VISION: A Single-arm, Open-label, Multicenter, Non-randomized, Multicohort Study in Adult Patients With Locally Advanced or Metastatic NSCLC[1]

ELIGIBILITY CRITERIA

PATIENT BASELINE CHARACTERISTICS

Median age is **72** **years**[2]

Patients with NSCLC carrying ***MET*ex14** skipping alterations[1-4]

TEPOTINIB DOSAGE AND ADMINISTRATION

450 mg[1,*] oral QD

EFFICACY

Primary Endpoint:

Confirmed ORR by RECIST v1.1 as evaluated by IRC[3]

Overall ORR was **50.8%**

(95% CI: 45.1, 56.5)

Treatment naive (n=164)	Previously treated, 2L only (n=92)	Previously treated (n=149)
ORR by IRC (95% CI: 48.1, 63.8)	ORR by IRC (95% CI: 35.2, 56.4)	ORR by IRC (95% CI: 36.8, 53.3)
56.1%	45.7%	45.0%

Secondary Endpoints[2,3,5]: BOR, DCR, DOR, PFS, OS

Exploratory analysis[5]: RANO-BM

SAFETY

TRAEs (any grade) occurring in **≥10%** of all patients[5]

TRAE, %	Overall (N=313)
Peripheral edema	66.5
Nausea	23.3
Hypoalbuminemia	23.0
Diarrhea	22.4
Blood creatinine increased	21.7
ALT increased	13.1
Decreased appetite	11.2

Indication and Usage

Tepotinib Warnings and Precautions

Important Safety Information

VISION cohorts A+C (*MET*ex14 skipping only)

*Equivalent to 500mg tepotinib hydrochloride hydrate.

2L, second line; ALT, alanine transaminase; BOR, best objective response; CI, confidence interval; DCR, disease control rate; DOR, duration of response; IRC, independent review committee; *MET*ex14, mesenchymal-epithelial transition exon 14; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; QD, once daily; RANO-BM, Response Assessment in Neuro-Oncology Brain Metastases; RECIST, Response Evaluation Criteria in Solid Tumors.

References: 1. TEPMETKO® [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021. **2.** Thomas M, et al. Presented at DGHO Annual Meeting 2021, Abstract 52. **3.** Smit EF, et al. Presented at ESMO, 2022, Abstract 985P. **4.** ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02864992?cond=NCT02864992 (accessed February 2023). **5.** Thomas M, et al. Presented at WCLC, 2022. Abstract OA03.05.

March 2023
US-TEP-00668

Eligibility Criteria

INCLUSION CRITERIA[1-4]

- Locally advanced or metastatic NSCLC (≥1 measurable lesion by RECIST v1.1)
- *MET*ex14 skipping alteration
  - Identification of *MET*ex14 skipping was prospectively determined using central laboratories employing either a PCR-based or NGS-based clinical trial assay using tissue and/or plasma samples*
- *EGFR* wild-type and *ALK* negative status
- Treatment-naive patients or pretreated patients with no more than 3 lines of prior therapy
- ECOG PS 0-1

EXCLUSION CRITERIA[1,2]

- Symptomatic CNS metastases
- Clinically significant uncontrolled cardiac disease
- Prior treatment with any MET or HGF inhibitor
- Prior anticancer therapy within 21 days of the first dose of study intervention
- Unresolved Grade ≥2 toxicity

*An FDA-approved test for detection of *MET*ex14 skipping alterations in NSCLC for selecting patients for treatment with tepotinib is not available.

ALK, anaplastic lymphoma kinase; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*, epidermal growth factor receptor; FDA, Food and Drug Administration; HGF, hepatocyte growth factor; MET, mesenchymal-epithelial transition; *MET*ex14, mesenchymal-epithelial transition exon 14; NSCLC, non-small cell lung cancer; NGS, next-generation sequencing; PCR, polymerase chain reaction; RECIST, Response Evaluation Criteria in Solid Tumors.

References: 1. TEPMETKO® [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021. **2**. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02864992?cond=NCT02864992&draw=2&rank=1 (accessed February 2023). **3**. Smit EF, et al. Presented at ESMO, 2022, Abstract 985P. **4**. Thomas M, et al. Presented at WCLC, 2022. Abstract OA03.05.

Patient Baseline Characteristics

AGE, ECOG PS

Treatment naive (n=164)		Previously treated (n=149)
74 years (range 47 to 94)	Median age	70.8 years (range 41 to 89)
27.4%	ECOG PS 0	24.2%
72.0%	ECOG PS 1	75.8%

DISEASE CHARACTERISTICS

Treatment naive (n=164)		Previously treated (n=149)
79.9%	Adenocarcinoma histology	81.2%

RACE* AND GENDER

Treatment naive (n=164)		Previously treated (n=149)
68.3%	White	55.7%
30.5%	Asian	37.6%
50.6%	Male	47.7%
49.4%	Female	52.3%

SMOKING HISTORY†

Treatment naive (n=164)		Previously treated (n=149)
53.7%	Yes	40.9%
45.7%	No	53.0%

*MET*ex14 SKIPPING ALTERATIONS WERE IDENTIFIED THROUGH PCR OR NGS TESTING

Treatment naive (n=164)		Previously treated (n=149)
67.7%	Enrolled by tissue (RNA-based) testing	65.1%
57.9%	Enrolled by plasma (ctDNA-based) testing	55.7%

VISION cohorts A+C (*MET*ex14 skipping only), Feb 2022 cut-off.

*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'. †Smoking history was missing in 10 patients.

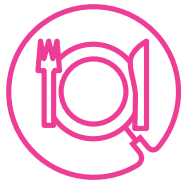
ctDNA, circulating tumor DNA; ECOG PS, Eastern Cooperative Oncology Group performance status; *MET*ex14, mesenchymal-epithelial transition exon 14; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; PCR, polymerase chain reaction.

Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Tepotinib Dosage and Administration

RECOMMENDED DOSAGE

- Recommended dosage: 450 mg* (two 225 mg tablets) orally once daily with food
  - ⚠ Until disease progression or unacceptable toxicity
- Dosage timing: approximately the same time every day



- Intake method: swallow whole (do not chew, crush, or split tablets)
- Missed dose: avoid taking within 8 hours of the next scheduled dose
  - ⚠ In case of vomiting after taking a dose, take the next dose at the scheduled time

DOSE MODIFICATIONS FOR ARs

- Recommended dose reduction: 225 mg of active moiety orally once daily
  - ⚠ Permanently discontinue tepotinib in patients who are unable to tolerate the 225 mg dose
  - ⚠ Management of some ARs may require temporary interruption or permanent discontinuation
- See the full Prescribing Information for recommended dosage modifications of tepotinib

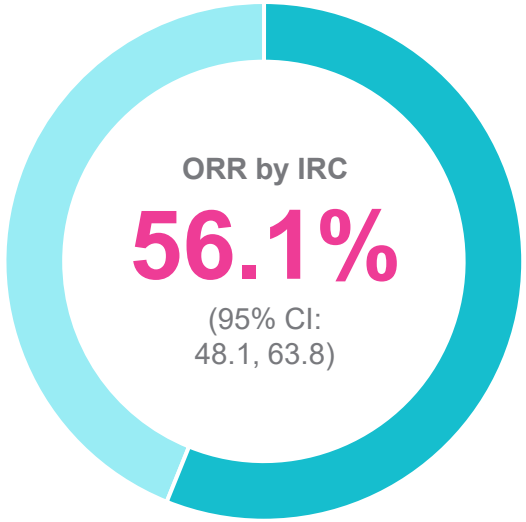
*Equivalent to 500 mg tepotinib hydrochloride hydrate.
AR, adverse reaction.
Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

Efficacy: Primary Endpoint

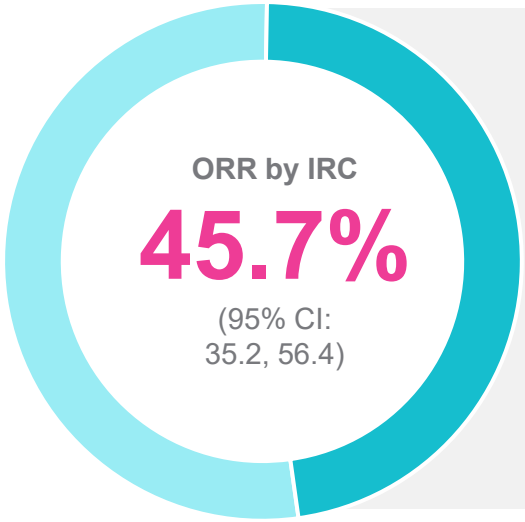
OBJECTIVE RESPONSE RATE BY PRIOR LINES OF THERAPY

Overall ORR was **50.8%** (95% CI: 45.1, 56.5)

Treatment naive (n=164)



Previously treated, 2L only (n=92)



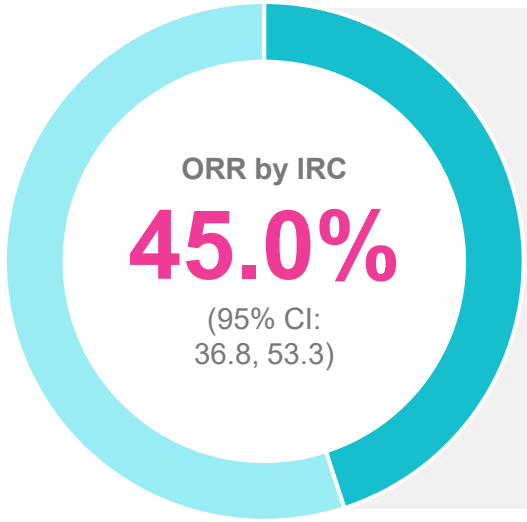
PRIOR THERAPY

IO* (n=36)
38.9%
(95% CI: 23.1, 56.5)

IO + CT (n=16)
62.5%
(95% CI: 35.4, 84.8)

CT (n=54)
50.0%
(95% CI: 36.1, 63.9)

Previously treated, 2L+ (n=149)



PRIOR THERAPY

IO* (n=79)
39.2%
(95% CI: 28.4, 50.9)

IO + CT (n=22)
54.5%
(95% CI: 32.2, 75.6)

CT (n=104)
48.1%
(95% CI: 38.2, 58.1)

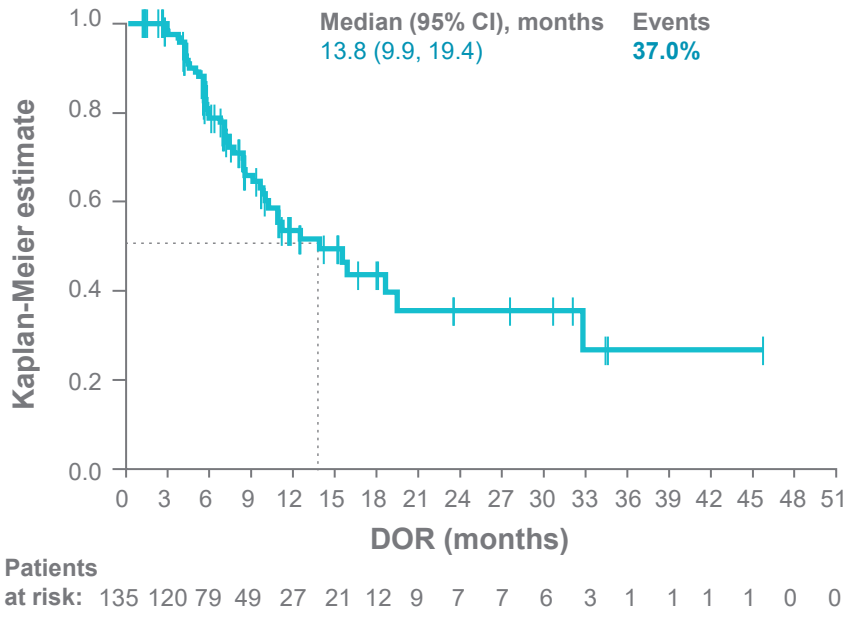
VISION cohorts A+C (*MET*ex14 skipping only), Feb 2022 cut-off.
*Patients received IO monotherapy or IO + platinum-based CT.
2L, second line; CI, confidence interval; CT, chemotherapy; IO, immunotherapy; IRC, independent review committee; *MET*ex14, mesenchymal-epithelial transition exon 14; ORR, objective response rate.
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Efficacy: Secondary Endpoints

