Tepotinib in patients with advanced non-small cell lung cancer (NSCLC) with *MET* amplification (*MET*amp)

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CONCLUSIONS

- **Tepotinib showed high and clinically meaningful activity in this first study of a MET inhibitor in advanced NSCLC with *MET*amp prospectively detected by liquid biopsy**
- **Patients who received tepotinib in 1L appeared to be more sensitive to therapy (ORR: 71.4%)**
- **Tepotinib was well tolerated, with mostly mild or moderate TRAEs and no discontinuations due to TRAEs**
- **Tepotinib warrants further evaluation in patients with advanced NSCLC with *MET*amp, who have an urgent unmet need for new treatment options**

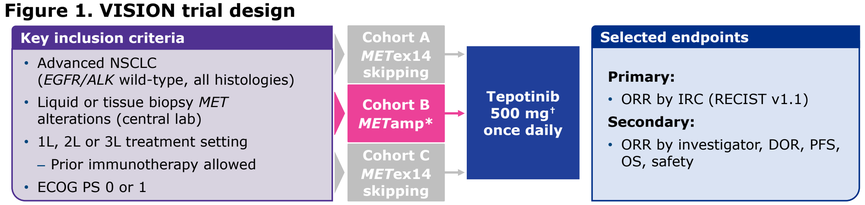
INTRODUCTION

- *MET*amp is an oncogenic driver that occurs in 1–5% of patients with NSCLC,[1] the majority of whom are current or former smokers[2]
- There is an urgent unmet need for new treatments for patients with NSCLC and *MET*amp, who have a poor prognosis[3] and lack approved therapies[1]
- Tepotinib is a highly selective, oral, once daily MET inhibitor[4] that was approved for metastatic NSCLC with *MET*ex14 skipping in Japan[5] and the US[6] based on Cohort A of the VISION trial[7,8]
- We report the first data from VISION Cohort B, which evaluated tepotinib in patients with advanced NSCLC and *MET*amp, as detected by a minimally invasive liquid biopsy assay, in the absence of *MET*ex14 skipping

METHODS

- VISION is an open-label, multicenter, multi-cohort, Phase II trial (NCT02864992) (**Figure 1**)[7]
- Cohort B enrolled patients with advanced *EGFR*/*ALK* wild-type NSCLC with *MET*amp and no *MET*ex14 skipping. *MET*amp was detected by liquid biopsy (Guardant360®; Guardant Health, Redwood City, CA) and defined as *MET* gene copy number ≥2.5
- The data cut-off for the present analysis was July 1, 2020

Figure 1. VISION trial design



*In the absence of *MET*ex14 skipping. †Containing 450 mg active moiety. Treatment was administered until disease progression, intolerable toxicity or withdrawal of consent.

RESULTS

Patients

- A total of 24 patients were enrolled and received tepotinib (**Table 1**)
- Tepotinib was administered to 7 patients (29.2%) in 1L, 10 patients (41.7%) in 2L, and 7 patients (29.2%) in 3L
- Treatment was ongoing in 5 patients at the data cut-off (July 1, 2020; 1L, n=2; 2L, n=2; 3L, n=1); as of November 2020, all 5 patients were continuing to receive tepotinib and had treatment duration >1 year

Table 1. Baseline characteristics

Characteristic		(n=24)
Male, n (%)		21 (87.5)
Median age, years (range)		63.4 (38–73)
Race, n (%)	White/Asian	17 (70.8)/7 (29.2)
Current/former smoker, n (%)		21 (87.5)
ECOG PS, n (%)	0/1	3 (12.5)/21 (87.5)
Median tumor load of target lesions (IRC), mm (range)		95.6 (26.9–231.9)
Number of prior lines of therapy, n (%)	0	7 (29.2)
	1	10 (41.7)
	2	7 (29.2)
Prior immunotherapy, n (%)		10 (41.7)
Best response to prior immunotherapy, n*	PR	1
	SD	1
	PD	5

*Best response to prior immunotherapy was unknown for 3 patients.

