A TREATMENT FOR PATIENTS WITH METASTATIC NSCLC HARBORING *MET*EX14 SKIPPING+ ALTERATIONS

EMD SERONO

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NSCLC, non-small cell lung cancer; USPI, United States Prescribing Information.

Important Notices

- Tepotinib is being investigated for treatment of various diseases. Efficacy and safety of this product is still under investigation in various indications. Regulatory approval is dependent on the completion of the study programs and review by local regulatory authorities and varies from country to country. Please check the **US Prescribing Information** label for US-specific information. Clinical trial information is available at www.clinicaltrials.gov
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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.

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NSCLC DISEASE AND BACKGROUND

Lung Cancer: Key US 2022 Statistics

236,740 new cases of lung cancer are diagnosed in the US annually[1]

71

Median age at diagnosis[1]
(all cases: patients with driver mutations tend to be younger)[2]

236,740
New cases of lung cancer[1]

118,830 in women[3]

117,910 in men[3]

130,180
Deaths from lung cancer[1]

61,360 in women[3]

68,820 in men[3]

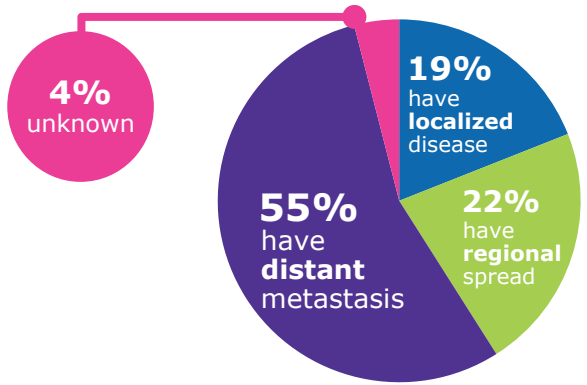
NSCLC accounts for 84% of these:
~198,862 patients[3]

~3% of these patients have *MET*ex14 skipping NSCLC:
~5,966 patients[4]

One patient with NSCLC harboring *MET*ex14 is diagnosed **every 90 minutes***

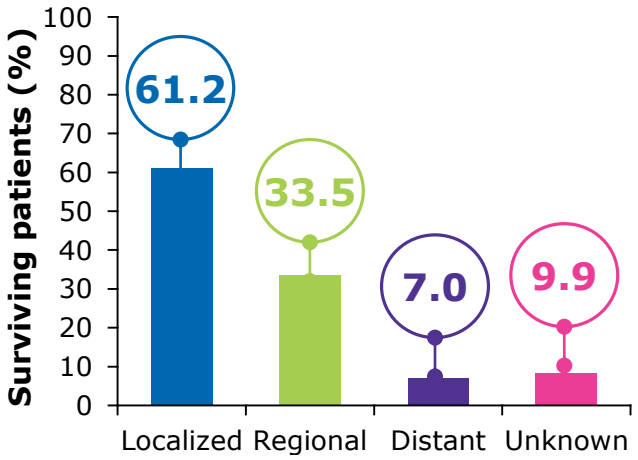
16 patients with NSCLC harboring *MET*ex14 are diagnosed **every day***

Spread at diagnosis[1]



~55% of patients with lung cancer are diagnosed with advanced or metastatic disease with a 5-year survival rate of 7%[1]

5-year relative survival by spread at diagnosis (2011–2017)[1]