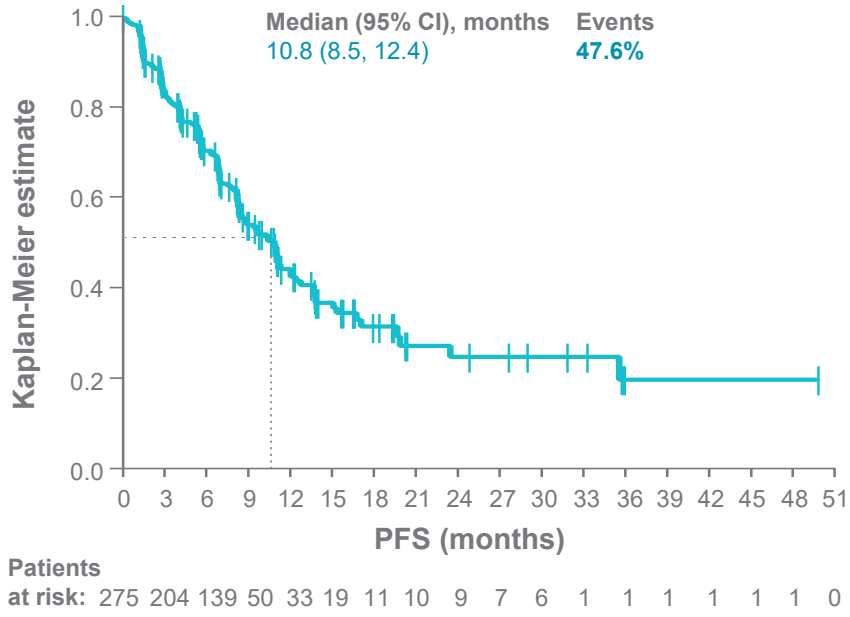
BEST OBJECTIVE RESPONSE, DISEASE CONTROL RATE, DURATION OF RESPONSE, AND PROGRESSION-FREE SURVIVAL

BOR	Overall (N=275)
CR, n (%)	0
PR, n (%)	135 (49.1)
SD, n (%)	71 (25.8)
PD, n (%)	34 (12.4)
NE, n (%)	35 (12.7)
DCR, % (95% CI)	74.9 (69.4, 79.9)

DOR



PFS



Overall, DCR was 74.9% (95% CI: 69.4, 79.9), median DOR was 13.8 months (95% CI: 9.9, 19.4), and median PFS was 10.8 months (95% CI: 8.5, 12.4)

Part 1 | Part 2 | Part 3

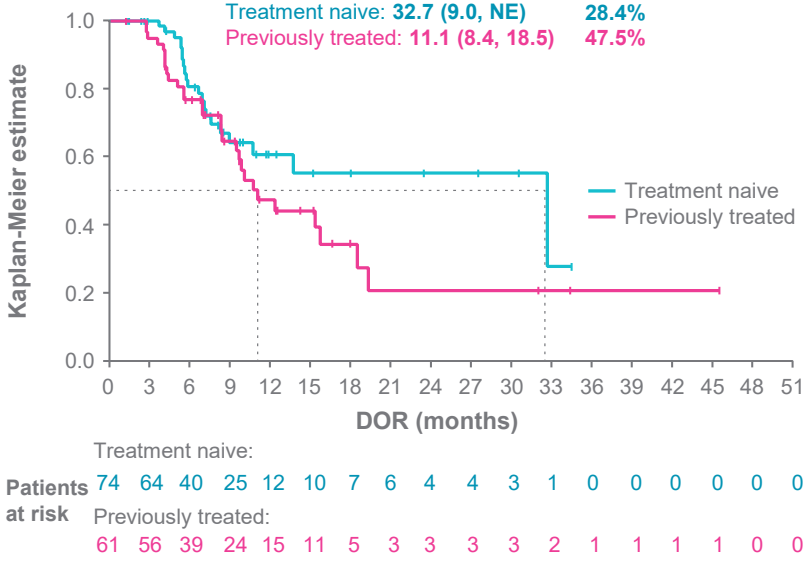
VISION cohorts A+C (*MET*ex14 skipping only), Feb 2021 cut-off.
BOR, best objective response; CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; IRC, Independent Review Committee; *MET*ex14, mesenchymal-epithelial transition exon 14; NE, not evaluable; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.
Reference: Thomas M, et al. Presented at DGHO Annual Meeting 2021, Abstract 52.

Efficacy: Secondary Endpoints

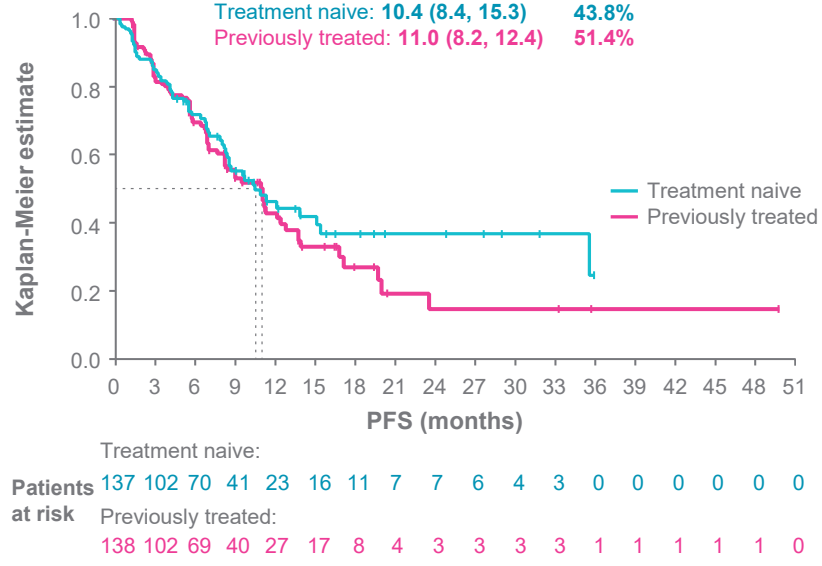
BEST OBJECTIVE RESPONSE, DISEASE CONTROL RATE, DURATION OF RESPONSE, AND PROGRESSION-FREE SURVIVAL BY PRIOR LINES OF THERAPY

