Health-related quality of life in patients with NSCLC harboring *MET* exon 14 skipping treated with tepotinib

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CONCLUSIONS

- **In patients with advanced NSCLC with *MET* exon 14 skipping, treatment with tepotinib resulted in a meaningful improvement in symptoms of cough, and patients did not experience deterioration in cough for a median of 19 months**
- **Symptoms of dyspnea and chest pain remained stable during the 24-week analysis**
- **Overall HRQoL remained stable, with no meaningful change in QLQ C30 or EQ-5D-5L scores up to 24 weeks, and median time to deterioration of ~1 year on both scales**
- **These findings, coupled with the efficacy and safety profile from the VISION study, support tepotinib as an effective treatment option in this patient population, who are typically elderly with a poor prognosis**

INTRODUCTION

- The oncogenic driver *MET* exon 14 skipping occurs in 3–4% of patients with NSCLC[1–4]
- Tepotinib is an oral, once-daily, highly selective MET TKI that blocks MET-mediated signaling pathways involved in tumorigenesis[5]
- In the Phase II VISION study (NCT02864992), tepotinib has shown promising efficacy across treatment lines in patients with advanced NSCLC with *MET* exon 14 skipping[6]
  - The primary analysis conducted in patients with 9 months' follow-up showed an objective response rate by independent review of 46.5–50.0% and 55.6–61.7% by investigator assessment; onset of response was mostly within 6 weeks with a long median duration of response of up to 15.7 months (data cut-off January 1, 2020)[6]
  - Results from this study led to regulatory approval of tepotinib and its companion diagnostic in Japan in March 2020;[6] updated efficacy results are presented in Poster 1283P (data cut-off July 1, 2020)
- NSCLC patients with *MET* exon 14 skipping are older than those with other actionable molecular alterations;[1,7-9] median age was 74 years in the VISION study;[6] for older patients, treatment effects on symptoms and functioning may be particularly important
- Little is known about the impact of targeted treatments on quality of life in this elderly patient population with *MET* exon 14 skipping NSCLC; in patients with *EGFR*-positive NSCLC, who are typically younger, EGFR TKIs in the first-line setting are associated with a median TTD in cough of ~2 years; median TTD of dyspnea varied from 3–10 months, and median TTD of chest pain varied from 4–21 months[10,11,12]
- Here, we present analysis of HRQoL PROs in the VISION study (data cut-off January 1, 2020)

METHODS

- VISION Cohort A enrolled patients with locally advanced or metastatic NSCLC with *MET* exon 14 skipping. Patients were *EGFR/ALK* wild-type, had ≤2 lines of prior therapy and received oral tepotinib 500 mg once daily until intolerable toxicity or disease progression
- PROs were assessed using the following:
  - EORTC QLQ-LC13[13] Cough, dyspnea and chest pain were pre-defined items of interest
  - EORTC QLQ-C30 global health status and 5 functional scales[14]
  - EQ-5D-5L questionnaire and VAS[15,16]
- Results were scored from 0 to 100 where a change of ≥10 points from baseline was considered to be the minimal clinically important difference; lower scores indicate reduced symptoms on EORTC QLQ-LC13 and higher scores indicate improvement on EORTC QLQ-C30 and global health status and EQ-5D-5L VAS scores
- Questionnaires were completed at baseline and every 6 weeks with a predefined analysis at week 12
- 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

RESULTS

Patients

- At data cut-off (January 1, 2020), 99 patients with at least 9 months' follow-up had been enrolled and were analyzed for HRQoL
- Over half the patients were male (55%) and were mostly older (median age 74.0 years) with an ECOG PS of 1 (77%), half were smokers (47%), and almost all had metastatic disease (97%) at study entry[6]
- Questionnaire completion rates were high (**Table 1**)

Table 1. Questionnaire completion rate at baseline and over time

Time	Number of patients on treatment	Completion rate; n (%)
Baseline	99	86 (86.9%)
Week 6	86	72 (83.7%)
Week 12	76	68 (89.5%)
Week 18	68	62 (91.2%)
Week 24	59	50 (84.7%)

At week 18, one patient did not complete the EORTC-5D-5L questionnaire (completion rate was 89.7%).

Baseline symptom burden

- Baseline scores showed moderate-to-high functioning and quality of life and moderate lung cancer symptom burden (**Table 2**)

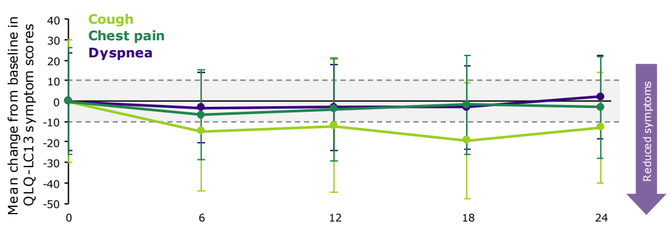
Table 2. Baseline symptom burden

	Mean (SD)
EORTC QLQ-LC13 symptom scores *Lower scores indicate milder symptoms (scale 0–100)*	
Cough	38.0 (29.9)
Chest pain	19.4 (26.3)
Dyspnea	30.9 (23.9)
EORTC QLQ-C30 *Higher scores indicate greater functioning (scale 0–100)*	
Global health score	53.7 (23.7)
EQ-5D-5L *Higher scores indicate greater functioning (scale 0–100)*	
VAS	59.0 (20.6)