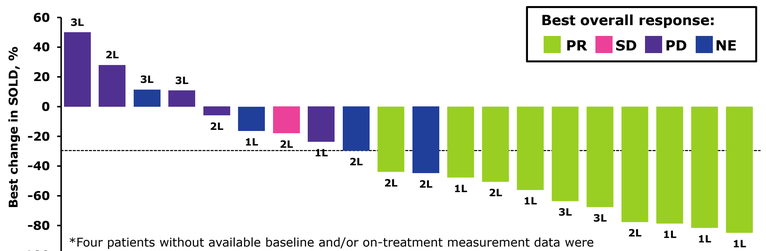
Efficacy

- ORR by IRC was 41.7% (95% CI: 22.1, 63.4) overall (**Table 2, Figure 2**)
- In subgroup analyses according to treatment line, ORR by IRC was 71.4% in 1L, 30.0% in 2L, and 28.6% in 3L
- Similar response rates were observed by investigator assessment

Table 2. Objective response by IRC, overall and by line of therapy

		Overall (n=24)	1L (n=7)	2L (n=10)	3L (n=7)
Best overall response, n (%)	PR	10 (41.7)	5 (71.4)	3 (30.0)	2 (28.6)
	SD	1 (4.2)	0	1 (10.0)	0
	PD	5 (20.8)	1 (14.3)	2 (20.0)	2 (28.6)
	NE	8 (33.3)	1 (14.3)	4 (40.0)	3 (42.9)
ORR, n (%) [95% CI]		10 (41.7) [22.1, 63.4]	5 (71.4) [29.0, 96.3]	3 (30.0) [6.7, 65.2]	2 (28.6) [3.7, 71.0]

Figure 2. Percent change in SOLD by IRC (n=20*)

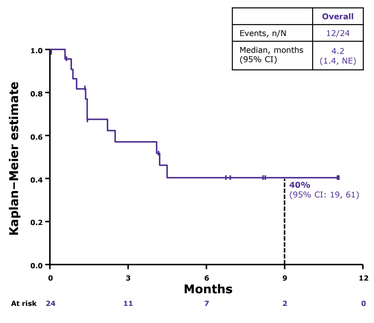


*Four patients without available baseline and/or on-treatment measurement data were excluded. 1L/2L/3L labels indicate line of tepotinib therapy.

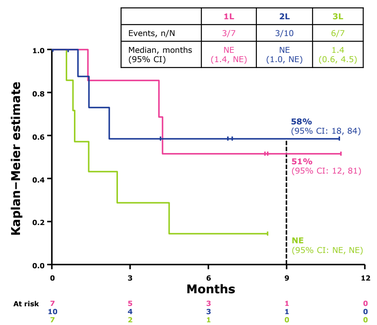
- In the overall population, the 9-month event-free rate for PFS by IRC was 40% (95% CI: 19, 61) and median PFS was 4.2 months (**Figure 3A**)
- The 9-month event-free rate for PFS was 51% in 1L, 58% in 2L, and NE in 3L (**Figure 3B**)

Figure 3. PFS

A. Overall



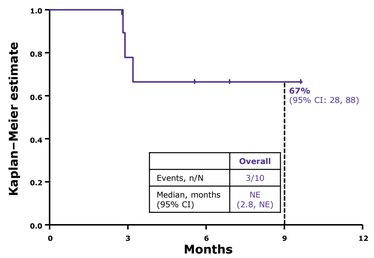
B. By line of therapy



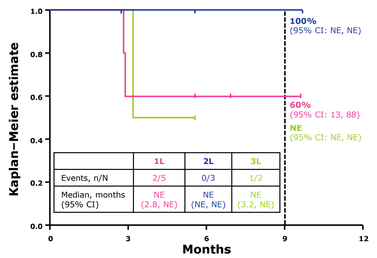
- In the overall population, the 9-month event-free rate for DOR by IRC was 67% (95% CI: 28, 88); median DOR was NE (**Figure 4A**)
- The 9-month event-free rate for DOR was 60% in 1L, 100% in 2L, and NE in 3L (**Figure 4B**)

Figure 4. DOR

A. Overall



B. By line of therapy



Safety

- Five patients (20.8%) discontinued due to AEs, all of which were considered to be unrelated to tepotinib (disease progression, n=2; respiratory failure, n=2; pneumonia, n=1; sepsis, n=1; septic shock, n=1)
- TRAEs of any grade were reported in 16 patients (66.7%), and TRAEs of Grade 3/4 were reported in 7 patients (29.2%) (**Table 3**)

Table 3. TRAEs reported in ≥5% of patients (n=24)

Patients, n (%)	Any grade	Grade 3	Grade 4
Peripheral edema	9 (37.5)	2 (8.3)	0
Generalized edema	4 (16.7)	2 (8.3)	0
Constipation	4 (16.7)	0	0
Diarrhea	2 (8.3)	0	0
Edema	2 (8.3)	0	0
Transaminases increased	2 (8.3)	1 (4.2)	0

Abbreviations: 1L, first line; 2L, second line; 3L, third line; AE, adverse event; *ALK*, anaplastic lymphoma kinase; CI, confidence interval; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*, epidermal growth factor receptor; IRC, independent review committee; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; *MET*ex14, *MET* exon 14; 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; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SOLD, sum of longest diameters; TRAE, treatment-related adverse event.