BOR	Treatment naive (n=137)	Previously treated (n=138)
CR, n (%)	0	0
PR, n (%)	74 (54.0)	61 (44.2)
SD, n (%)	28 (20.4)	43 (31.2)
PD, n (%)	16 (11.7)	18 (13.0)
NE, n (%)	19 (13.9)	16 (11.6)
DCR, % (95% CI)	74.5 (66.3, 81.5)	75.4 (67.3, 82.3)

DOR



PFS



- In treatment-naive patients (n=137), DCR was 74.5 (95% CI: 66.3, 81.5), median DOR was 32.7 months (95% CI: 9.0, NE), and median PFS was 10.4 months (95% CI: 8.4, 15.3)
- In previously treated patients (n=138), DCR was 75.4 (95% CI: 67.3, 82.3), median DOR was 11.1 months (95% CI: 8.4, 18.5), and median PFS was 11 months (95% CI: 8.2, 12.4)

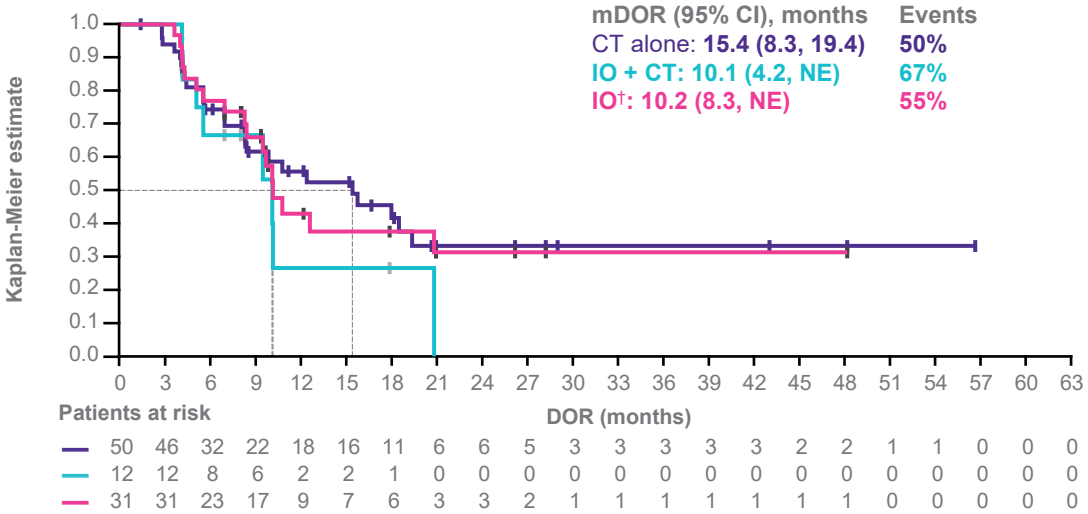
Part 1 | Part 2 | Part 3

VISION cohorts A+C (*MET*ex14 skipping only), Feb 2021 cut-off.
BOR, best objective response; CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; IRC, Independent Review Committee; *MET*ex14, mesenchymal-epithelial transition exon 14; NE, not evaluable; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.
Reference: Thomas M, et al. Presented at DGHO Annual Meeting 2021, Abstract 52.

