Health utility with tepotinib in patients with *MET* exon 14 (*MET*ex14) skipping non-small cell lung cancer (NSCLC)

Niels Reinmuth[1], Sanjay Popat[2], Luis Paz-Ares[3], Emma Knowles[4], Anthony Hatswell[4], Thomas McLean[5], Svenja Adrian[6], Bruce Gaumond[7], Helene Vioix[6], Paul Paik[8,9]

[1]Asklepios Clinics Munich-Gauting, Department of Thoracic Oncology, Gauting, Germany; [2]The Royal Marsden Hospital, London, UK; [3]Hospital Universitario 12 deOctubre, Madrid, Spain; [4]Delta Hat, Nottingham, UK; [5]Merck Serono Limited, Feltham, UK, an affiliate of Merck KGaA; [6]Merck Healthcare KGaA, Darmstadt, Germany; [7]EMD Serono, Rockland, MA, USA, an affiliate of Merck KGaA; [8]Thoracic Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [9]Weill Cornell Medical College, New York, NY, USA

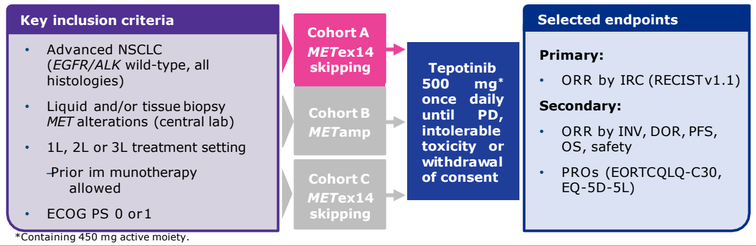
CONCLUSIONS

- **VISION is the first trial of a MET inhibitor to provide data on health utilities (preference-based measures of HRQoL) in patients with *MET*ex14 skipping NSCLC**
- **Overall HRQoL scores remained stable with tepotinib treatment, with no meaningful change in EORTC QLQ-C30 or EQ-5D-5L scores up to 84 weeks**
- **EORTC QLU-C10D and EQ-5D utilities showed moderate-to-high functioning and quality of life during tepotinib therapy until progression**
- **The increase in EQ-5D utilities with tepotinib, before IRC-assessed progression, exceeds the previously reported minimally important difference in cancer of 0.08[1]**
- **Utility with tepotinib did not vary by prior treatment status, or by adenocarcinoma or squamous histology**
- **EORTC QLU-C10D and EQ-5D utilities from matched data collection points were highly correlated, suggesting similarities between both utility instruments**

INTRODUCTION

- Tepotinib is a highly selective, oral, once daily MET inhibitor[2,3] that has been approved in several countries for treatment of advanced NSCLC harboring *MET*ex14 skipping[4,5]
- Approval was based on the Phase II VISION trial (**Figure 1**), in which tepotinib showed durable clinical activity, and was well tolerated in patients with advanced *MET*ex14 skipping NSCLC[6,7]
- PROs were evaluated as a secondary endpoint using EORTC QLQ-C30 and EQ-5D-5L questionnaires, and showed maintenance of overall HRQoL during tepotinib treatment[6,8]
- 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-5D-5L VAS scores
- Health utilities are HRQoL metrics reflecting patients' preferences for different health states, and are expressed on a scale from 0 (dead) to 1 (full health)[9]
- Utilities are widely used to inform cost-effectiveness analyses in Health Technology Assessment (HTA), such as those included in NICE technology appraisal[9]
- To complement the clinical findings of VISION, we used PRO data collected in the trial to evaluate utilities in tepotinib-treated patients with *MET*ex14 skipping NSCLC (Cohort A; data cut-off: February 1, 2021)

Figure 1. VISION: Open-label, multicenter, multicohort, Phase II trial (NCT02864992)[6]

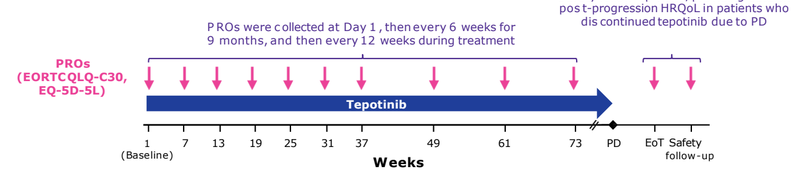


*Containing 450 mg active moiety.

