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# Safety and Patient-Reported Outcomes with Tepotinib in Patients with *MET*ex14 Skipping NSCLC: ≥3-years Follow-Up of VISION

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# CONCLUSIONS

- In patients enrolled in the VISION study with ≥3-years follow-up, tepotinib continues to demonstrate a manageable safety profile with no new safety signals, consistent with earlier findings
- Overall, HRQoL PRO scores remained stable with tepotinib, with no meaningful change in EORTC QLQ-C30 or EQ-5D-5L scores up to 228 weeks
- The favorable safety of tepotinib and maintained patient HRQoL benefits this often elderly population of patients with NSCLC

## PLAIN LANGUAGE SUMMARY



- Tepotinib, an anticancer drug taken by mouth, is approved in many countries based on the results of a clinical trial called VISION
- This trial investigated the effectiveness of tepotinib in patients with non-small cell lung cancer that has a
  particular mutation called MET exon 14 skipping
- This poster reports long-term safety and quality of life outcomes from patients in the VISION trial who have been monitored for at least 3 years



characteristics

**Quality of life** 

 313 patients participated in the VISION trial, with an average age of 72 years
 Patients received tenotinib for

Patients received tepotinib for an average duration of 7.5 months



Approximately 90% of patients experienced side effects related to tepotinib treatment
 16% experienced serious side effects

- The most common side effects were swelling in the extremities (such as hands and feet), low blood albumin protein levels, and nausea
- Additionally, 15.7% of patients had to stop treatment due to side effects
- Throughout the VISION trial, patients completed questionnaires evaluating their quality of life before and while receiving tepotinib
- Patient scores relating to their overall health and quality of life **remained stable** while receiving tepotinib
  Specific scores relating to symptoms experienced by patients with lung cancer were improved during
- treatment with tepotinib for cough and chest pain, or remained stable for shortness of breath

# INTRODUCTION

- Typically, 3-4% of patients with NSCLC harbor *MET*ex14 skipping; these patients are usually elderly and have a poor prognosis, and therefore treatments with a manageable safety profile are especially relevant  $^{1-4}$
- Tepotinib is an oral, once-daily, and highly selective MET TKI, approved in many countries for the treatment of advanced/metastatic NSCLC with METex14 skipping based on outcomes from the VISION trial<sup>5,6</sup>
- Safety outcomes and HRQoL PROs of tepotinib in VISION have previously been reported from earlier data cuts (safety: data cut-off: November 20, 2022; HRQoL PROs: data cut-off: February 20, 2022)<sup>4,6,7</sup>
- Here, we report long-term safety outcomes and HRQoL PROs from VISION in patients with ≥3-years follow-up (data cut-off: May 20, 2024)



# **METHODS**

- VISION (NCT02864992) is a single-arm, Phase II trial of tepotinib in patients with advanced NSCLC harboring METex14 skipping (Supplementary Figure S1)
- Secondary endpoints included safety and HRQoL PROs
- PROs were assessed using the following:
- EORTC QLQ-C30 global health status and 5 functional scales; EQ-5D-5L questionnaire and EQ-VAS; EORTC QLQ-LC13: cough, dyspnea, and chest pain were predefined items of interest
- Results were scored from 0 to 100 where a change of ≥10 points from baseline was considered to be the minimal clinically important difference; higher scores indicate improvement on EORTC QLQ-C30 global health status and EQ-VAS scores, and lower scores indicate reduced symptoms on EORTC QLQ-LC13
- PROs were collected at Day 1, every 6 weeks for 9 months, and then every 12 weeks during treatment
- TTD was defined as time from baseline to first 10-point deterioration using Kaplan-Meier estimates;
- the proportion of patients without deterioration was estimated every 3 months
- An MMRM analysis was used to evaluate longitudinal changes from baseline in EORTC QLQ-LC13 symptom scores