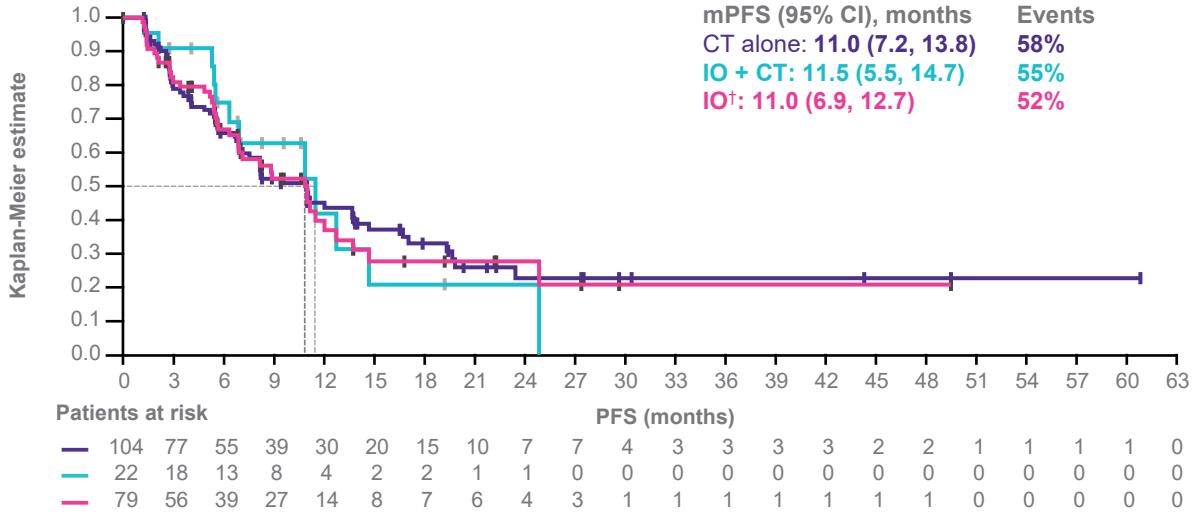
Efficacy: Secondary Endpoints

DURATION OF RESPONSE,* PROGRESSION-FREE SURVIVAL, AND OVERALL SURVIVAL BY PRIOR THERAPY TYPES

DOR



PFS



- In treatment-naive patients (n=164), mDOR was 46.4 months (95% CI: 13.8, NE), mPFS was 12.6 months (95% CI: 9.6, 17.7), and mOS was 19.1 months (95% CI: 13.7, 23.7)
- In previously treated patients, 2L only (n=92), mDOR was 12.6 months (95% CI: 8.3, 20.8), mPFS was 10.9 months (95% CI: 8.2, 13.8), and mOS was 20.0 months (95% CI: 15.8, 23.7)
- In previously treated, 2L+ patients (n=149), mDOR was 12.4 months (95% CI: 9.5, 18.5), mPFS was 11.0 months (95% CI: 8.2, 13.7), and mOS was 19.6 months (95% CI: 15.2, 22.3)

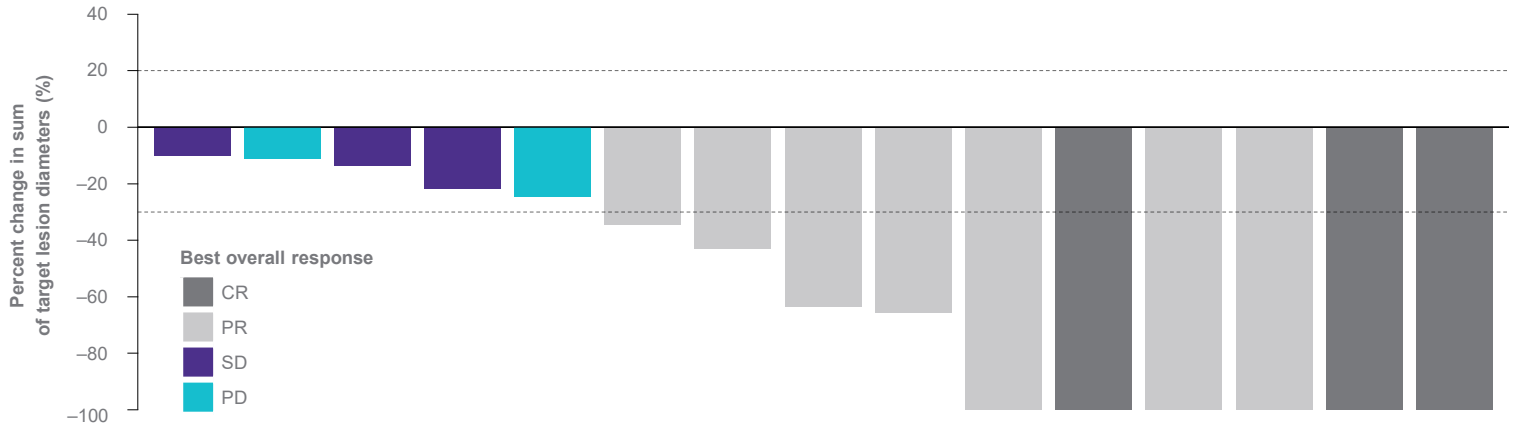
Updated efficacy outcomes by treatment experience

Part 1	Part 2	Part 3

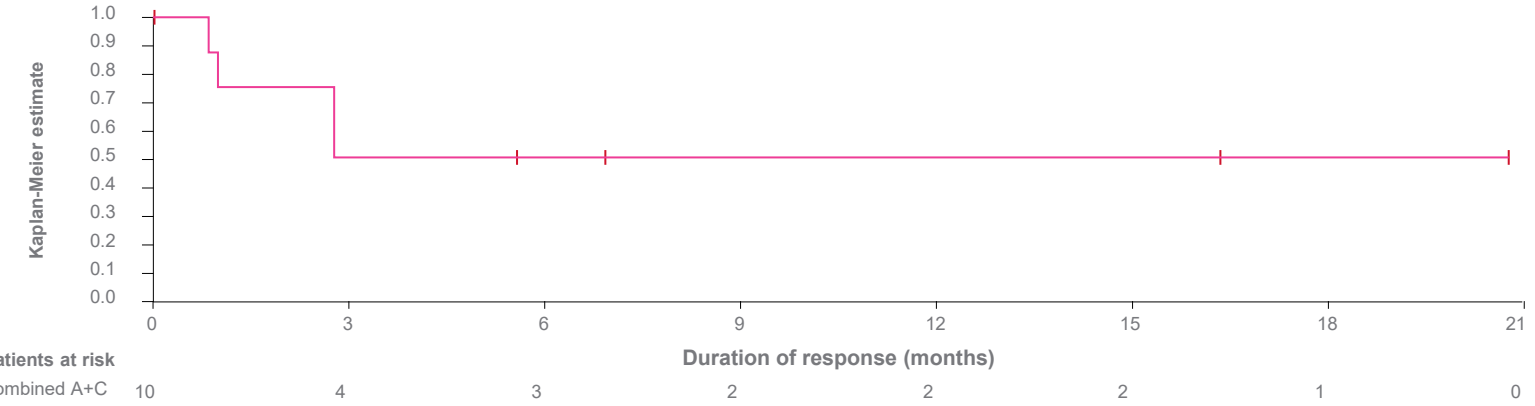
VISION cohorts A+C (*MET*ex14 skipping only), Feb 2022 cut-off.
*By IRC. †Patients received IO monotherapy or IO + platinum-based CT.
2L, second line; CI, confidence interval; CT, chemotherapy; DOR, duration of response; IO, immunotherapy; IRC, Independent Review Committee; m, median; *MET*ex14, mesenchymal-epithelial transition exon 14; NE, not estimable; OS, overall survival; PFS, progression-free survival.
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Efficacy: Exploratory Analysis of Patients With Brain Metastases

