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Treatment (Tx) sequencing of tepotinib in patients (pts) with MET exon 14 (METex14) skipping non-small lung cancer (NSCLC): Outcomes from ≥3 years follow-up of the VISION study

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CONCLUSIONS

- In VISION, outcomes with tepotinib across treatment lines in patients with ≥3 years follow-up demonstrated robust and durable efficacy consistent with previous reports, particularly in the 1L-setting, supporting its early use in the treatment sequence
- TRAEs, particularly peripheral edema, were common but manageable, with dose reductions and treatment interruptions enabling prolonged treatment durations in many patients
- Many patients who discontinued tepotinib went on to receive and have their disease controlled by subsequent therapy, including rechallenge with MET inhibitors

PLAIN LANGUAGE SUMMARY

Background

Tepotinib, an anticancer drug taken by mouth, is approved in many countries in patients with non-small cell lung cancer (NSCLC) that has spread through the body and carries a particular genetic alteration called MET exon 14 (METex14) skipping

Tepotinib is approved in Europe and other countries to treat this cancer, either after or regardless of previously received chemotherapy or immunotherapy

On this poster, we show results from the VISION study of patients with NSCLC with the METex14 skipping alteration who were treated with tepotinib and followed up for 3 years or more

The results show how long the patients received tepotinib and how their cancer responded to tepotinib, as well as the effectiveness of the therapies they received before and after tepotinib

313 patients participated in the VISION trial, with an average age of 72 years

Before entering the VISION study and receiving tepotinib treatment, 149 patients received chemotherapy and/or immunotherapy

Treatment outcomes

The percentage of patients whose cancer responded to chemotherapy and/or immunotherapy, before entering the VISION study was 28.9%

For patients receiving tepotinib in VISION, after receiving chemotherapy and/or immunotherapy previously, 45.0% had cancer which responded to tepotinib treatment

In patients who received tepotinib as their first cancer therapy, 57.9% had cancer which responded to tepotinib treatment

19 patients stayed on tepotinib treatment in VISION for 4 years or more

145 patients went on to receive another treatment after stopping tepotinib treatment in the VISION study

What do these results mean?

Tepotinib continues to show benefits in patients with NSCLC with METex14 skipping alterations who have been followed for 3 years or more, especially when used early in the treatment plan

Patients who received tepotinib after other therapies also saw improvements, and some stayed on tepotinib treatment for years



RESULTS

Baseline characteristics

- In VISION Cohorts A+C, 313 patients with METex14 skipping NSCLC were included
- 52.4% (n=164) patients received tepotinib in 1L while 47.6% (n=149) patients received tepotinib in 2L+ (**Supplementary Table S1**)
 - Patients who received tepotinib in 1L had a median age of 74.0 years (range: 47–94), 49.4% were female, and median duration of treatment was 8.1 months (0.03–71.52), with 13 patients receiving treatment for ≥48 months; the longest duration of tepotinib treatment was 71.5 months
 - Patients who received tepotinib in 2L+ had a median age of 70.8 years (41–89), 52.3% patients were female, and median duration of treatment was 7.0 months (0.03–83.12), with six patients receiving treatment for ≥48 months; the longest duration of tepotinib treatment was 83.1 months
 - Prior to enrolling in VISION, 104 (69.8%) patients received platinum-based CT without IO, 59 (39.6%) received IO monotherapy, and 22 (14.8%) received IO + platinum-based CT

Efficacy outcomes prior to and with tepotinib

- Patients who received tepotinib in 1L had an ORR of 57.9%, while those who received tepotinib in 2L+ had an ORR of 45.0% (**Table 1**)
 - Across all treatment lines received prior to tepotinib, ORR was 28.9%; outcomes with tepotinib in 2L+ were improved compared with all treatment lines received prior to tepotinib