METHODS

- PROs were assessed in VISION according to the schedule in **Figure 2**

Figure 2. VISION: Schedule of PRO assessments



- PRO questionnaire responses were used to derive utilities using UK weights:
  - EORTC QLU-C10D utilities were derived from EORTC QLQ-C30 responses using UK value sets[10]
  - For EQ-5D utilities, EQ-5D-5L data were mapped to EQ-5D-3L responses using a crosswalk algorithm[11], and utilities were obtained using the value set for EQ-5D-3L weights for England[12]
- To account for dependencies within the data (i.e., correlated repeated measurements within patients) when evaluating mean change over time, utilities were analyzed using linear mixed modeling
- The linear mixed models included a random intercept and fixed effects for baseline utility and progression status (i.e., pre- or post-progression health states, as assessed by IRC or INV):
  - Utility ~ (1 | patient ID) + baseline + progression status
- Exploratory analyses also evaluated the impact of prior treatment status, or adenocarcinoma or squamous histology
- Model fit was evaluated using the AIC and BIC

RESULTS

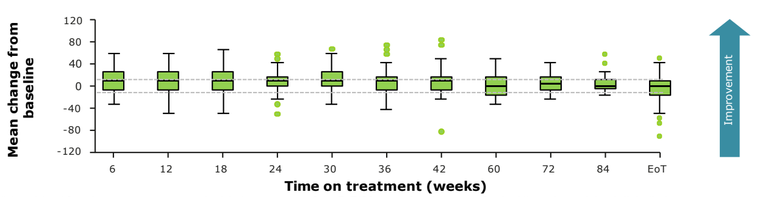
Patients

- At data cut-off (February 1, 2021), 151 patients were analyzed for HRQoL, with a median follow-up of 16.5 months
- Half of the patients were male (52%) and were mostly older (median age 73.0 years) with an ECOG PS of 1 (73.5%), half had a history of nicotine use (51.7%), and almost all had metastatic disease (98%) at study entry
- Questionnaire completion rates were high (**Table S1:** scan QR code below to access supplementary results)

Global health and VAS scores

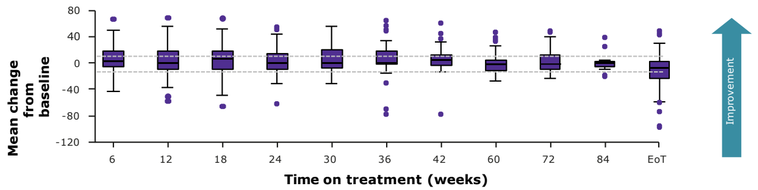
- Mean baseline scores of EORTC QLQ-C30 global health and EQ-5D-5L VAS showed moderate-to-high functioning and quality of life (54.3 [SD: 24.2] and 62 [SD: 20.4], respectively)
- Mean change from baseline in EORTC QLQ-C30 global health and EQ-5D-5L VAS scores demonstrated stability in patient quality of life over time (**Figures 3** and **4**)

Figure 3. 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.

Figure 4. Mean change from baseline in EQ-5D-5L VAS score



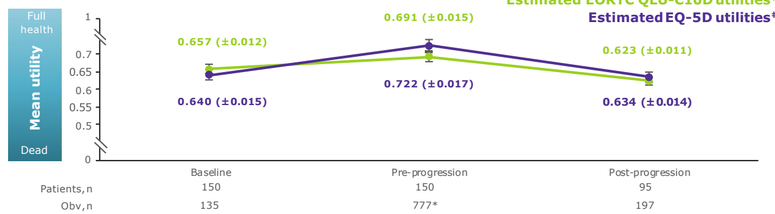
Visits with ≤10 patients are not presented, with the exception of the EoT/30 day safety follow-up. Dashed lines show minimal clinically-important difference of +/- 10 points.

RESULTS (CONTINUED)

