologically confirmed NSCLC with *MET*ex14 skipping detected by TBx or LBx
- 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

RESULTS

OVERALL POPULATION

VISION comprises a large population of elderly patients with *MET*ex14 skipping NSCLC

- Overall, most patients in Cohorts A and C that were assessed for efficacy (N=275) were elderly (median age 72.4 years [range 41–94]), about half were male, half had smoking history, and most had adenocarcinoma
- Baseline characteristics were similar in younger and older patients

Table 1. Baseline characteristics

Baseline characteristics		Overall (N=275)
Sex, %	Male	49.1
ECOG PS, %	0	27.6
	1	72.0
Smoking history*, %	Yes	46.5
Histology, adenocarcinoma, %		80.0
Treatment-naïve, %		49.8
Age, %	<65 years	20.4
	≥65–<75 years	36.7
	≥75–<85 years	34.2
	≥85 years	8.7

*Smoking history was missing in ten patients.

Tepotinib demonstrated an overall robust clinical activity

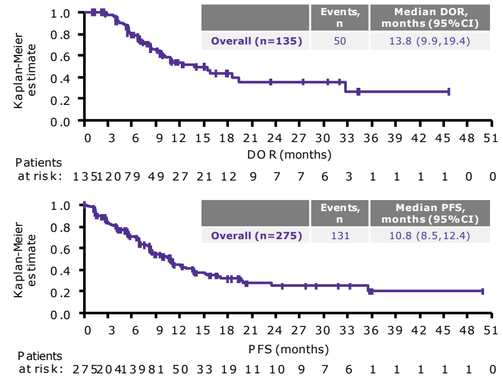
- Overall, ORR was 49.1%, median DOR was 13.8 months and median PFS was 10.8 months

Table 2. Overall efficacy of tepotinib

Efficacy (IRC)	Overall (N= 275)
BOR, n (%)	
CR	0
PR	135 (49.1)
SD	71 (25.8)
PD	34 (12.4)
NE	35 (12.7)
ORR, % (95% CI)	49.1 (43.0, 55.2)
DCR, % (95% CI)	74.9 (69.4, 79.9)
mDOR, months (95% CI)	13.8 (9.9, 19.4)
mPFS, months (95% CI)	10.8 (8.5, 12.4)

- Outcomes in patients enrolled based on liquid or tissue biopsy testing for *MET*ex14 skipping have been presented previously by Felip E, et al.[6] (scan QR code to view)

Figure 2. Overall DOR and PFS



EFFICACY ACCORDING TO AGE

Responses were durable, including in patients above 75 years of age

- ORR was 52.2% and 44.9%, median DOR was 12.4 and 13.8 months, and median PFS was 11.0 and 10.4 months in patients below and above 75 years of age, respectively

Table 3. Objective response to tepotinib

Efficacy (IRC)	<75 years n=157	≥75 years n=118
BOR, n (%)		
CR	0	0
PR	82 (52.2)	53 (44.9)
SD	35 (22.3)	36 (30.5)
PD	21 (13.4)	13 (11.0)
NE	19 (12.1)	16 (13.6)
ORR, % (95% CI)	52.2 (44.1, 60.3)	44.9 (35.7, 54.3)
DCR, % (95% CI)	74.5 (67.0, 81.1)	75.4 (66.6, 82.9)
mDOR, months (95% CI)	12.4 (9.5, 32.7)	13.8 (9.0, ne)
mPFS, months (95% CI)	11.0 (8.2, 13.7)	10.4 (8.2, 13.7)