Intracranial response in patients with target lesions (n=15)



Intracranial duration of response



- Tepotinib crosses the blood-brain barrier to a significant extent, leading to concentrations of unbound tepotinib in the brain of 25% compared to plasma ($Kp_{u,u}$=0.25), within a similar range to other CNS-penetrant TKIs
- Across Cohorts A+C, 43 patients with brain metastases were evaluable by RANO-BM (1L, n=23; 2L+, n=20)
- 30 patients (69.8%) received prior brain radiotherapy or surgery
- In patients with target or non-target lesions (n=43), **intracranial disease control rate was 88.4%** (95% CI: 74.9, 96.1) with **intracranial mPFS of 20.9 months** (95% CI: 5.7, NE)
- In patients with target lesions (n=15), **intracranial ORR was 66.7%** (95% CI: 38.4, 88.2) with **intracranial mDOR NE** (95% CI: 0.9, NE)

Due to the single-arm design of the VISION Trial, no formal statistical comparisons were conducted; data were analyzed in a descriptive manner. For analysis of intracranial activity, brain imaging had no mandatory schedule and, as such, data for this retrospective ad hoc analysis were incomplete, and confirmation of response was not required. Impact of prior radiotherapy on this analysis should be considered. Results are subject to change based on updated analyses. For these reasons, results from these analyses should be interpreted with caution.

VISION cohorts A+C (*MET*ex14 skipping only), Feb 2022 cut-off.
1L, first line; 2L+, second-or-later line; CI, confidence interval; CNS, central nervous system; CR, complete response; DOR, duration of response; Kpu,u, unbound partition coefficient; m, median; *MET*ex14, mesenchymal-epithelial transition exon 14; NE, not estimable; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; RANO-BM, Response Assessment in Neuro-Oncology Brain Metastases; SD, stable disease; TKI, tyrosine kinase inhibitor.
Reference: Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05.

Safety: Most Common TRAEs and AEs of Clinical Interest

TRAEs, %	Cohorts A+C (N=313*)
Any grade	91.7
Grade ≥3	34.2
Leading to dose reduction	33.5
Leading to treatment interruption	42.5
Leading to permanent discontinuation	14.7

Reported in ≥10% of patients, %	All grades	Grades ≥3
Peripheral edema	66.5	10.9
Nausea	23.3	0.6
Hypoalbuminemia	23.0	3.2
Diarrhea	22.4	0.3
Blood creatinine increase	21.7	0.6
ALT increase	13.1	2.2
Decreased appetite	11.2	0.3

- Tepotinib was generally well tolerated, with mostly mild-moderate AEs and few discontinuations
- Overall (N=313), TRAEs occurred in 91.7% of patients, 34.2% had Grade ≥3 TRAEs, and 14.7% discontinued due to TRAEs

Part 1 | Part 2

VISION cohorts A+C (*MET*ex14 skipping only), Feb 2022 cut-off.
*Safety population comprised all patients from VISION Cohorts A and C.
AE, adverse event; ALT, alanine transaminase; *MET*ex14, mesenchymal-epithelial transition exon 14; TRAE, treatment-related adverse event.
Reference: Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05.

Safety: TRAE By Prior Lines of Therapy

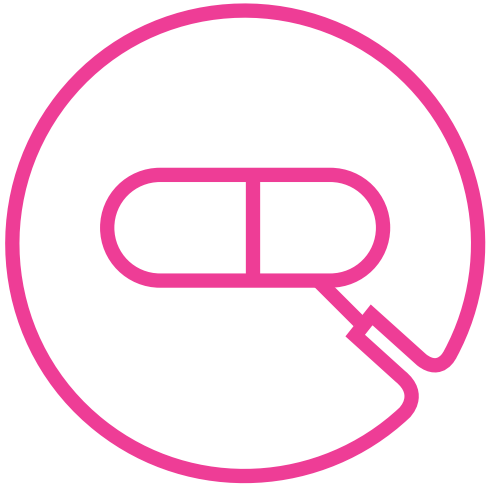
TRAEs, n (%)	Treatment naive (n=164)	Previously treated (n=149)	Prior IO (n=81)
Any grade	155 (94.5)	132 (88.6)	73 (90.1)
Grade ≥3	67 (40.9)	40 (26.8)	22 (27.2)
Leading to dose reduction	64 (39.0)	41 (27.5)	21 (25.9)
Leading to temporary interruption	79 (48.2)	54 (36.2)	31 (38.3)
Leading to permanent discontinuation	25 (15.2)	21 (14.1)	14 (17.3)
All-cause AEs in ≥20% of all patients, n (%)			
Peripheral edema	123 (75.0)	102 (68.5)	57 (70.4)
Nausea	55 (33.5)	41 (27.5)	21 (25.9)
Diarrhea	47 (28.7)	43 (28.9)	21 (25.9)
Hypoalbuminemia	57 (34.8)	44 (29.5)	28 (34.6)
Blood creatinine increase	46 (28.0)	45 (30.2)	27 (33.3)
Dyspnea	44 (26.8)	23 (15.4)	14 (17.3)
Decreased appetite	37 (22.6)	27 (18.1)	17 (21.0)

- In treatment-naive patients (n=164), Grade ≥3 TRAEs occurred in 40.9% of patients and 15.2% of patients discontinued due to TRAEs
- In previously treated patients (n=149), Grade ≥3 TRAEs occurred in 26.8% of patients and 14.1% of patients discontinued due to TRAEs; in patients with prior IO, Grade ≥3 TRAEs occurred in 27.2% of patients and 17.3% of patients discontinued due to TRAEs
- Peripheral edema was the most common all-cause AE, occurring in 75.0% of treatment-naive patients, 68.5% of previously treated patients, and 70.4% of patients with prior IO
- The safety profile of tepotinib was consistent in patients with prior IO