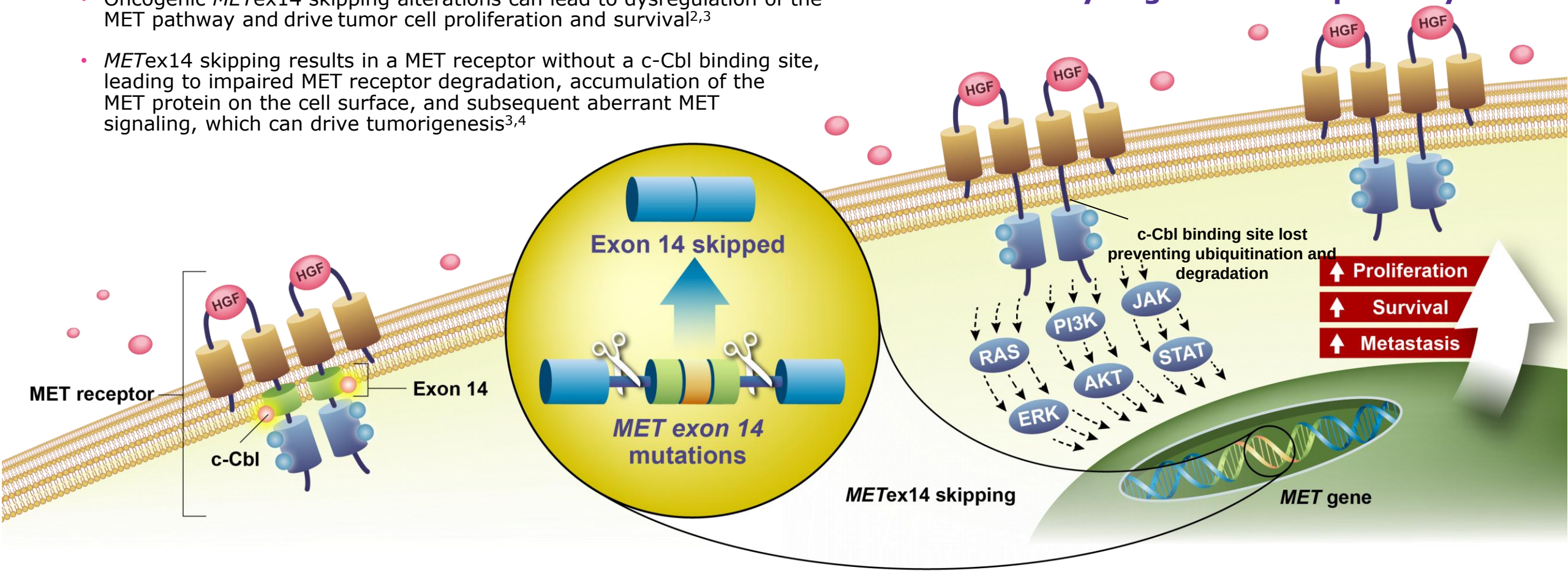


*Calculation: number of patients per year (5,966)/days in calendar year (365)=16.
NSCLC, non-small cell lung cancer; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14.
References: 1. Cancer Stat Facts: Lung and Bronchus Cancer. SEER Program, National Cancer Institute. https://seer.cancer.gov/statfacts/html/lungb.html (accessed October 2022); **2.** Suidan AM, et al. J Glob Oncol. 2019;5:1–8; **3.** Key Statistics for Lung Cancer. American Cancer Society. https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html (accessed October 2022); **4.** Salgia R, et al. Can Treat Rev. 2020;87:102022.

MET Signaling Can Drive Tumor Growth and Progression[1]

- MET is a receptor tyrosine kinase encoded by the *MET* gene[1]
- Oncogenic *MET*ex14 skipping alterations can lead to dysregulation of the MET pathway and drive tumor cell proliferation and survival[2,3]
- *MET*ex14 skipping results in a MET receptor without a c-Cbl binding site, leading to impaired MET receptor degradation, accumulation of the MET protein on the cell surface, and subsequent aberrant MET signaling, which can drive tumorigenesis[3,4]

*MET*ex14 skipping and dysregulated MET pathway[4,5]



AKT, protein kinase B; c-Cbl, casitas B-lineage lymphoma; ERK, extracellular regulatory kinase; HGF, hepatocyte growth factor; JAK, Janus kinase; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; PI3K, phosphoinositide 3-kinase; STAT, signal transducer and activator of transcription.

References: 1. Paik PK, et al. N Engl J Med. 2020;383(10):1–40; **2.** Tong JH, et al. Clin Cancer Res. 2016;22(12):3048–3056; **3.** Liang H, Wang M. Onco Targets Ther. 2020;13:2491–2510; **4.** Drilon A, et al. J Thorac Oncol. 2017;12(1):15–26; **5.** Wu YL, et al. Cancer Treat Rev. 2017; 61:70–81.

*MET*ex14 Skipping Alterations Are Primary Oncogenic Drivers in NSCLC[1–6]

Patients with *MET*ex14 skipping alterations:

Have been associated with **advanced disease** and a **poor prognosis**[2]

Tend to be **considerably older** vs patients with other oncogenic drivers (average age of 54 to 65 years in *ALK, ROS1, EGFR, KRAS, and BRAF*)[1]

Are more frequently current or former smokers (60%) than never smokers (40%)[6]

_MET_ex14 skipping is the primary oncogenic driver in:

- 3% of adenocarcinomas[4,5]
- 2% of squamous cell carcinomas[5]
- 8% of sarcomatoid carcinomas[5]

Average age at diagnosis in patients with *MET*ex14 skipping alterations[1]:

~74 years

Testing to identify patients with *MET*ex14 skipping alterations can help inform treatment decisions[2,3]

ALK, anaplastic lymphoma kinase gene; *BRAF*, proto-oncogene B-Raf; *EGFR*, epidermal growth factor receptor gene; *KRAS*, Ki-ras2 gene; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer; *ROS1*, ROS proto-oncogene 1.

References: 1. Tong JH, et al. Clin Cancer Res. 2016;22(12):3048–3056; **2.** Awad MM, et al. Lung Cancer. 2019;133:96–102; **3.** Salgia R. Mol Cancer Ther. 2017;16(4):555–565; **4.** Frampton GM, et al. Cancer Discov. 2015;5:850–859; **5**. Schrock AB, et al. J Thorac Oncol. 2016;11:1493–5102; **6.** Wolf J, et al. Presented at ENA, 2018, Poster 403.

IMPORTANT SAFETY INFORMATION

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 one 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 one patient (0.2%)
- The median time-to-onset of Grade 3 or higher increased ALT/AST was 30 days (range 1–178)

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

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

Important Safety Information (continued)

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 one 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 one patient (0.4%) due to pneumonitis, in one patient (0.4%) due to hepatic failure, and in one 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.

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Important Safety Information (continued)

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 3-4 laboratory abnormalities

- **The most common Grade 3-4 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.

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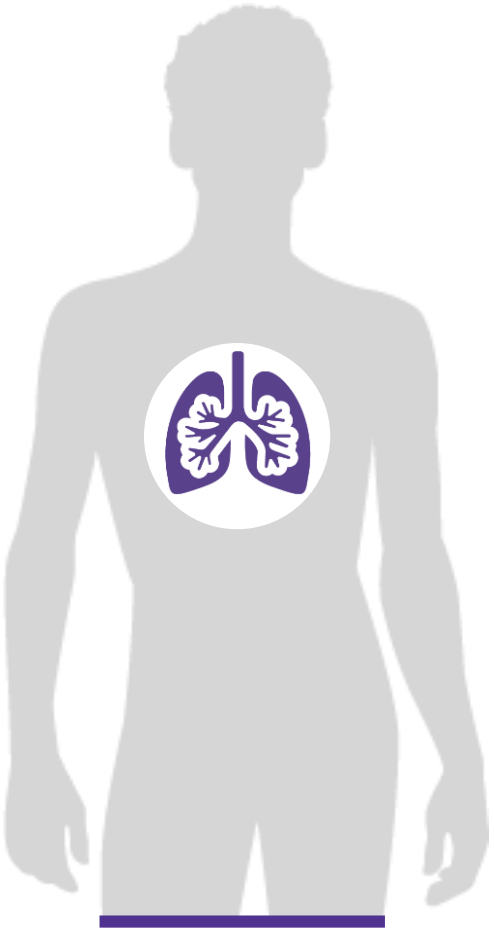
TEPOTINIB WARNINGS AND PRECAUTIONS