Table 1. Efficacy outcomes prior to and with tepotinib

Outcomes with:	Patients, n	ORR, % (95% CI)	mDOR, months (IQR or 95% CI)*	mPFS, months (IQR or 95% CI)*
All treatment lines prior to tepotinib[†]	149	28.9	6.0 (4.0–12.0)	5.0 (2.0–11.0)
Tepotinib in 1L[‡]	164	57.9 (50.0, 65.6)	31.7 (13.8, 46.4)	12.6 (9.7, 17.7)
Tepotinib in 2L[‡]	92	45.7 (35.2, 56.4)	12.6 (8.3, 18.5)	10.9 (8.2, 13.8)
Tepotinib in 2L+[‡]	149	45.0 (36.8, 53.3)	12.6 (9.5, 18.5)	11.0 (8.2, 13.7)
Tepotinib in 3L+[‡]	57	43.9 (30.7, 57.6)	10.8 (8.3, NE)	11.0 (5.7, 14.7)
Tepotinib in 2L+ according to prior treatment received[‡]				
Platinum-based CT alone	104	48.1 (38.2, 58.1)	15.4 (8.3, 33.6)	11.0 (7.2, 13.8)
IO monotherapy	59	33.9 (22.1, 47.4)	12.6 (8.3, NE)	8.9 (5.7, 13.8)
IO-CT	22	54.5 (32.2, 75.6)	10.1 (4.2, NE)	11.5 (5.5, 14.7)

*95% confidence intervals for efficacy outcomes with tepotinib and IQR for other treatments. [†]Assessed by investigator; mDOR and mPFS were based on descriptive analyses. [‡]Assessed by independent review committee.

Dose reductions and interruptions

- Overall, in patients who had dose reductions and/or interruptions (n=197), the median duration of tepotinib treatment was 10.7 months (range: 0.7–83.1) (**Table 2**)
 - In patients with dose reductions only, the median duration of treatment was 11.0 months (1.4–71.5), while in patients with treatment interruptions only, the median duration of treatment was 11.0 months (0.7–83.1)
- TRAEs led to dose reductions in 104 patients (33.2%) and treatment interruptions in 137 patients (43.8%); permanent discontinuation was reported for 49 patients (15.7%)
 - Treatment-related deaths were reported in three patients (1.0%)⁴
- Peripheral edema was the most common treatment-related adverse event observed in 212 patients (67.7%); Grade ≥3: 11.8%
 - To manage peripheral edema, 48 (15.3%) patients had a dose reduction of tepotinib, 59 (18.8%) patients had dose interruptions, and 19 (6.1%) patients discontinued treatment permanently
- These dose reductions and/or interruptions often enabled continued therapy and were associated with prolonged treatment durations (**Supplementary Figure S2**)

Table 2. Duration of tepotinib treatment in patients with dose reductions and/or interruptions

	Overall (n=197)	1L (n=108)	2L+ (n=89)
Mean ± std dev, months	16.6 ± 16.3	18.8 ± 17.2	14.0 ± 14.8
Median (range), months	10.7 (0.7–83.1)	11.1 (0.7–71.5)	9.4 (0.7–83.1)
Treatment ongoing, n (%)	15 (7.6)	11 (10.2)	4 (4.5)

Outcomes with subsequent treatments

- Overall, 295 (94.2%) patients discontinued tepotinib, of whom 145 (46.3%) started a subsequent treatment
 - Among patients who received tepotinib in 1L, 152 (92.7%) discontinued tepotinib, of whom 72 (43.9%) started a subsequent treatment (**Figure 1**)
 - Among patients who received tepotinib in 2L+, 143 (96.0%) discontinued tepotinib, of whom 73 (49.0%) started a subsequent treatment (**Figure 2**)

Outcomes with subsequent treatments (cont'd)