Part 1 | Part 2

VISION cohorts A+C (*MET*ex14 skipping only), Feb 2022 cut-off.
*Safety population comprised all patients from VISION Cohorts A and C.
AE, adverse event; IO, immunotherapy; *MET*ex14, mesenchymal-epithelial transition exon 14; TRAE, treatment-related adverse event.
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

FDA-Approved Indication and Usage*

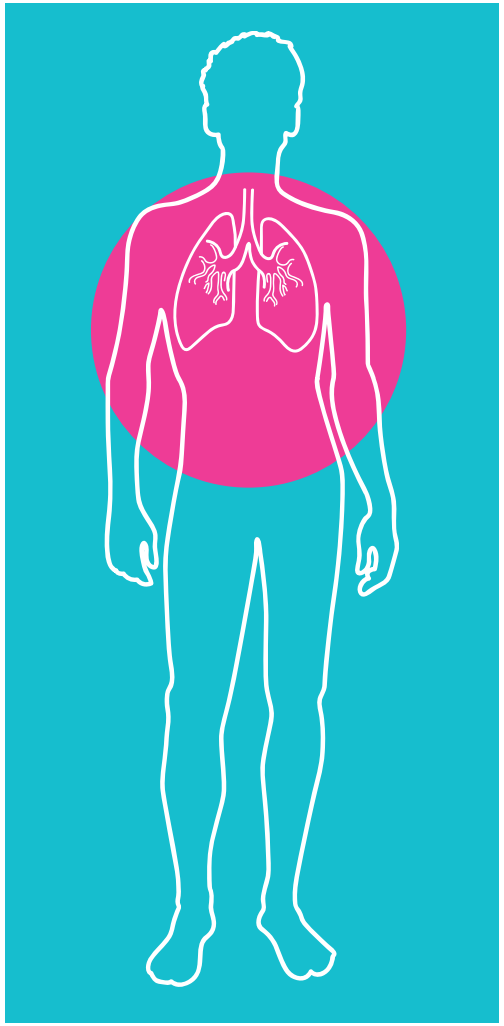


- TEPMETKO® (tepotinib) is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (mNSCLC) harboring mesenchymal-epithelial transition (*MET*) exon 14 skipping alterations
- This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials
- The recommended dosage of tepotinib is 450 mg (two 225 mg tablets) orally once daily with food until disease progression or unacceptable toxicity

*See full Prescribing Information at TEPMETKO.com.

Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

Tepotinib Warnings and Precautions



INTERSTITIAL LUNG DISEASE (ILD)/PNEUMONITIS

ILD/pneumonitis, which can be fatal, occurred in patients treated with tepotinib

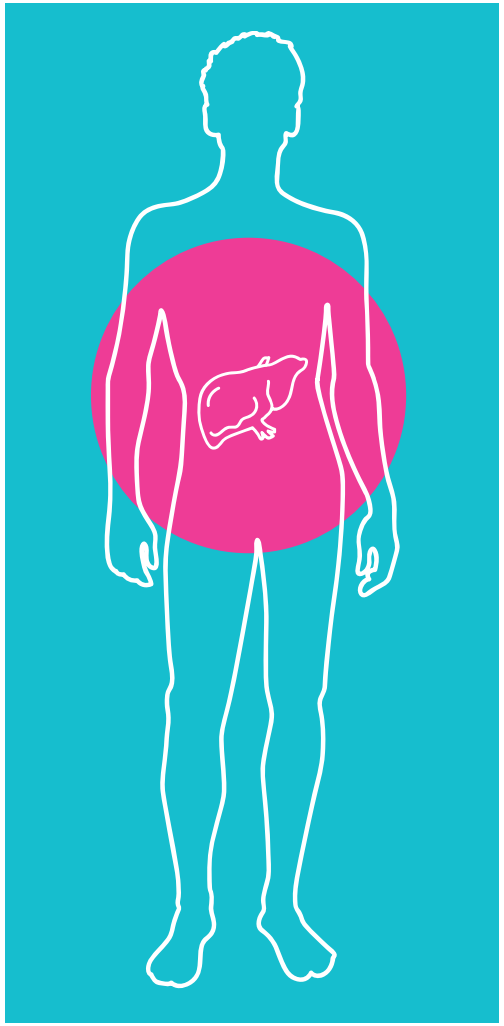
ILD/pneumonitis	
All grades	2.2%
Grade ≥3	1 case; this event resulted in death
Discontinuation of tepotinib due to ILD/ pneumonitis	0.9% (n=4)

Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever)

Immediately **withhold** tepotinib in patients with suspected ILD/pneumonitis and **permanently discontinue** if no other potential causes of ILD/pneumonitis are identified

Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

Tepotinib Warnings and Precautions



HEPATOTOXICITY

Hepatotoxicity occurred in patients treated with tepotinib

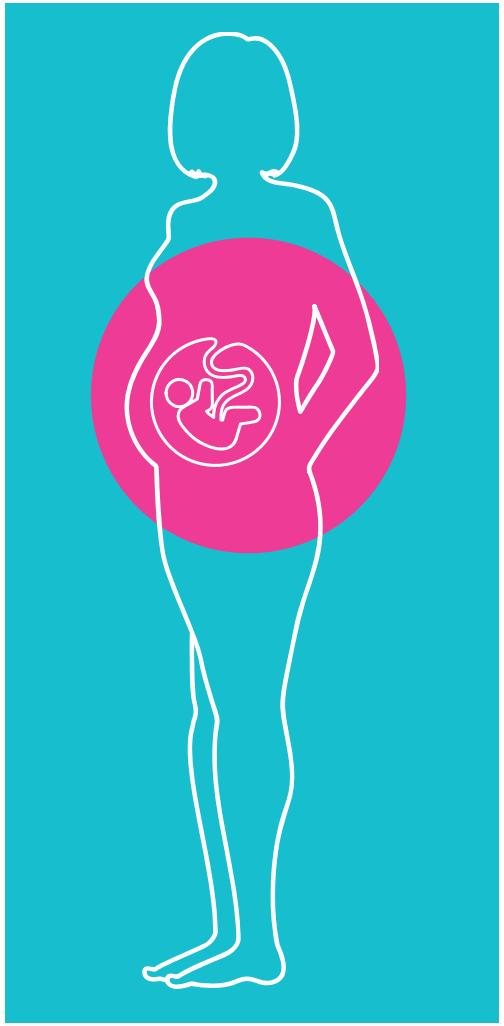
Increased ALT/AST	
All grades	13%
Grade 3 or 4	4.2%
Fatal AR of hepatic failure	0.2% (n=1)
Discontinuation of tepotinib due to increased ALT/AST	0.7% (n=3)
Median time to onset of Grade ≥3 increased ALT/AST	30 days (range: 1 to 178)