Tepotinib Warnings and Precautions: Interstitial Lung Disease/Pneumonitis



ILD/pneumonitis, which can be fatal, occurred in patients treated with tepotinib	
ILD/pneumonitis All grades ≥Grade 3	2.2% 1 case; this event resulted in death
Discontinuation of tepotinib due to ILD/pneumonitis	0.9% (n=4)

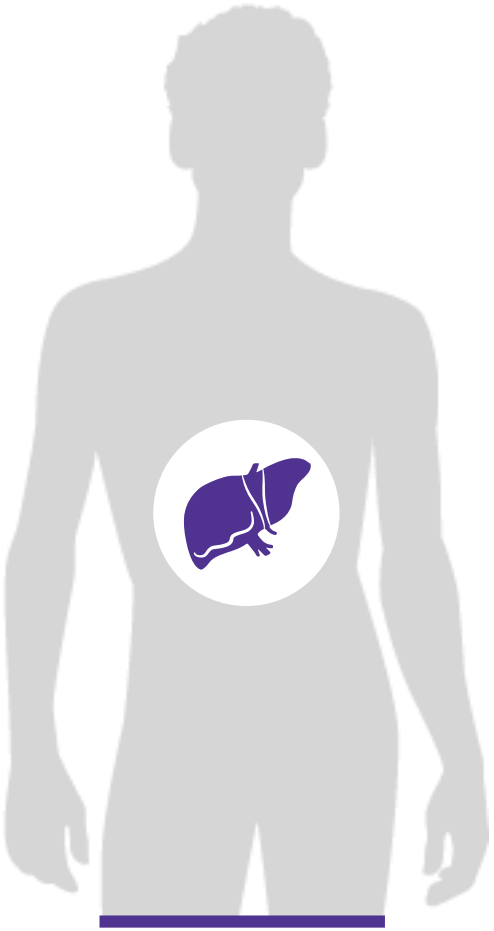
Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever)

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

ILD, interstitial lung disease.

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/increased AST All grades Grade 3 or 4 increased ALT/AST	 13% 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: 1–178)

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 one week after the final dose

AUC, area under the curve.

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

TEPOTINIB DOSAGE AND ADMINISTRATION

Tepotinib Dosage and Administration: Patient Selection

- Select patients for treatment with tepotinib based on the presence of *MET*ex14 skipping alterations in plasma or tumor specimens
- Testing for the presence of *MET*ex14 skipping alterations in plasma specimens is recommended only in patients for whom a tumor biopsy cannot be obtained
- If an alteration is not detected in a plasma specimen, re-evaluate the feasibility of biopsy for tumor tissue testing
- An FDA-approved test for the detection of *MET*ex14 skipping alterations in NSCLC to select patients for treatment with tepotinib is not available

FDA, US Food and Drug Administration; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer.

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

Tepotinib Dosage and Administration: Recommended Dosage and Modification

Recommended dosage

- The recommended dosage of tepotinib is 450 mg* (two 225 mg tablets) orally **once daily with food** until disease progression or unacceptable toxicity
- Instruct patients to take their dose at approximately the same time every day and to swallow tablets whole. Do not chew, crush, or split tablets
- Advise patients not to make up a missed dose within 8 hours of the next scheduled dose
- If vomiting occurs after taking a dose, advise patients to take the next dose at the scheduled time

Dose modifications for ARs

- The recommended dose reduction of tepotinib for the management of ARs is 225 mg 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.

VISION CLINICAL TRIAL

VISION: A Single-arm, Open-label, Multicenter, Non-randomized, Multicohort Study

Tepotinib in adult patients with advanced or metastatic NSCLC harboring *MET*ex14 skipping alterations

Eligibility:

- Advanced, metastatic *MET*ex14+ NSCLC*
- *EGFR* wild-type and *ALK* negative status
- ≥1 measurable lesion by RECIST v1.1
- 1L, 2L, or 3L of therapy[2,3]
- ECOG PS 0–1

Exclusions:

- Symptomatic CNS metastases
- Clinically significant uncontrolled cardiac disease
- Prior treatment with any MET or HGF inhibitor

Cohort A†
*MET*ex14 skipping
Detection of alterations in plasma or tissue

Cohort B:
MET amplification
Not included in this presentation

Cohort C‡
*MET*ex14 skipping
Detection of alterations in plasma or tissue

Confirmatory Part 2 of study

Tepotinib
500 mg§ oral QD

Tepotinib was administered until disease progression or unacceptable toxicity

Major efficacy outcome

- Confirmed ORR by RECIST v1.1 as evaluated by BIRC‖

Additional efficacy outcome

- DOR by BIRC‖, PFS[2,3], OS[2,3]
- Safety (per NCI-CTCAE v4.03)[2,3]

Exploratory RANO-BM analysis[3,¶]

BOR per RANO-BM (patients with ≥1 evaluable post-baseline tumor assessment): disease control was defined as CR/PR/SD, or non-CR/non-PD

*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. An FDA-approved test for detection of *MET*exon14 skipping alterations in NSCLC for selecting patients for treatment with tepotinib is not available. †Cohort A enrollment began on September 13, 2016. ‡Cohort C enrolment began on August 8, 2019. §450 mg active moiety. ‖Per IRC for February 20, 2022, cut-off.[2,3] ¶Composite of radiographic responses, corticosteroid use, and clinical status, giving a more comprehensive overview of the patient compared with RECIST.[4] For patients with non-measurable lesions only (enhancing and non-enhancing NTLs), non-CR/non-PD was defined as a best objective response of disease control, ie, persistence of at least one non-progressing NTL. Brain imaging had no mandatory schedule and, as such, data for this analysis were incomplete, and confirmation of response was not required.