Figure 1. Sankey plots for patients receiving tepotinib in 1L

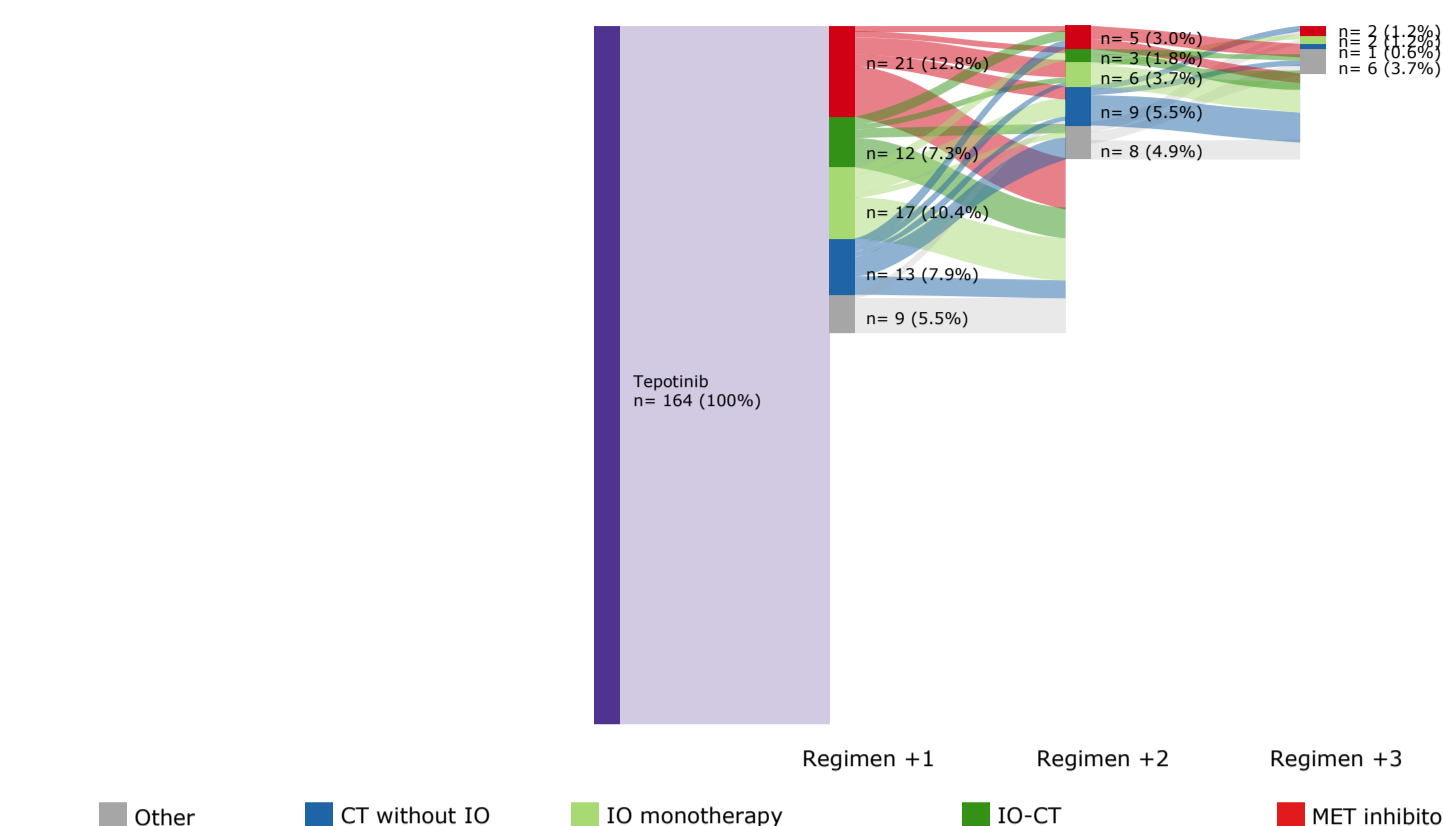
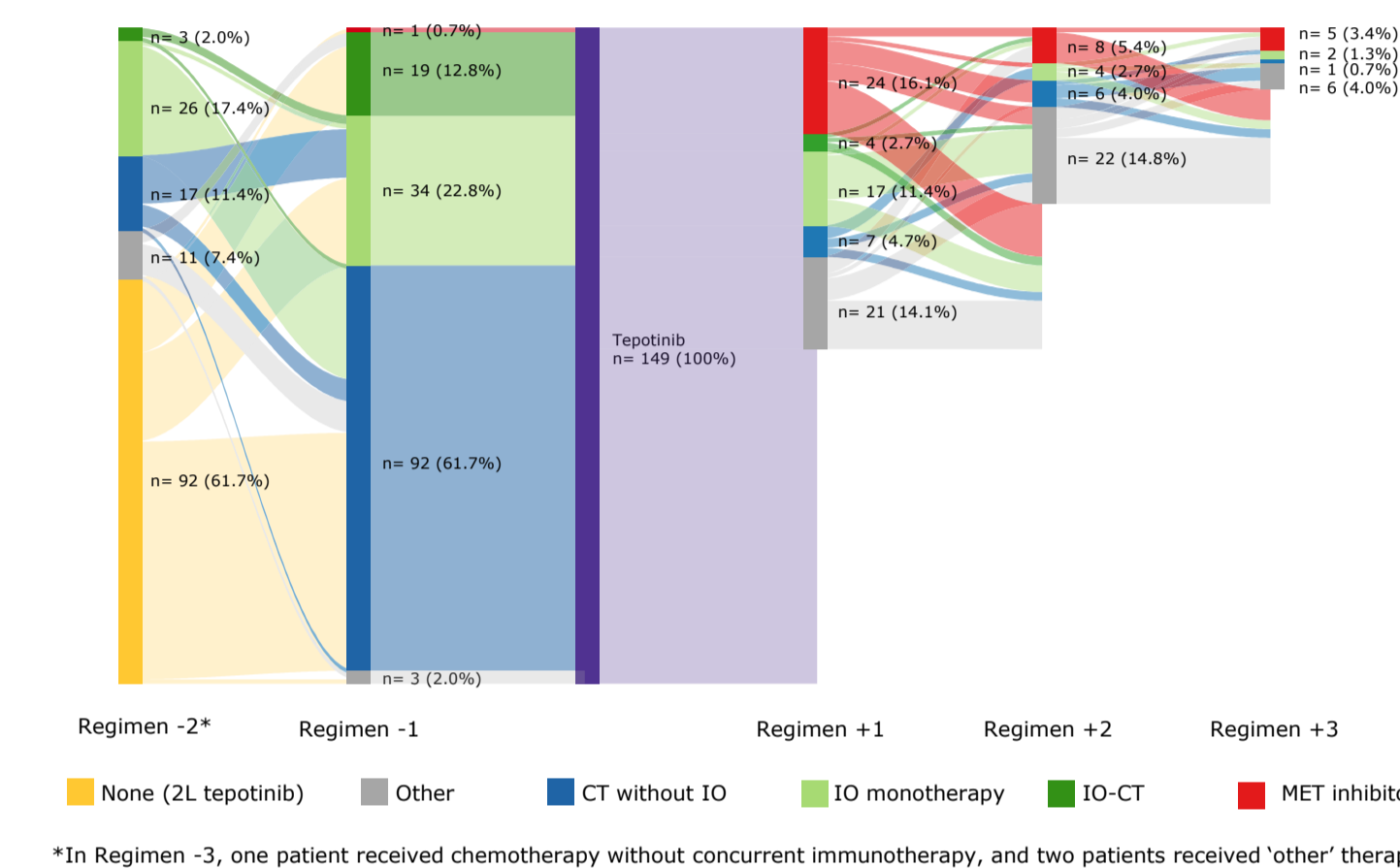