### **Baseline characteristics**

- VISION included 313 patients with *MET*ex14 skipping NSCLC in Cohorts A and C (**Supplementary Figure S1**)
- Median age of the patients was 72.0 years (range: 41–94), 50.8% were female, 73.8% had an ECOG PS of 1, and 47.6% were previously treated (Supplementary Table S1)
- Patients had a median treatment duration of 7.5 months (range: 0.03-83.12) and 19 patients received treatment for ≥48 months

## **Safety outcomes**

- All patients were analyzed for safety; all-cause any grade adverse events occurred in 310 patients (99.0%; Grade  $\geq$ 3: 68.4%), while any grade TRAEs occurred in 287 patients (91.7%; Grade  $\geq$ 3: 36.1%) (**Table 1**)
- Any grade serious TRAEs were observed in 50 (16.0%) patients
- TRAEs led to dose reduction in 104 (33.2%) patients, treatment interruption in 137 (43.8%) patients, and permanent discontinuation in 49 (15.7%) patients

Table 1. Summary of all-cause AEs and TRAEs

	Cohort A+C (N=313)	
Patients with at least one, n (%)	All-cause AEs	TRAEs
Any AE	310 (99.0)	287 (91.7)
Serious AE	171 (54.6)	50 (16.0)
Grade ≥3 AE	214 (68.4)	113 (36.1)
Grade ≥4 AE	59 (18.8)	12 (3.8)
AE leading to death	43 (13.7)	3 (1.0)
AE leading to dose reduction	114 (36.4)	104 (33.2)
AE leading to temporary discontinuation (interruption)	172 (55.0)	137 (43.8)
AE leading to permanent discontinuation	84 (26.8)	49 (15.7)

The most common TRAEs were peripheral edema in 212 patients (67.7%;
 Grade ≥3: 11.8%), hypoalbuminemia in 79 patients (25.2%; Grade ≥3: 3.8%),
 and nausea in 73 patients (23.3%; Grade ≥3: 0.6%) (Table 2)

Table 2. Summary of TRAEs in >10% of patients

	Any grade n (%)	Grade ≥3 n (%)
Peripheral edema	212 (67.7)	37 (11.8)
Hypoalbuminemia	79 (25.2)	12 (3.8)
Nausea	73 (23.3)	2 (0.6)
Diarrhea	71 (22.7)	1 (0.3)
Blood creatinine increased	69 (22.0)	4 (1.3)
Alanine aminotransferase increased	44 (14.1)	7 (2.2)
Decreased appetite	36 (11.5)	1 (0.3)
Aspartate aminotransferase increased	35 (11.2)	6 (1.9)
Amylase increased	33 (10.5)	6 (1.9)

- Out of 313 patients, no dose reductions were observed in 196 (62.6%) patients, while 117 (37.4%) experienced at least one dose reduction during treatment
- Peripheral edema was the most common TRAE that led to dose reduction in 48 (15.3%) patients, treatment interruptions in 59 (18.8%) patients, and treatment discontinuation in 19 (6.1%) patients (**Tables 3–5**)

Table 3. TRAEs leading to dose reductions in ≥1% of patients

	Any grade n (%)
Peripheral edema	48 (15.3)
Generalized edema	10 (3.2)
Edema	7 (2.2)
Pleural effusion	5 (1.6)
Blood creatinine increased	8 (2.6)
Hypoalbuminemia	4 (1.3)
Fatigue	3 (1.0)
Asthenia	3 (1.0)
Localized edema	3 (1.0)

Questionnaire-Core 30; EORTC QLQ-LC13, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Lung Cancer 13; EoT, end-of-treatment; EQ-5D-5L, European Quality of Life 5-dimension 5-level scale; EQ-VAS, European Quality Visual Analog Scale; GHS, global health status; HRQoL, health-related quality of life;