1L, first line; 2L, second line; 3L, third line; *ALK*, anaplastic lymphoma kinase; BIRC, Blinded Independent Review Committee; BOR, best overall response; CNS, central nervous system; CR, complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*, epidermal growth factor receptor; FDA, US Food and Drug Administration; HGF, hepatocyte growth factor; IRC, independent review committee; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NCI-CTCAE, National Cancer Institute - Common Terminology Criteria for Adverse Events; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; NTL, non-target lesion; ORR, objective response rate; OS, overall survival; PCR, polymerase chain reaction; PD, progressive disease; PFS, progression-free survival; PR, partial response; QD, once daily; RANO-BM, Response Assessment in Neuro-Oncology Brain Metastases; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

References: 1. TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021; **2.** Smit EF, et al. Presented at ESMO, 2022, Abstract 985P; **3.** Thomas M, et al. Presented at WCLC, 2022. Abstract OA03.05. **4.** Lin NU, et al. Lancet Oncol. 2015;16(6):e270–e278.

*MET*ex14 Skipping Patient Populations in VISION

Main data cut-offs:

- Primary efficacy analysis (not included in this deck): January 2020 data cut-off when 99/152 patients in Cohort A had ≥9 months of follow-up data[1]
- Data submitted to FDA and included in USPI (full Cohort A and safety data for Cohorts A+C): July 2020 main data cut-off[2,3]
- Updated analysis: February 2021 (see Backup section)[4,5] and February 2022 data cut-offs[6,7]

July 2020 Data Cut-off[2,3]

Safety set (N=255)
All treated patients in Cohorts A + C

Efficacy analysis set (N=152)
Full Cohort A

Treatment naive	2L+
n=69	n=83

February 2022 Data Cut-off[6,7]

Safety set (N=313)
All treated patients in Cohorts A + C

Confirmatory efficacy analysis set (N=161)
Full Cohort C

Treatment naive	2L+
n=95	n=66

Efficacy analysis set (N=313)
Cohorts A + C

Treatment naive	2L+
n=164	n=149

2L, second line; 2L+. second-or-later line; FDA, US Food and Drug Administration; *MET*ex14, *MET* exon 14; USPI, United States Prescribing Information.

References: 1. Paik PK, et al. N Engl J Med. 2020;383(10):931–943; **2.** TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021; **3.** Le X, et al. Clin Cancer Res. 2022;28(6):1117–1126; **4.** Thomas M, et al. Presented at DGHO Annual Meeting, 2021, Abstract 52; **5.** Garassino M, et al. Presented at AMCP Annual Meeting, 2022, Abstract C6. **6.** Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05; 7. Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Timeline

January 2020 data cut-off

Paik PK, et al. *N Engl J Med*. 2020 (Cohort A, ≥9 months follow-up, N=99 [efficacy], N=152 [safety])[1]

July 2020 data cut-off

Le X, et al. *Clin Cancer Res*. 2022 (Cohort A, 16.4 months median follow-up, N=152 [efficacy], N=255 [safety])[2]

USPI Feb 2021[3]

February 2021 data cut-off

Thomas M, et al. DGHO, 2021 (Cohorts A+C, ≥3 months follow-up)[4]

Garassino M, et al. AMCP, 2022 (Cohorts A+C, ≥3 months follow-up)[5]

N=275 (efficacy), N=291 (safety)[4,5]

February 2022 data cut-off

Thomas M, et al. WCLC, 2022 (Cohort C, >9 months follow-up, N=161 [efficacy & safety])[6]

Smit EF, et al. ESMO, 2022 (Cohorts A+C, N=313 [efficacy & safety])[7]

USPI, United States Prescribing Information.

References: 1. Paik PK, et al. N Engl J Med. 2020;383(10):931–943; **2.** Le X, et al. Clin Cancer Res. 2022;28(6):1117–1126; **3.** TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021; **4.** Thomas M, et al. Presented at DGHO Annual Meeting, 2021, Abstract 52; **5.** Garassino M, et al. Presented at AMCP Annual Meeting, 2022, Abstract C6. **6.** Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05; 7. Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

PIVOTAL COHORT A EFFICACY AND SAFETY DATA

VISION Cohort A

July 2020 cut-off

Patient Characteristics

Age and ECOG PS

- **Median age of 73 years** (range 41–94)
- **27%** had ECOG PS 0
- **73%** had ECOG PS 1

Disease characteristics

- **98%** of patients had metastatic disease
- **86%** had adenocarcinoma histology
- **10%** had CNS metastases

Race and gender

- **71%** White
- **25%** Asian

- **52%** male
- **48%** female

Smoking status

- **43%** never smokers

Line of therapy

- **45%** (n=69) treatment naive
- **55%** (n=83) previously treated
  - **89%** prior platinum-based chemotherapy

*MET*ex14 skipping alterations were identified through PCR or NGS testing*

- **58%** of patients were enrolled by tissue (RNA-based) testing
- **65%** of patients were enrolled by plasma (ctDNA-based) testing

*Some patients tested positive using both methodologies.
CNS, central nervous system; ctDNA, circulating tumor DNA; ECOG PS, Eastern Cooperative Oncology Group performance status; *MET*ex14, *MET* exon 14; NGS, next-generation sequencing; PCR, polymerase chain reaction.
Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

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Baseline Characteristics

	Treatment-naive (n=69)	Previously treated (n=83)	Overall (n=152)
Age, median years (range)	74.0 (56–94)	72.6 (41–88)	73.1 (41–94)
Male/female, %	52.2/47.8	51.8/48.2	52.0/48.0
Race*, %			
White	81.2	62.7	71.1
Asian	17.4	31.3	25.0
ECOG PS 0/1, %	36.2/63.8	19.3/80.7	27.0/73.0
Smoking history yes/no†, %	62.3/37.7	43.4/47.0	52.0/42.8
Histology‡, %			
Adenocarcinoma	84.1	88.0	86.2
Squamous	8.7	10.8	9.9
Brain metastases at baseline§, %	14.5	15.7	15.1

*Race was unknown or missing in 4 patients; 1 patient was Black/African American, and 1 patient was 'other'. †Smoking history was missing in 8 patients. ‡Two patients had adenosquamous histology (1 treatment naive and 1 previously treated), 3 patients had sarcomatoid (all treatment naive), and 1 patient had NSCLC-NOS (treatment naive). §Baseline brain metastases identified by IRC or investigator.
ECOG PS, Eastern Cooperative Oncology Group performance status; IRC, Independent Review Committee; NSCLC-NOS, non-small cell lung cancer – not otherwise specified.
Reference: Paik PK, et al. Presented at WCLC, 2020, Presentation MA11.05.