Symptom scores

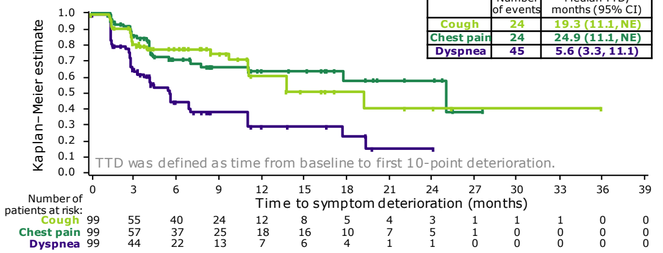
- For the QLQ-LC13 symptoms, a clinically meaningful improvement in cough was observed, with a time to improvement paralleling the onset of objective response (within first 6 weeks)[6]
- Numerical improvements in the mean change from baseline for dyspnea (–3.1 at Week 12) and chest pain (–4.0 at Week 12) were also observed (**Figure 1**)
- Median TTD in EORTC QLQ-LC13 cough, chest pain and dyspnea symptom scores were 19.3 months, 24.9 months and 5.6 months, respectively (**Figure 2**)

Figure 1. Mean change from baseline in EORTC QLQ-LC13 cough, chest pain and dyspnea symptom scores



An increase or decrease of >10 points was considered to be clinically meaningful (shaded area).

Figure 2. TTD in EORTC QLQ-LC13 cough, dyspnea, and pain symptom scores



	Number of events	Median TTD, months (95% CI)
Cough	24	19.3 (11.1, NE)
Chest pain	24	24.9 (11.1, NE)
Dyspnea	45	5.6 (3.3, 11.1)

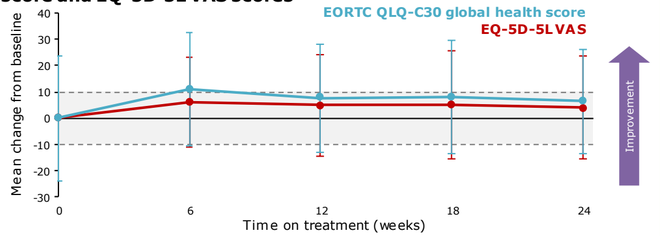
Number of patients at risk:

Cough	99	55	40	24	12	8	5	4	3	1	1	1	0	0
Chest pain	99	57	37	25	18	16	10	7	5	1	0	0	0	0
Dyspnea	99	44	22	13	7	6	4	1	1	0	0	0	0	0

Global health and VAS scores

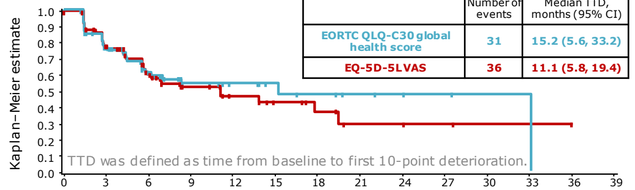
- Mean change from baseline in QLQ-C30 global health score and EQ-5D-5L VAS scores demonstrated stability in patient quality of life over time (**Figure 3**)
- QLQ-C30 functional subscales (physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning) were also stable up to 24 weeks (not shown)
- The median TTD in QLQ-C30 global health and EQ-5D-5L VAS scores were 15.2 and 11.1 months, respectively, for patients treated with tepotinib (**Figure 4**)

Figure 3. Mean change from baseline in EORTC QLQ-C30 global health score and EQ-5D-5L VAS scores



An increase or decrease of >10 points was considered to be clinically meaningful (shaded area).

Figure 4. TTD in EORTC QLQ-C30 global health score and EQ-5D-5L VAS scores



	Number of events	Median TTD, months (95% CI)
EORTC QLQ-C30 global health score	31	15.2 (5.6, 33.2)
EQ-5D-5L VAS	36	11.1 (5.8, 19.4)

Number of patients at risk:

EORTC QLQ-C30	99	52	32	19	11	8	6	4	3	2	1	1	0	0
EQ-5D-5L VAS	99	53	35	22	13	9	6	3	3	2	1	1	0	0

- The proportion of patients without deterioration was relatively high at 3 months: 81%, 86% and 65% for QLQ-LC13 symptoms of cough, chest pain and dyspnea, respectively (**Table 3**)

Table 3. Number of patients without deterioration in QLQ–LC13 symptom scores, QLQ-C30 global health and EQ-5D-5L VAS scores

Measure		Patients without deterioration; % (95% CI)		
		3 months	6 months	9 months
EORTC QLQ-LC13 symptom score	Cough	81 (69, 88)	78 (66, 86)	75 (62, 84)
	Chest pain	86 (75, 92)	71 (58, 80)	66 (53, 77)
	Dyspnea	65 (53, 75)	45 (32, 56)	38 (26, 51)
EORTC QLQ-C30 global health score		77 (65, 85)	61 (48, 72)	55 (41, 66)
EQ-5D-5L VAS		78 (66, 86)	60 (47, 71)	52 (39, 64)

Abbreviations: ALK, anaplastic lymphoma kinase; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; EORTC, European Organisation for Research and Treatment of Cancer; EQ-5D-5L, EuroQol Five Dimension Five Level Scale; HRQoL, health-related quality of life; MET, mesenchymal-epithelial transition factor; NE, not evaluable; NSCLC, non-small cell lung cancer; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire – Core Questionnaire; QLQ-LC13, Quality of Life Questionnaire – Lung Cancer Module; SD, standard deviation; TKI, tyrosine kinase inhibitor; TTD, time to deterioration; VAS, visual analog scale.

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