Figure 2. Sankey plots for patients receiving tepotinib in 2L+



*In Regimen -3, one patient received chemotherapy without concurrent immunotherapy, and two patients received 'other' therapy.

- In all patients who received subsequent treatment after tepotinib (n=145), the ORR was 7.0%, mDOR was 4.0 months (IQR: 4.0–6.0), and mPFS was 4.0 months (IQR: 2.0–7.0)
- Outcomes with platinum-based CT, IO-containing regimens, and MET inhibitors received after discontinuing tepotinib were lower than those obtained with tepotinib during study treatment in VISION (**Table 3**)

Table 3. Efficacy outcomes with subsequent treatments after tepotinib

Efficacy outcomes in subsequent treatments	Platinum-based CT alone (n=38)	IO monotherapy (n=51)	IO + platinum-based CT (n=19)	MET inhibitor (n=65)
ORR, %	5.3	15.7	15.8	9.2
Best response, n (%)				
CR	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
PR	2 (5.3)	8 (15.7)	3 (15.8)	6 (9.2)
SD	16 (42.1)	15 (29.4)	5 (26.3)	15 (23.1)
PD	5 (13.2)	12 (23.5)	2 (10.5)	6 (9.2)
mDOR*, months (IQR)	3.0 (3.0–3.0)	11.0 (4.0–16.0)	4.0 (4.0–4.0)	4.0 (4.0–5.0)
mPFS*, months, median (IQR)	2.0 (2.0–2.0)	3.0 (2.0–8.0)	5.5 (3.5–7.5)	5.0 (2.0–7.0)

*Assessed by investigator; mDOR and mPFS were based on descriptive analyses.