Monitor liver function tests (including ALT, AST, and total bilirubin) prior to the start of tepotinib, every 2 weeks during the first 3 months of treatment, then once a month or as clinically indicated, with more frequent testing in patients who develop increased transaminases or bilirubin*

Based on the severity of the AR, **withhold, dose reduce**, or **permanently discontinue** tepotinib

*Please note that this is as per Prescribing Information but could be inconsistent with practice patterns.
ALT, alanine aminotransferase; AR, adverse reaction; AST, aspartate aminotransferase.
Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

Tepotinib Warnings and Precautions



EMBRYO-FETAL TOXICITY

- Based on findings in animal studies and its mechanism of action, tepotinib can cause fetal harm when administered to pregnant women
- Oral administration of tepotinib to pregnant rabbits during the period of organogenesis resulted in malformations (teratogenicity) and anomalies at exposures less than the human exposure based on AUC at the 450 mg daily clinical dose

Advise pregnant women of the potential risk to a fetus

Advise females of reproductive potential or males with female partners of reproductive potential to use effective contraception during treatment with tepotinib and for 1 week after the final dose

AUC, area under the curve.

Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

Important Safety Information

INTERSTITIAL LUNG DISEASE/PNEUMONITIS

- Tepotinib can cause **ILD/pneumonitis**, which can be fatal
- Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever)
- Immediately withhold tepotinib in patients with suspected ILD/pneumonitis and permanently discontinue if no other potential causes of ILD/pneumonitis are identified
- ILD/pneumonitis occurred in 2.2% of patients treated with tepotinib, with 1 patient experiencing Grade 3 or higher event; this event resulted in death

HEPATOTOXICITY

- Tepotinib can cause **hepatotoxicity**, which can be fatal
- Monitor liver function tests (including ALT, AST, and total bilirubin) prior to the start of tepotinib, every 2 weeks during the first 3 months of treatment, then once a month or as clinically indicated, with more frequent testing in patients who develop increased transaminases or total bilirubin
- Based on the severity of the adverse reaction, withhold, dose reduce, or permanently discontinue tepotinib
- Increased ALT/AST occurred in 13% of patients treated with tepotinib. Grade 3 or 4 increased ALT/AST occurred in 4.2% of patients
- A fatal adverse reaction of hepatic failure occurred in 1 patient (0.2%)
- The median time-to-onset of Grade 3 or higher increased ALT/AST was 30 days (range 1 to 178)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ILD, interstitial lung disease.

Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

Important Safety Information

EMBRYO-FETAL TOXICITY

- Tepotinib can cause **embryo-fetal toxicity**
- Based on findings in animal studies and its mechanism of action, tepotinib can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus
- Advise females of reproductive potential or males with female partners of reproductive potential to use effective contraception during treatment with tepotinib and for 1 week after the final dose

DRUG INTERACTIONS

- Avoid concomitant use of tepotinib with dual strong inhibitors of **CYP3A** and **P-gp inhibitors** and strong **CYP3A inducers**
- Avoid concomitant use of tepotinib with certain **P-gp substrates** where minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, reduce the P-gp substrate dosage if recommended in its approved product labeling

FATAL ADVERSE REACTIONS

- **Fatal adverse reactions** occurred in 1 patient (0.4%) due to pneumonitis, in 1 patient (0.4%) due to hepatic failure, and in 1 patient (0.4%) due to dyspnea from fluid overload

SERIOUS ADVERSE REACTIONS

- **Serious adverse reactions** occurred in 45% of patients who received tepotinib. Serious adverse reactions in >2% of patients included pleural effusion (7%), pneumonia (5%), edema (3.9%), dyspnea (3.9%), general health deterioration (3.5%), pulmonary embolism (2%), and musculoskeletal pain (2%)

MOST COMMON ADVERSE REACTIONS

- **The most common adverse reactions** (≥20%) in patients who received tepotinib were edema, fatigue, nausea, diarrhea, musculoskeletal pain, and dyspnea

Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

EMD SERONO

Important Safety Information

CLINICALLY RELEVANT ADVERSE REACTIONS

- **Clinically relevant adverse reactions** in <10% of patients who received tepotinib included ILD/pneumonitis, rash, fever, dizziness, pruritis, and headache

SELECTED LABORATORY ABNORMALITIES

- **Selected laboratory abnormalities (≥20%)** from baseline in patients receiving tepotinib in descending order were decreased albumin (76%), increased creatinine (55%), increased ALP (50%), decreased lymphocytes (48%), increased ALT (44%), increased AST (35%), decreased sodium (31%), decreased hemoglobin (27%), increased potassium (25%), increased GGT (24%), increased amylase (23%), and decreased leukocytes (23%)

MOST COMMON GRADE 3 TO 4 LABORATORY ABNORMALITIES:

- **The most common Grade 3 to 4 laboratory abnormalities (≥2%)** in descending order were decreased lymphocytes (11%), decreased albumin (9%), decreased sodium (8%), increased GGT (5%), increased amylase (4.6%), increased ALT (4.1%), increased AST (2.5%), and decreased hemoglobin (2%)

CLINICALLY RELEVANT LABORATORY ABNORMALITY

- **A clinically relevant laboratory abnormality** in <20% of patients who received tepotinib was increased lipase in 18% of patients, including 3.7% Grades 3 to 4

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; ILD, interstitial lung disease.

Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.