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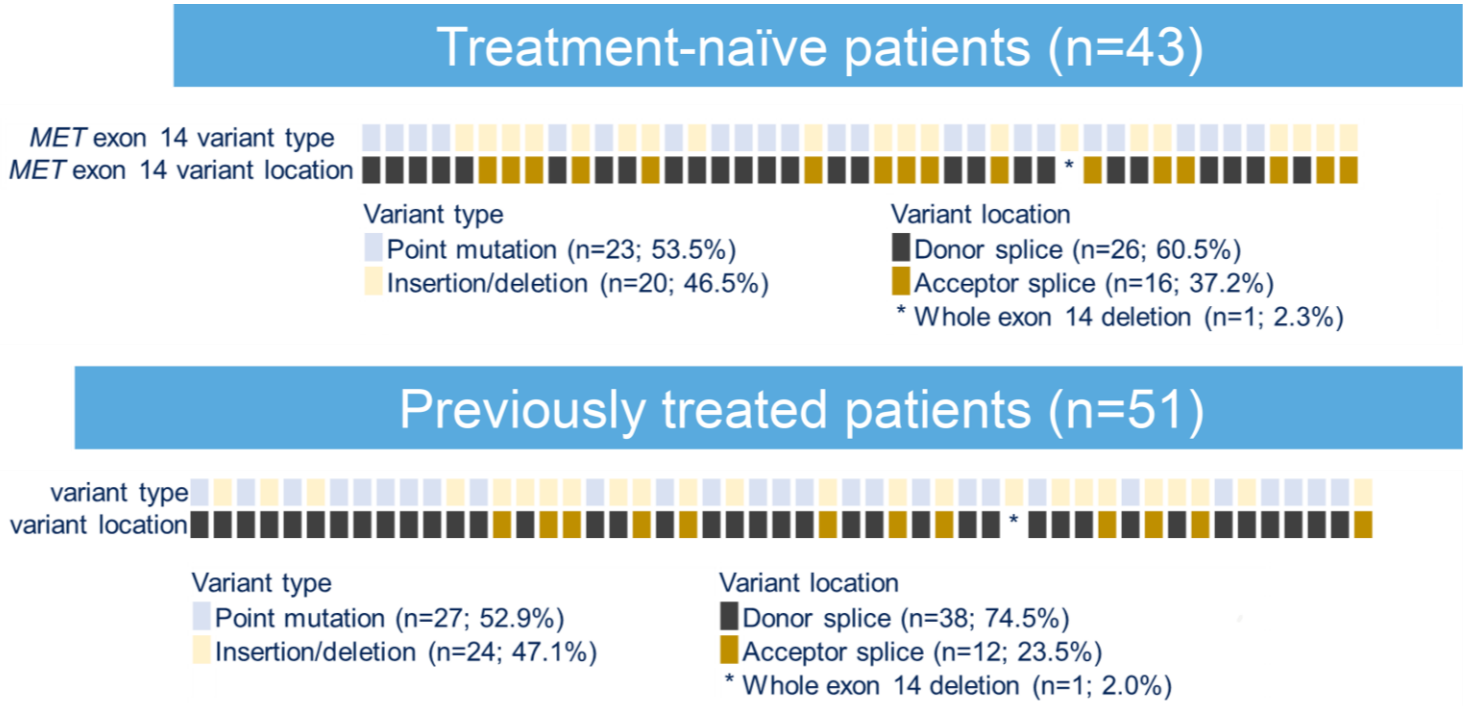
Mutational Profile at Baseline

Mutational profile of *MET*-skipping alterations



Mutational profile based on liquid biopsies indicated a balanced distribution between *MET* indels and point mutations, as well as donor and acceptor splice sites in both treatment-naive and previously treated patients

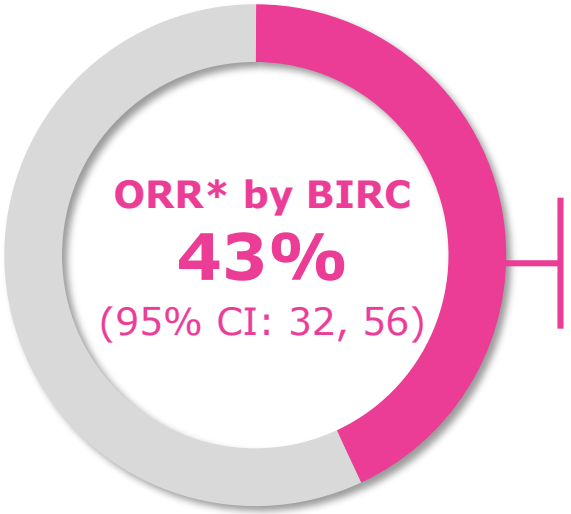
EGFR amplification occurred in 1/43 treatment-naive patients (2.3%) and 8/51 previously treated patients (15.7%)

EGFR, epidermal growth factor receptor gene; *MET*, mesenchymal-epithelial transition.

Reference: Paik PK, et al. Presented at ASCO Annual Meeting, 2021, Abstract 9012.

