# 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**

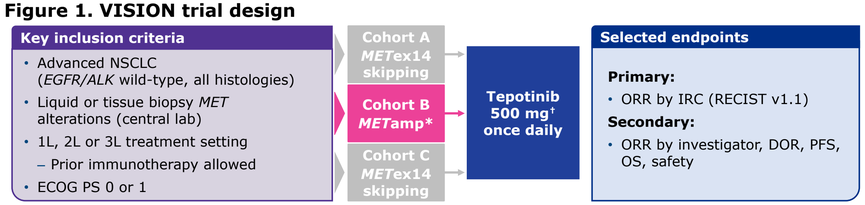
## INTRODUCTION

- *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.

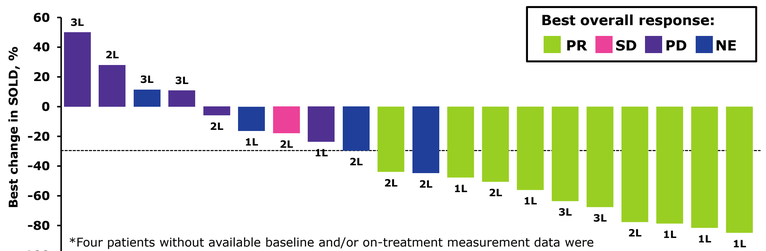
### Efficacy

- 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] |

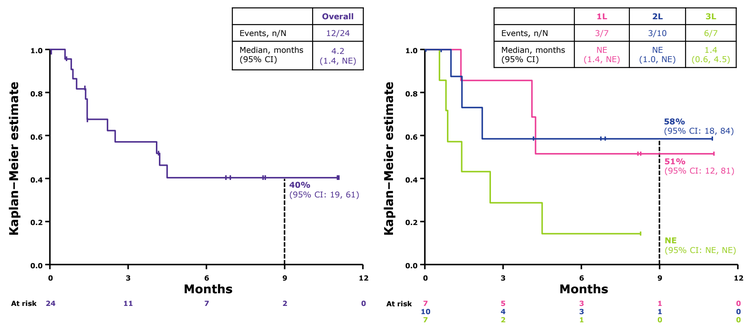
**Figure 2. Percent change in SOLD by IRC (n=20*)**




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

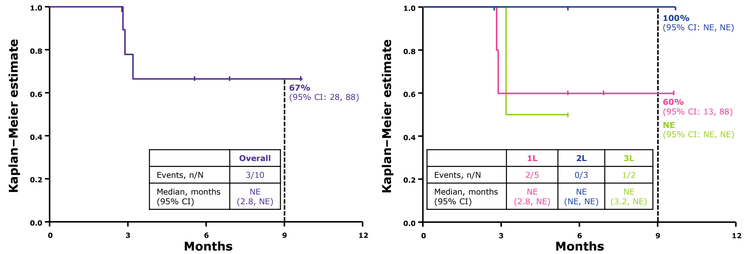
- In the overall population, the 9-month event-free rate for PFS by IRC was 40% (95% CI: 19, 61) and median PFS was 4.2 months (**Figure 3A**)
- The 9-month event-free rate for PFS was 51% in 1L, 58% in 2L, and NE in 3L (**Figure 3B**)

**Figure 3. PFS**




- 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**




### 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].

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