Outcomes with METi rechallenge

- Overall, 65 patients received subsequent treatment with a METi (21 crizotinib, 21 capmatinib, 7 tepotinib, 4 amivantamab, 3 cabozantinib, 3 savolitinib, 2 Sym015, 1 elzoventinib, and 1 telisotuzumab vedotin) (**Supplementary Table S2**)
 - Best response was PR in six (9.2%) patients and SD in 15 (23.1%) patients; longest PFS (median [IQR]) was 5.0 months (2.0–7.0)
 - Of the six patients with PRs, two patients received MET inhibitors as their next subsequent treatment, and four patients received other subsequent therapies with a duration of 2–33 months before receiving MET inhibitor rechallenge
 - Among seven patients who received subsequent tepotinib, best response was PR in one patient, and SD in two patients; longest DOR (median) was 4.0 months (3.0–5.0) while longest PFS (median) was 6.5 months (5.5–10.0)

INTRODUCTION

- Tepotinib, an oral, once-daily, and highly selective MET inhibitor, is approved in multiple countries for the treatment of patients with advanced/metastatic METex14 skipping NSCLC, and after immunotherapy and/or platinum-based chemotherapy in the EU^{1,2}
- The VISION study demonstrated robust and durable efficacy and safety of tepotinib in patients with METex14 skipping NSCLC with ≥3 years of follow-up (data cut-off: May 20, 2024)³
- Here, we report long-term efficacy data prior/peri/post-tepotinib treatment, tepotinib treatment interruption details, and duration of treatment with tepotinib in patients from the VISION study with ≥3 years of 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
- Patients received tepotinib 500 mg (450 mg active moiety) QD
 - Primary endpoint was objective response (RECIST v1.1) by IRC (**Supplementary Figure S1**)
- Prior or post-tepotinib treatment was investigator's choice, and the outcomes were reported as per investigator
- Regimens evaluated: platinum-based CT without IO, IO monotherapy, IO + platinum-based CT, and METi

Abbreviations: 1L, first line; 2L+, second-or-later line; 3L+, third-or-later line; CR, complete response; CT, chemotherapy; DOR, duration of response; IO, immunotherapy; IQR, interquartile range; IRC, independent review committee; m, median; MET, mesenchymal-epithelial transition factor; METex14, MET exon 14; METi, MET inhibitor; NE, not estimable; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; QD, once daily; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease; std dev., standard deviation; TRAE, treatment-related adverse events.
References: 1. TEPINETX. Tepotinib (see) from https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/214095d01/label.pdf. Accessed October 13, 2025. 2. TEPINETX® (tepotinib). Summary of product characteristics. 2024. Available from: https://www.ema.europa.eu/en/documents/product-information/tepotinib-epar-product-information_en.pdf. Accessed September 28, 2025. 3. Mazieres J, et al. *J Thorac Oncol*. 2025;20(3):559–560. 4. Mazieres J, et al. *JAMA Oncol*. 2023;9(9):1260–1266.
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Poster PDF



Supplementary file



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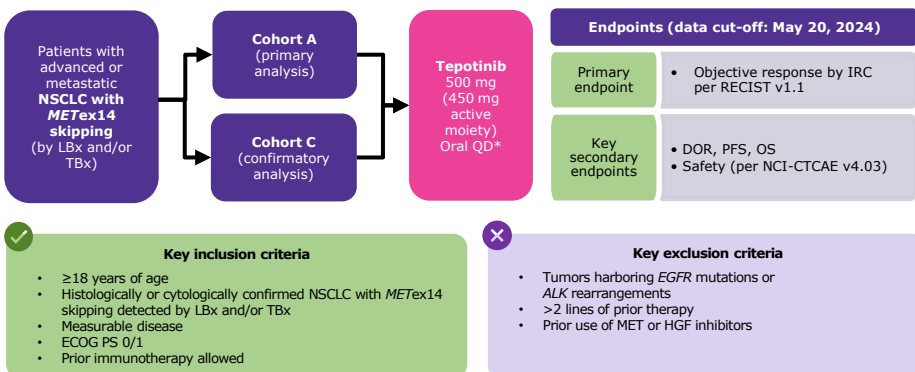
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SUPPLEMENTARY RESULTS