Efficacy by Previous Treatment Status

Treatment naive (n=69)

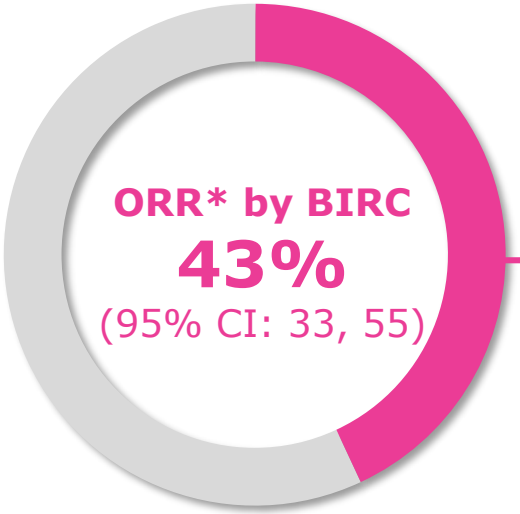


ORR* by BIRC
43%
(95% CI: 32, 56)

mDOR† by BIRC
10.8 mo
(95% CI: 6.9, NE)

Patients with DOR:
≥6 mo, 67%
≥9 mo, 30%

Previously treated (n=83)



ORR* by BIRC
43%
(95% CI: 33, 55)

mDOR† by BIRC
11.1 mo
(95% CI: 9.5, 18.5)

Patients with DOR:
≥6 mo, 75%
≥9 mo, 50%

*Confirmed responses. †Product-limit (Kaplan-Meier) estimates, 95% CI for the median using the Brookmeyer and Crowley method.
BIRC, Blinded Independent Review Committee; CI, confidence interval; DOR, duration of response; mDOR, median duration of response; mo, months; NE, not estimable; ORR, objective response rate.
Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

Physician-Evaluated Responses to Prior Therapies Among Previously Treated Patients

VISION Cohort A

July 2020 cut-off

	Most recent anticancer therapy (n=83)	Prior Pt-based CT (n=74)	Prior ICI + Pt-based CT (n=10)
Best response, n (%)			
Complete response	1 (1.2)	2 (2.7)	0
Partial response	20 (24.1)	19 (25.7)	3 (30.0)
Stable disease	25 (30.1)	22 (29.7)	1 (10.0)
Progressive disease	24 (28.9)	21 (28.4)	3 (30.0)
Non–complete response/non–progressive disease	1 (1.2)	1 (1.4)	0
Not assessable/unknown	12 (14.5)	9 (12.2)	3 (30.0)
DOR Patients for whom data are available Median longest DOR, months (range)	 n=16 4.5 (1–17)	 n=16 5.0 (1–17)	 n=2 6.5 (5–8)
PFS Patients for whom data are available Median longest PFS, months (range)	 n=59 4.0 (0–36)	 n=55 3.0 (0–26)	 n=5 2.0 (0–6)

Of the 83 previously treated patients, 21 had a documented OR to their most recent anticancer therapy

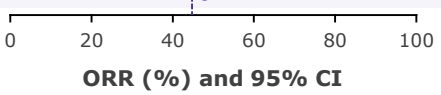
CT, chemotherapy; DOR, duration of response; ICI, immune checkpoint inhibitor; OR, objective response; PFS, progression-free survival; Pt, platinum.

Reference: Le X, et al. Clin Cancer Res. 2022;28(6):1117–1126.

EMD SERONO

ORR by Baseline Characteristics

Subgroup	n	ORR by IRC	
Overall	152	44.7	(36.7,53.0)
Sex			
Male	79	45.6	(34.3,57.2)
Female	73	43.8	(32.2,55.9)
Race			
Caucasian/White	108	42.6	(33.1,52.5)
Asian	38	50.0	(33.4,66.6)
ECOG PS			
0	41	56.1	(39.7,71.5)
1	111	40.5	(31.3,50.3)
Smoking history			
Yes	79	49.4	(37.9,60.9)
No	65	38.5	(26.7,51.4)
Histological subtype*			
Adenocarcinoma	131	48.1	(39.3,57.0)
Squamous	15	20.0	(4.3,48.1)
Other	6	33.3	(4.3,77.7)
Age			
<65 years	27	48.1	(28.7,68.1)
≥65 years	125	44.0	(35.1,53.2)
<75 years	84	48.8	(37.7,60.0)
≥75 years	68	39.7	(28.0,52.3)
<85 years	115	47.8	(38.4,57.3)
≥85 years	37	35.1	(20.2,52.5)
Lines of prior therapy for advanced/metastatic disease			
Treatment naive	69	44.9	(32.9,57.4)
Previously treated	83	44.6	(33.7,55.9)
1 line of prior therapy	49	44.9	(30.7,59.8)
≥2 lines of prior therapy	34	44.1	(27.2,62.1)
Prior therapies			
Pt-based CT	74	48.6	(36.9,60.6)
Also received ICI	29	41.4	(23.5,61.1)
As combination†	10	40.0	(12.2,73.8)
As single agent in a separate line†,‡	20	40.0	(19.1,63.9)
Brain metastases at baseline			
Present (by RECIST v1.1)	23	47.8	(26.8,69.4)



Overall, 57 of 68 responses (83.8%) were recorded at the first (6 weeks) or second (12 weeks) tumor assessments

*Of 15 patients with squamous-cell histology: 9 (60.0%) had a smoking history and 6 (40.0%) were never smokers; 7 were from the US (46.7%), 5 from Europe (33.3%), and 3 from Asia (20.0%). 'Other' histologies included sarcomatoid (n=3), adenosquamous (n=2), and NSCLC-NOS (n=1). †One patient received ICI as monotherapy and in combination with Pt-based CT and, as such, is included in both subgroups. ‡Patients could have received 1L Pt-based CT followed by 2L single-agent ICI, or vice versa.

1l, first line; 2L, second line; CI, confidence interval; CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; ICI, immune checkpoint inhibitor; IRC, Independent Review Committee; NSCLC-NOS, non-small cell lung cancer - not otherwise specified; ORR, objective response rate; Pt, platinum; RECIST, Response Evaluation Criteria in Solid Tumors.

Reference: Le X, et al. Clin Cancer Res. 2022;28(6):1117–1126.