References: 1. Drilon A, et al. *J Thorac Oncol*. 2017;12(1):15–26; 2. Wolf J, et al. EORTC/NCI/AACR 2018 (Poster 403): 3. Dimou A, et al. *PLoS One*. 2014;9(9):e107677; 4. Falchook GS, et al. *Clin Cancer Res*. 2020;26(6):1237–1246; 5. Tepotinib Japanese Package Insert, 2020; 6. Tepotinib US Prescribing Information, 2021; 7. Paik PK, et al. *N Engl J Med*. 2020;383(10):931–943; 8. Paik PK, et al. *J Thorac Oncol*. 2021;16(3S):S174[MA11.05].

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

Disclosures: Xiuning Le has acted in a consulting or advisory role for AstraZeneca, Lilly, EMD Serono, Spectrum Pharmaceuticals and Daiichi Sankyo/Lilly, and has received research funding from Lilly and Boehringer Ingelheim. Luis G. Paz-Ares is part of the leadership team at Genomica and ALTUM Sequencing, has received speakers' bureau fees from MSD Oncology, Bristol-Myers Squibb, Roche/Genentech, Pfizer, Lilly, AstraZeneca, and Merck Serono, has received travel expenses from Roche, AstraZeneca, MSD, Bristol-Myers Squibb, Pfizer, and Takeda, has received honoraria from Roche/Genentech, Lilly, Pfizer, Bristol-Myers Squibb, MSD, AstraZeneca, Merck Serono, PharmaMar, Novartis, Celgene, Amgen, Sanofi, Ipsen, Servier, Bayer, Blueprint Medicines, Mirati Therapeutics, and Takeda, and has received research funding from Bristol-Myers Squibb, AstraZeneca, PharmaMar, Kuro Oncology, and MSD; also has other relationships with Novartis, Ipsen, Pfizer, Servier, Sanofi, Roche, Amgen, and Merck. Jan Van Meerbeeck has performed a consulting or advisory role for Amgen and has received travel expenses from Bristol-Myers Squibb, Santiago Viteri Ramirez has performed a consulting or advisory role for AbbVie, Bristol-Myers Squibb, and Roche, has received speakers' bureau fees from Bristol-Myers Squibb, MSD, and Roche, and has received travel expenses from Roche, OSE Pharma, Bristol-Myers Squibb, Merck, Merck Serono, Puma Biotechnology, and Janssen Cilag. Carlos Cabrera Galvez has received honoraria from Roche and Boehringer Ingelheim, has performed a consulting or advisory role for Boehringer Ingelheim, and has received travel expenses from Roche. David Vincente Baz has acted in a consultancy or advisory role for Roche, Merck KGaA, Bristol-Myers Squibb, AstraZeneca, Pfizer, Boehringer Ingelheim, and Takeda, and has received speakers' bureau fees from Roche, Merck KGaA, Bristol-Myers Squibb, AstraZeneca, Pfizer, and Boehringer Ingelheim. Young-Chul Kim has received honoraria from AstraZeneca, Roche, and Boehringer Ingelheim, and has received research funding from AstraZeneca, Roche, and Boehringer Ingelheim. Jin-Hyoung Kang has received honoraria from Roche, Boehringer Ingelheim, MSD, and Bristol-Myers Squibb, has performed a consulting or advisory role for Roche, Boehringer Ingelheim, MSD, AstraZeneca, and Yuhan, has received speakers' bureau fees from Pfizer, MSD, and Roche, and has received research funding from Boehringer Ingelheim, AstraZeneca, Daiichi Sankyo, and Yuhan. Karl-Maria Schumacher, Niki Karachaliou, and Svenja Adrian are employees of Merck KGaA, Darmstadt, Germany. Rolf Bruns is an employee of Merck KGaA, Darmstadt, Germany, and holds stock in Merck KGaA Darmstadt, Germany. Paul Paik has performed a consulting or advisory role for EMD Serono, Takeda, Calithera Biosciences, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Xencor, and Bicara, has received honoraria from Takeda, Calithera Biosciences, Boehringer Ingelheim, EMD Serono, AstraZeneca, Xencor, Bicara, and GlaxoSmithKline, and has received research funding from EMD Serono, Boehringer Ingelheim, and Bicara.

Abstract 9021 presented at the American Society of Clinical Oncology 2021 Annual Meeting | Virtual format