Table 4. TRAEs leading to treatment interruptions in >2% of patients

	Any grade n (%)
Peripheral edema	59 (18.8)
Alanine aminotransferase increased	8 (2.6)
Generalized edema	15 (4.8)
Edema	11 (3.5)
Pleural effusion	10 (3.2)
Blood creatinine increased	18 (5.8)
Localized edema	7 (2.2)
Nausea	7 (2.2)

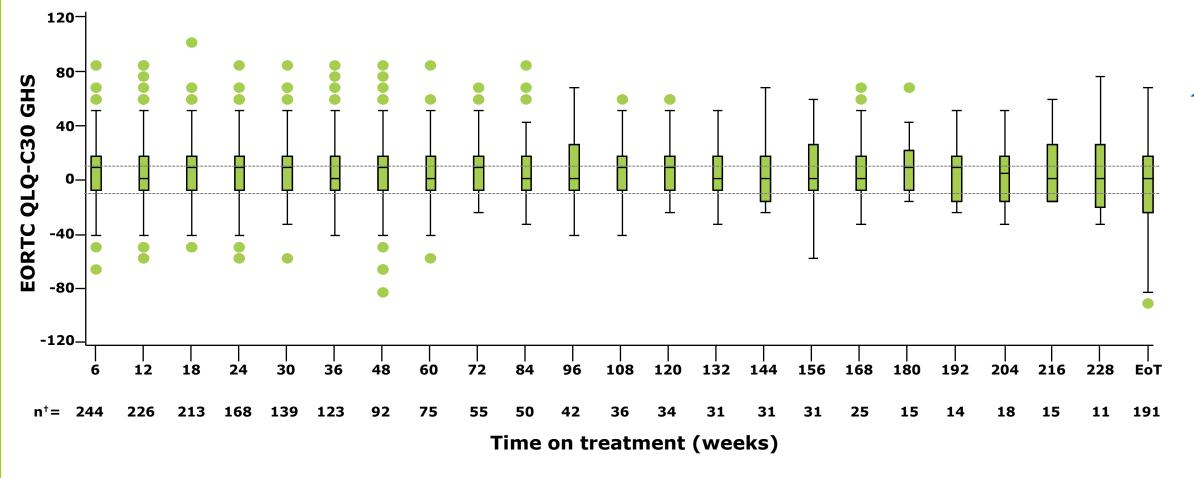
Table 5. TRAEs leading to treatment discontinuation in ≥1% of patients

	Any grade n (%)
Peripheral edema	19 (6.1)
Generalized edema	3 (1.0)
Edema	4 (1.3)
Pleural effusion	3 (1.0)
Interstitial lung disease	3 (1.0)
Pneumonitis	3 (1.0)