Clinical Outcomes by the Type or Location of *MET*ex14 Skipping Alterations Assessed by Liquid Biopsy[1]

VISION Cohort A

July 2020 cut-off

Efficacy according to *MET*ex14 variant type	Insertion/deletion (n=44)		Point mutation (n=50)	
	IRC	Investigator	IRC	Investigator
ORR (95% CI), %	40.9 (26.3, 56.8)	47.7 (32.5, 63.3)	50.0 (35.5, 64.5)	54.0 (39.3, 68.2)
DOR, median (95% CI), months	8.4 (5.5, NE)	8.3 (5.3, NE)	9.9 (7.2, NE)	14.0 (9.7, NE)
PFS, median (95% CI), months	7.8 (4.1, 9.7)	6.7 (4.2, 9.5)	8.5 (5.7, 11.3)	8.3 (5.1, 11.1)

Efficacy according to *MET*ex14 variant location*	Donor splice (n=64)		Acceptor splice (n=28)	
	IRC	Investigator	IRC	Investigator
ORR (95% CI), %	46.9 (34.3, 59.8)	56.2 (43.3, 68.6)	46.4 (27.5,66.1)	42.9 (24.5, 62.8)
DOR, median (95% CI), months	9.9 (7.2, NE)	12.5 (7.2, NE)	9.5 (5.5, NE)	8.3 (4.2, NE)
PFS, median (95% CI), months	8.5 (6.7, 11.0)	8.3 (5.1, 11.0)	6.8 (3.0, 10.9)	5.8 (2.8, 9.7)

These data confirm previous observations from the VISION study, in a larger patient population[2]

*Whole exon 14 skipping was detected in 2 patients, who are therefore not included in analysis of efficacy according to *MET*ex14 variant location.
CI, confidence interval; DOR, duration of response; IRC, Independent Review Committee; *MET*, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NE, not estimable; ORR, objective response rate; PFS, progression-free survival.
References: 1. Paik PK, et al. Presented at ASCO Annual Meeting, 2021, Abstract 9012; **2.** Paik PK, et al. N Engl J Med. 2020;383(10):931–943.

EMD SERONO

Safety and Tolerability Profile of Tepotinib as Studied in 255 Patients

VISION Cohorts A + C

July 2020 cut-off

- Fatal ARs occurred in one patient (0.4%) due to pneumonitis, one patient (0.4%) due to hepatic failure, and one patient (0.4%) due to dyspnea from fluid overload
- Serious ARs occurred in 45% of patients who received tepotinib. Serious ARs 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%)

Permanent discontinuation due to an AR occurred in 20% of patients who received tepotinib

- The most frequent ARs (>1%) leading to permanent discontinuations of tepotinib were edema (5%), pleural effusion (2%), dyspnea (1.6%), general health deterioration (1.6%), and pneumonitis (1.2%)

Dosage interruptions due to an AR occurred in 44% of patients who received tepotinib

- ARs that required dosage interruption in >2% of patients who received tepotinib included edema (23%), increased blood creatinine (6%), pleural effusion (4.3%), increased ALT (3.1%), and pneumonia (2.4%)

Dose reductions due to an AR occurred in 30% of patients who received tepotinib

- ARs that required dose reductions in >2% of patients who received tepotinib included edema (19%), pleural effusion (2.7%), and increased blood creatinine (2.7%)

ALT, alanine aminotransferase; AR, adverse reaction.

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

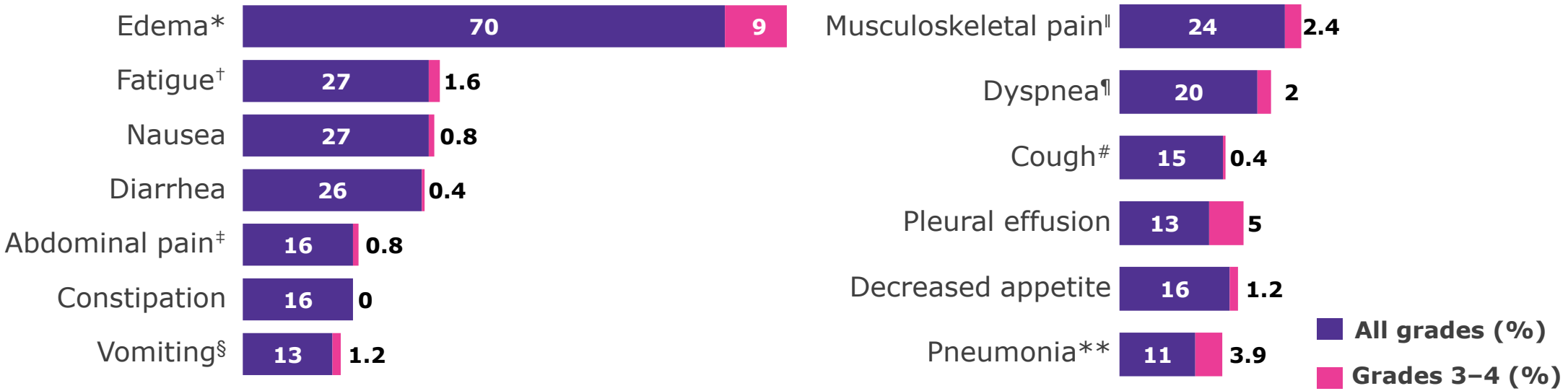
EMD SERONO

Safety and Tolerability Profile of Tepotinib as Studied in 255 Patients (continued)

VISION Cohorts A + C

July 2020 cut-off

ARs in ≥10% of patients with NSCLC with *MET*ex14 skipping alterations who received tepotinib in VISION (N=255)



Clinically relevant ARs in <10% of patients who received tepotinib included ILD/pneumonitis, rash, fever, dizziness, pruritus, and headache