Figure 3. DOR in patients <75 years and ≥75 years

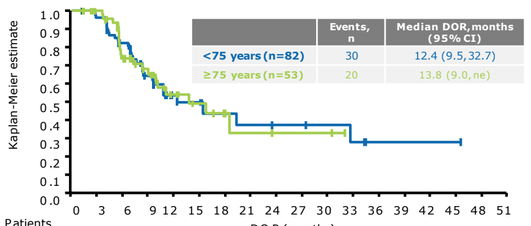
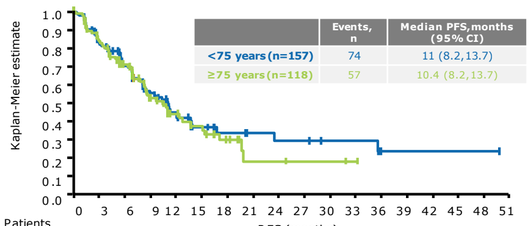


Figure 4. PFS in patients <75 years and ≥75 years



- Patient-reported outcomes indicated quality of life was maintained while on tepotinib treatment, in patients above and below 75 years of age (scan QR code to access supplementary HRQoL results)

SAFETY

Tepotinib was generally well tolerated with low proportion of TRAEs leading to discontinuation

- Grade ≥3 TRAEs occurred in 29.6% of patients, 30.9% of patients had TRAEs leading to dose reduction, 39.2% temporary interruption, and 14.1% permanent discontinuation
- The most common adverse event was peripheral edema, occurring in 66% of patients, which was considered treatment-related in 60% of patients

Table 4. Treatment-related adverse events

TRAE, n (%)	Overall (N=291)	Age subgroup, years			
		<65 (n=64)	≥65–<75 (n=107)	≥75–<85 (n=96)	≥85 (n=24)
Any grade	264 (90.7)	52 (81.3)	105 (98.1)	84 (87.5)	23 (95.8)
Grade ≥3	86 (29.6)	9 (14.1)	28 (26.2)	39 (40.6)	10 (41.7)
Leading to dose reduction	90 (30.9)	10 (15.6)	36 (33.6)	36 (37.5)	8 (33.3)
Leading to temporary interruption	114 (39.2)	14 (21.9)	39 (36.4)	46 (47.9)	15 (62.5)
Leading to permanent discontinuation	41 (14.1)	4 (6.3)	14 (13.1)	17 (17.7)	6 (25.0)

Table 5. Adverse events of any cause (any grade) occurring in ≥15% of all patients

AE, n (%)	Overall (N=291)	Age subgroup, years			
		<65 (n=64)	≥65–<75 (n=107)	≥75–<85 (n=96)	≥85 (n=24)
Peripheral edema	191 (65.6)	35 (54.7)	75 (70.1)	61 (63.5)	20 (83.3)
Nausea	87 (29.9)	16 (25.0)	35 (32.7)	32 (33.3)	5 (20.8)
Diarrhea	81 (27.8)	17 (26.6)	27 (25.2)	30 (31.3)	7 (29.2)
Hypoalbuminemia	81 (27.8)	15 (23.4)	27 (25.2)	31 (32.3)	8 (33.3)
Blood creatinine increase	76 (26.1)	13 (20.3)	30 (28.0)	29 (30.2)	4 (16.7)
Dyspnea	60 (20.6)	9 (14.1)	21 (19.6)	22 (22.9)	8 (33.3)
Decreased appetite	48 (16.5)	3 (4.7)	21 (19.6)	22 (22.9)	2 (8.3)
Constipation	46 (15.8)	9 (14.1)	17 (15.9)	19 (19.8)	1 (4.2)
Fatigue	45 (15.5)	8 (12.5)	16 (15.0)	20 (20.8)	1 (4.2)

Abbreviations: AE, adverse event; ALK, anaplastic lymphoma kinase; BOR, best objective response; CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HRQoL, health-related quality of life; KRAS, kirsten rat sarcoma virus; IRC, independent review committee; LBx, liquid biopsy; MET, mesenchymal–epithelial transition factor; mDOR, median duration of response; *MET*ex14, MET exon 14; mPFS, median progression free survival; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; ne, not estimable; NE, not evaluable; 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; TKI, tyrosine kinase inhibitor; TRAE, treatment-related adverse event.

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