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



*Treatment continues until disease progression, intolerable toxicity, or withdrawal of consent.

Supplementary Table S1. Baseline characteristics by line of therapy

Baseline characteristics	1L (n=164)	2L+			
		2L+ (n=149)	2L (n=92)	3L+ (n=57)	
Median age, years (range)	74.0 (47–94)	70.8 (41–89)	70.4 (41–89)	71.9 (52–88)	
Sex, n (%)	Male	83 (50.6)	71 (47.7)	46 (50.0)	25 (43.9)
	Female	81 (49.4)	78 (52.3)	46 (50.0)	32 (56.1)
Race*, n (%)	White	112 (68.3)	83 (55.7)	51 (55.4)	32 (56.1)
	Asian	50 (30.5)	56 (37.6)	36 (39.1)	20 (35.1)
ECOG PS[†], n (%)	0	45 (27.4)	36 (24.2)	23 (25.0)	13 (22.8)
	1	118 (72.0)	113 (75.8)	69 (75.0)	44 (77.2)
	Yes	88 (53.7)	61 (40.9)	36 (39.2)	25 (43.9)
Smoking history[‡], n (%)	Patients with a former smoking history	81 (49.4)	59 (39.6)	34 (37.0)	25 (43.9)
	Patients with a current smoking history	7 (4.3)	2 (1.3)	2 (2.2)	0
	No	75 (45.7)	79 (53.0)	50 (54.3)	29 (50.9)
Histology, n (%)	Adenocarcinoma	131 (79.9)	121 (81.2)	73 (79.3)	48 (84.2)
	TBx	111 (67.7)	97 (65.1)	65 (70.6)	32 (56.1)
<i>MET</i>Ex14 skipping detection method, n (%)	LBx	95 (57.9)	83 (55.7)	46 (50.0)	37 (64.9)
	LBx	95 (57.9)	83 (55.7)	46 (50.0)	37 (64.9)
Tumor load of target lesions (IRC), mean mm (±SD)	70.2 ± 45.61	62.0 ± 34.35	59.7 ± 34.81	65.7 ± 33.58	

*Race was missing/not collected at the study site for eight patients, three patients were Black/African American, and one patient was recorded as 'Other'.

[†]One patient receiving tepotinib in 1L was ECOG PS 2. [‡]Smoking history was missing in ten patients.

Treatment (Tx) sequencing of tepotinib in patients (pts) with *MET* exon 14 (*MET*ex14) skipping non-small lung cancer (NSCLC): Outcomes from ≥ 3 years follow-up of the VISION study

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SUPPLEMENTARY RESULTS

Supplementary Table S2. Efficacy outcomes with subsequent MET inhibitors after tepotinib

Outcomes* with:	Patients, n	ORR, %	mDOR, months (IQR)	mPFS, months (IQR)
MET inhibitors	65 [†]	9.2	4.0 (4.0–5.0)	5.0 (2.0–7.0)
Crizotinib	21	9.5	6.0 (6.0–6.0)	2.5 (1.5–4.5)
Capmatinib	21	9.5	4.0 (4.0–4.0)	2.0 (2.0–6.5)
Tepotinib	7	14.3	4.0 (3.0–5.0)	6.5 (5.5–10.0)
Amivantamab	4	25.0	NE	NE
Cabozantinib	3	0	NE	NE
Sym015	2	0	NE	11.0 (11.0–11.0)
Savolitinib	3	0	NE	NE
Elzoventinib	1	0	NE	4.0 (4.0–4.0)
Telisotuzumab vedotin	1	0	NE	5.0 (5.0–5.0)

*Assessed by investigator; mDOR and mPFS were based on descriptive analyses. [†]Data for two patients who received subsequent MET inhibitors was not available.