## **HRQoL** outcomes

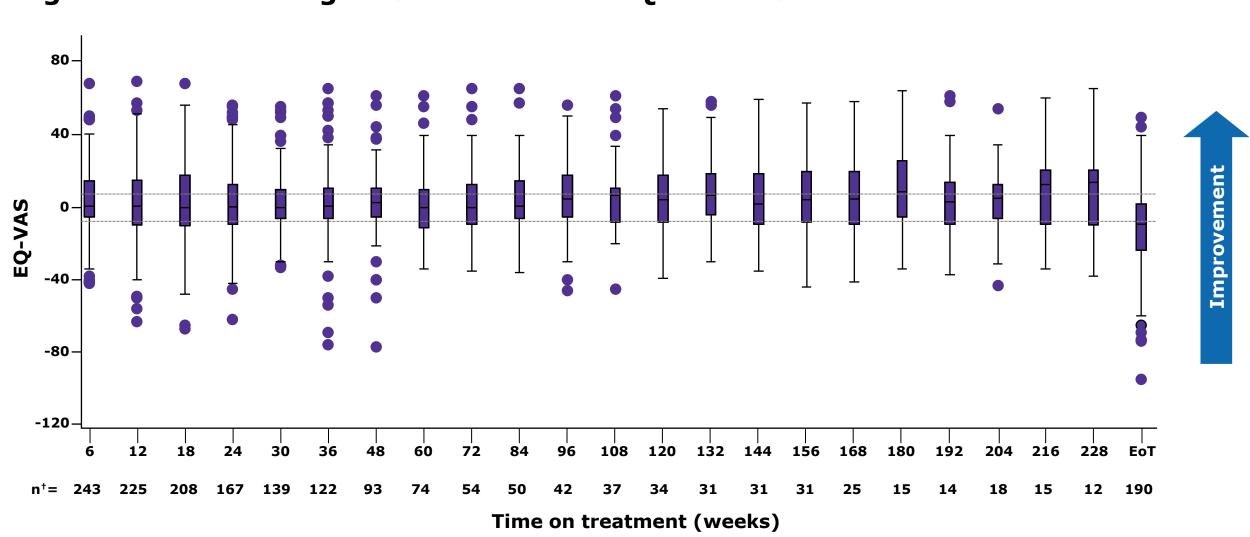
- At the end of treatment, in patients analyzed for HRQoL, the mean change (±SD) from baseline for EORTC QLQ-C30 GHS was -7.1 (26.66) (n=174) and for EQ-VAS was -10 (23.7) (n=172), with positive values indicating an improvement (**Figures 1-2**)
- Mean change (±SD) from baseline in EORTC QLQ-LC13 symptom scores for cough, dyspnea, and chest pain were -6.1 (28.16) (n=175), 7.1 (21.05) (n=175), and -2.3 (28.13) (n=174), respectively, with negative values indicating improvement (Supplementary Figure S2)
- Median time to deterioration of EORTC QLQ-LC13 symptom scores was 36.5 months for cough, 30.4 months for chest pain, and 5.5 months for dyspnea

Figure 1. Mean change from baseline in EORTC QLQ-C30 global health score\*



\*Visits with <10 patients are not presented, with the exception of the EoT/30-day safety follow-up. Dashed lines show minimal clinically important difference of ±10 points. In each box plot, horizontal lines indicate the medians, boxes indicate the interquartile ranges, whiskers indicate the ranges (excluding outliers), and circles indicate outliers.

Figure 2. Mean change from baseline in EQ-VAS score\*



\*Visits with <10 patients are not presented, with the exception of the EoT/30-day safety follow-up. Dashed lines show minimal clinically important difference of ±10 points. In each box plot, horizontal lines indicate the medians, boxes indicate the interquartile ranges, whiskers indicate the ranges (excluding outliers), and circles indicate outliers.

†Number of patients who completed the questionnaire at each visit.



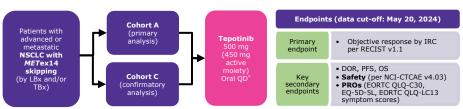
#### **Safety and Patient-Reported Outcomes with** Tepotinib in Patients with METex14 Skipping NSCLC: ≥3-years Follow-Up of VISION

Enriqueta Felip<sup>1</sup>, Roberto Ferrara<sup>2,3</sup>, Remi Veillon<sup>4</sup>, Xiuning Le<sup>5</sup>, Egbert F. Smit<sup>6</sup>, Julien Mazières<sup>7</sup>, Alexis B. Cortot<sup>8</sup>, Jo Raskin<sup>9</sup>, Michael Thomas<sup>10,11</sup>, **Niels Reinmuth**<sup>12</sup>, James Chih-Hsin Yang<sup>13</sup>, Myung-Ju Ahn<sup>14</sup>, Jun Zhao<sup>15</sup>, Frank Griesinger<sup>16</sup>, Santiago Viteri<sup>17</sup>, Erica Velthuis<sup>18</sup>, Chris Pescott<sup>19</sup>, Andreas Johne<sup>20</sup>, Rolf Bruns<sup>21</sup>, Paul K. Paik<sup>22</sup>