EORTC QLU-C10D and EQ-5D utilities

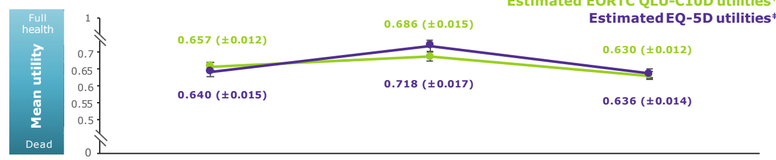
- Of 151 patients analyzed for HRQoL, 974 or 973 observations were available for EORTC QLU-C10D or EQ-5D utilities to be estimated, respectively
- In linear mixed model analyses:
  - EORTC QLU-C10D health utilities were found to be significantly associated with baseline utility and progression status by IRC, but not with prior treatment status (**Table S2**)
  - EQ-5D utilities were found to be significantly associated with baseline utility and progression status by IRC, but not with prior treatment status or histology (**Table S3**)
- Therefore, separate utility values for baseline, and pre- and post-progression health states were included in the analysis, irrespective of prior treatment for EORTC QLU-C10D health utilities, and irrespective of prior treatment or histologic subtype for EQ-5D utilities
- Estimated mean EORTC QLU-C10D utilities increased after tepotinib initiation, from 0.657 at baseline to 0.691 in the IRC-assessed progression-free period, and decreased after progression (0.623; **Figure 5**)
- Estimated mean EQ-5D utilities increased after tepotinib initiation, from 0.640 at baseline to 0.722 in the IRC-assessed progression-free period, and decreased after progression (0.634; **Figure 5**)
- Similar trends were seen when progression was based on INV assessment (**Figure 6**)

Figure 5. Estimated EORTC QLU-C10D and EQ-5D utilities, according to baseline utility and progression status (IRC-assessed)



Error bars: standard error. *776 observations for EQ-5D utilities. †Estimated using Model 1 (see Table S2). ‡Estimated using Model 3 (see Table S3).

Figure 6. Estimated EORTC QLU-C10D and EQ-5D utilities, according to baseline utility and progression status (INV-assessed)

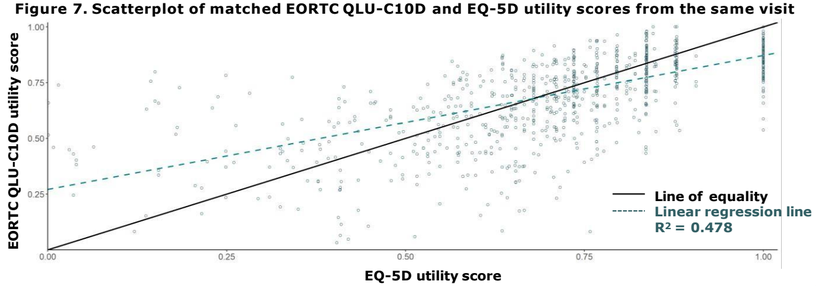


Error bars: standard error. *165 observations for EQ-5D utilities. †Estimated using a linear mixed model with a random intercept (coefficient: 0.686; SE: 0.015; p<0.001) and fixed effects for baseline utility (coefficient: -0.030; SE: 0.012; p=0.014) and progression status (coefficient: -0.057; SE: 0.012; p<0.001). ‡Estimated using a linear mixed model with a random intercept (coefficient: 0.718; SE: 0.017; p<0.001) and fixed effects for baseline utility (coefficient: -0.078; SE: 0.015; p<0.001) and progression status (coefficient: -0.082; SE: 0.014; p<0.001).

Correlation between EORTC QLU-C10D and EQ-5D utilities

- Utilities measured with each method (EORTC QLU-C10D and EQ-5D) were generally similar, in all health states (**Figures 5** and **6**)
- Matched EORTC QLU-C10D and EQ-5D utilities derived from data collected at the same visit were generally highly correlated (Pearson's correlation coefficient: 0.692; **Figure 7**)

Figure 7. Scatterplot of matched EORTC QLU-C10D and EQ-5D utility scores from the same visit



Abbreviations: 1L, first line; 2L, second line; 3L, third line; AIC, Akaike information criterion; ALK, anaplastic lymphoma kinase; BIC, Bayesian information criterion; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; EORTC QLU-C10D, European Organization for Research and Treatment of Cancer Quality of Life Utility Measure-Core 10 dimensions; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC, European Organisation for Research and Treatment of Cancer; EoT, end of treatment; EQ-5D-3L, EuroQol 5-dimension 3-level scale; EQ-5D-5L, EuroQol 5-dimension 5-level scale; EQ-5D, EuroQol 5-dimension; HRQoL, health-related quality of life; HTA, Health Technology Assessment; INV, investigator; IRC, independent review committee; MET, mesenchymal-epithelial transition factor; *METamp*, *MET* amplification; *METex14*, *MET* exon 14; NICE, National Institute for Health and Care Excellence; NSCLC, non-small cell lung cancer; Obv, observation; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PRO, patient-reported outcome; RECIST, Response Evaluation Criteria in Solid Tumours; SE, standard error; SD, standard deviation; VAS, visual analog score