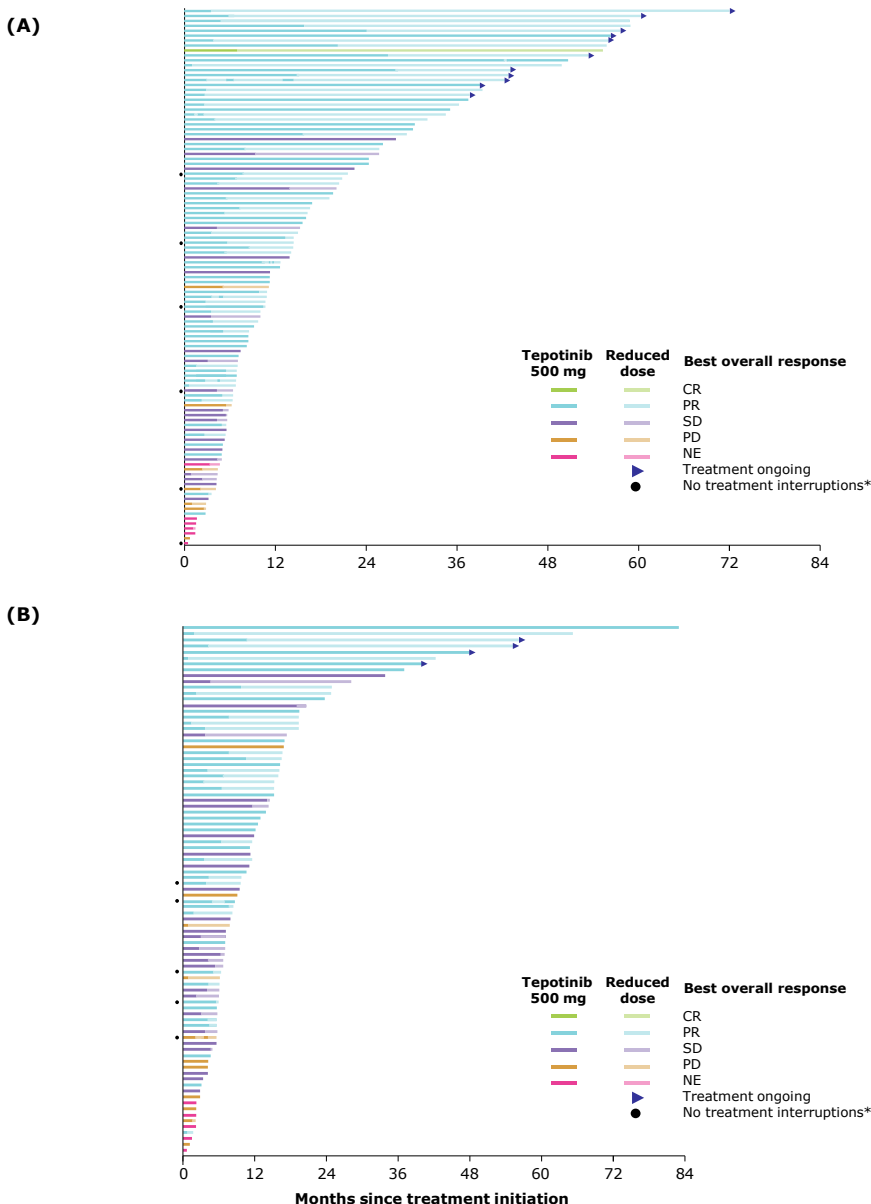
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SUPPLEMENTARY RESULTS

Supplementary Figure S2. Swimmer plots highlighting the duration of treatment in patients with dose reductions and/or treatment interruptions receiving tepotinib in (A) 1L (n=108) and (B) 2L+ (n=89)



Abbreviations: 1L, first line; 2L+, second-or-later line; BOR, best overall response; CR, complete response; NE, not estimable; PD, disease progression; PR, partial response; SD, stable disease.
*All patients had treatment interruptions except those indicated with a circle.