#### SUPPLEMENTARY RESULTS

#### Supplementary Figure S1. Study design, endpoints, and eligibility criteria of VISION





#### Key inclusion criteria

- ≥18 years of age
- Histologically or cytologically confirmed NSCLC with METex14 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 or HGF inhibitors

#### Supplementary Table S1. Baseline characteristics

Parameter		Cohort A+C (N=313)
Sex, n (%)	Male	154 (49.2)
	Female	159 (50.8)
Race*, n (%)	White	195 (62.3)
	Asian	106 (33.9)
	Black/African American	3 (1.0)
Age, years	Median (range)	72.0 (41-94)
Histology <sup>†</sup> , n (%)	Adenocarcinoma	252 (80.5)
	Squamous	28 (8.9)
	Sarcomatoid	10 (3.2)
Smoking history*, n (%)	No	154 (49.2)
	Yes	149 (47.6)
ECOG PS§, n (%)	0	81 (25.9)
	1	231 (73.8)
Line of treatment, n (%)	1L	164 (52.4)
	2L+	149 (47.6)

<sup>\*</sup>Nine patients had race reported as 'other' or was missing. †21 patients had other histologies and two were missing. ‡Smoking history was missing for 10 patients. §One patient had ECOG PS 2.

<sup>\*</sup>Treatment continues until disease progression, intolerable toxicity, or withdrawal of consent.

## Safety and Patient-Reported Outcomes with Tepotinib in Patients with *MET*ex14 Skipping NSCLC: ≥3-years Follow-Up of VISION

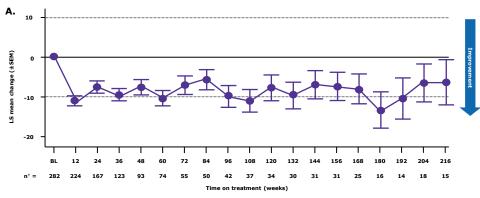
Enriqueta Felip<sup>1</sup>, Roberto Ferrara<sup>2,3</sup>, Remi Veillon<sup>4</sup>, Xiuning Le<sup>5</sup>, Egbert F. Smit<sup>6</sup>, Julien Mazières<sup>7</sup>, Alexis B. Cortot<sup>8</sup>, Jo Raskin<sup>9</sup>, Michael Thomas<sup>10,11</sup>, **Niels Reinmuth**<sup>12</sup>, James Chih-Hsin Yang<sup>13</sup>, Myung-Ju Ahn<sup>14</sup>, Jun Zhao<sup>15</sup>, Frank Griesinger<sup>16</sup>, Santiago Viteri<sup>17</sup>, Erica Velthuis<sup>18</sup>, Chris Pescott<sup>19</sup>, Andreas Johne<sup>20</sup>, Rolf Bruns<sup>21</sup>, Paul K. Paik<sup>22</sup>

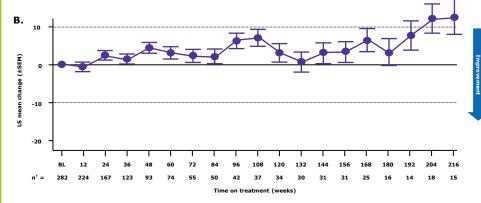
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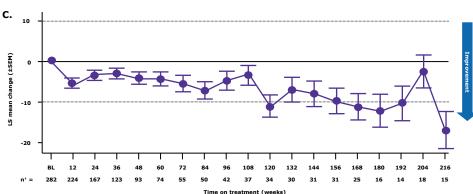


#### SUPPLEMENTARY RESULTS

Supplementary Figure S2. LS mean change from baseline in EORTC QLQ LC-13 symptom scales\* A. Cough, B. Dyspnea, C. Chest pain







\*Visits with <10 patients are not presented. Dashed lines show minimal clinically important difference of ±10 points. †Number of patients who completed the questionnaire at each visit.