References: 1. Pickard AS, et al. *Health Qual Life Outcomes*. 2007;5:70; 2. Bladt F, et al. *Clin Cancer Res*. 2013;19(11):2941–2951; 3. Falchook GS, et al. *Clin Cancer Res*. 2020;26(6):1237–1246; 4. Tepotinib Japanese Package Insert, 2020; 5. Tepotinib US Prescribing Information, 2021; 6. Paik PK, et al. *N Engl J Med*. 2020;383(10):931–943; 7. Paik PK, et al. *J Thorac Oncol*. 2021;16(3S):S174(MA11.05); 8. Garassino MC, et al. *Ann Oncol*. 2020;31(S4):S864(1347P); 9. Tosh JC, et al. *Value Health*. 2011;14(1):102–109; 10. Norman R, et al. *Health Economics*. 2019;28(12):1385–1401; 11. van Hout B, et al. *Value Health*. 2012;15(5):708–715; 12. Dolan P. *Med Care* 1997;35(11):1095–1108.

Acknowledgements: Study sponsored by Merck Healthcare KGaA, Darmstadt, Germany. The authors would like to thank patients, all investigators and co-investigators, and the study teams at all participating centers and at Merck Healthcare KGaA, Darmstadt, Germany. Medical writing and editorial assistance was provided by Mark Dyson, DPhil (Berlin, Germany), Syneos Health Medical Communications (London, UK), and funded by Merck Healthcare KGaA, Darmstadt, Germany.

Disclosures: Niels Reinmuth reports honoraria for scientific meetings and travel support from BMS, MSD, AstraZeneca, Roche, Takeda, Boehringer Ingelheim, Pfizer; advisory board honoraria from BMS, MSD, AstraZeneca, Roche, Takeda, Boehringer Ingelheim, Pfizer; honoraria for advisory and speaker activities from Amgen, AstraZeneca, BMS, Boehringer Ingelheim, Hoffmann-La Roche, MSD, Merck, Pfizer, Sanofi and Takeda. Sanjay Popat reports an advisory role at Amgen, AstraZeneca, Bayer, Beigene, Blueprint, BMS, Boehringer Ingelheim, Daiichi Sankyo, Guardant Health, Janssen, Lilly, Merck Healthcare KGaA, Darmstadt, Germany, Novartis, Roche, Takeda; other COIs at Amgen and MSD; is a coordinating PI at Ariad, Boehringer Ingelheim, Celgene, Daiichi Sankyo, Takeda and Turning Point Therapeutics; is a local PI at AstraZeneca, GlaxoSmithKline, Roche and Trizel; reports non-financial interests of acting in an advisory role with ALK Positive UK, Lung Cancer Europe, International Association for the Study of Lung Cancer and Ruth Strauss Foundation; a leadership role with British Thoracic Oncology Group and European Thoracic Oncology Platform; is an officer with European Society of Medical Oncology; is a member of board of directors with Mesothelioma Applied Research Foundation. Luis Paz-Ares reports consultancy fees from AstraZeneca, Lilly, END, Spectrum Pharmaceuticals, Daiichi Sankyo/Lilly; research activities at Lilly, Boehringer Ingelheim; a leadership role at Genomica, ALTUM Sequencing; is a member of the speaker's bureau at MSD, BMS, Roche, Pfizer, Lilly, AstraZeneca, Merck; travel grants from Roche, AstraZeneca, MSD, BMS, Pfizer, Takeda; honoraria from Roche, Lilly, Pfizer, BMS, MSD, AstraZeneca, Merck, PharmaMar, Novartis, Celgene, Amgen, Sanofi, Ipsen, Servier, Bayer, Blueprint Medicines, Mirati Therapeutics, Takeda. Emma Knowles and Anthony Hatswell are employees of Delta Hat. Thomas McLean is an employee of Merck Serono Limited, an affiliate of Merck KGaA. Svenja Adrian and Helene Vioix are employees of Merck Healthcare KGaA, Darmstadt, Germany. Bruce Gaumond is an employee of EMD Serono, an affiliate of Merck KGaA. Paul Paik reports an advisory role at AbbVie, AstraZeneca, Calithera, Celgene, Lilly, Takeda; EMD Serono, an affiliate of Merck KGaA, Xencor, Bicara, Boehringer Ingelheim, GlaxoSmithKline, EMD Serono, an affiliate of Merck KGaA; his research institution has received research expenses from Celgene, EMD Serono, an affiliate of Merck KGaA.

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Supplementary materials

Post er recording

1255P | Presented at the European Society for Medical Oncology (ESMO) Annual Meeting | Virtual Format; 16–21 September 2021