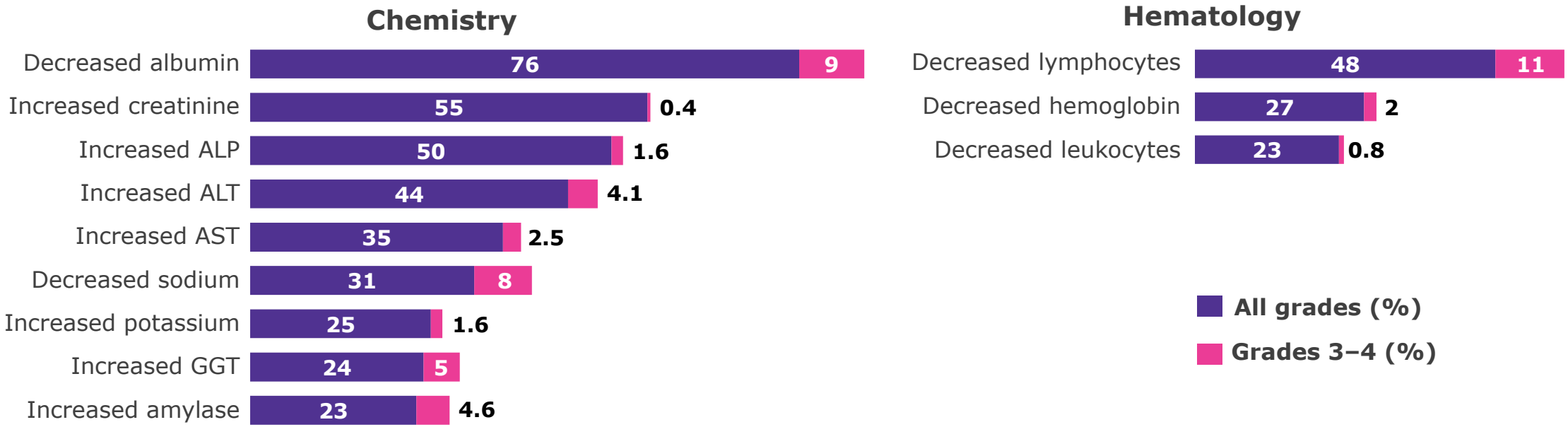
*Edema includes eye edema, face edema, generalized edema, localized edema, edema, genital edema, peripheral edema, peripheral swelling, periorbital edema, and scrotal edema. †Fatigue includes asthenia and fatigue. ‡Abdominal pain includes abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper, gastrointestinal pain, and hepatic pain. §Vomiting includes retching and vomiting. ‖Musculoskeletal pain includes arthralgia, arthritis, back pain, bone pain, musculoskeletal chest pain, musculoskeletal pain, myalgia, neck pain, non-cardiac chest pain, pain in extremity, and spinal pain. ¶Dyspnea includes dyspnea, dyspnea at rest, and dyspnea exertional. #Cough includes cough, productive cough, and upper-airway cough syndrome. **Pneumonia includes pneumonia, pneumonia aspiration, and pneumonia bacterial.
AR, adverse reaction; ILD, interstitial lung disease; *MET*ex14, *MET* exon 14.
Reference: TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

Safety and Tolerability Profile of Tepotinib as Studied in 255 Patients (continued)

VISION Cohorts A + C

July 2020 cut-off

Select laboratory abnormalities (≥20%) that worsened from baseline in patients who received tepotinib in VISION*



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

*The denominator used to calculate the rate varied from 207 to 246 based on the number of patients with a baseline value and at least one post-treatment value.
ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase.

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

EMD SERONO

Most Common (≥5%) TRAEs and TRAEs Leading to Dose Reduction/Interruption

VISION Cohorts A + C

July 2020 cut-off

TRAEs, n (%)	Tepotinib 500 mg* QD (N=255)	
	All grades	Grades 3–4
Any	220 (86.3)	62 (24.3)
Leading to dose reduction	71 (27.8)	NR
Leading to temporary interruption	90 (35.3)	NR
Leading to permanent interruption	27 (10.6)	NR
Reported in ≥5% of patients		
Peripheral edema	138 (54.1)	19 (7.5)
Nausea	51 (20.0)	1 (0.4)
Diarrhea	50 (19.6)	1 (0.4)
Blood creatinine increased	45 (17.6)	1 (0.4)
Hypoalbuminemia	37 (14.5)	6 (2.4)
ALT increased	22 (8.6)	5 (2.0)
Decreased appetite	21 (8.2)	1 (0.4)
Amylase increased	19 (7.5)	5 (2.0)
Fatigue	18 (7.1)	1 (0.4)
Alopecia	18 (7.1)	0
Lipase increased	17 (6.7)	7 (2.7)
Pleural effusion	16 (6.3)	8 (3.1)
Edema	16 (6.3)	0
AST increased	15 (5.9)	3 (1.2)
Constipation	15 (5.9)	0
Asthenia	14 (5.5)	1 (0.4)
Vomiting	14 (5.5)	1 (0.4)
Upper abdominal pain	14 (5.5)	0

- Most TRAEs were similar to the known safety profile for tepotinib

Peripheral edema was the most common TRAE leading to **dose reduction** (14.1%) or **permanent discontinuation** (3.5%)

Peripheral edema led to **dose interruption** in 16.1% of patients

Peripheral edema can be considered a class effect of MET TKIs and should be proactively managed

*500 mg tepotinib refers to 500 mg tepotinib hydrochloride hydrate, which is equivalent to 450 mg tepotinib (the active moiety).
ALT, alanine aminotransferase; AST, aspartate aminotransferase; MET, mesenchymal-epithelial transition; NR, not reported; QD, once daily; TKI, tyrosine kinase inhibitor; TRAE, treatment-related adverse event.
Reference: Le X, et al. Clin Cancer Res. 2022;28(6):1117–1126.

EMD SERONO

AEs of Clinical Interest

AEs (all cause) of clinical interest, n (%)	Overall N=255		
	All grades	Grade 3	Grade 4
Edema (composite term)	178 (69.8)	24 (9.4)	0
Peripheral edema	153 (60.0)	20 (7.8)	0
Edema	18 (7.1)	0	0
Generalized edema	13 (5.1)	5 (2.0)	0
Face edema	7 (2.7)	0	0
Localized edema	6 (2.4)	1 (0.4)	0
Genital edema	6 (2.4)	3 (1.2)	0
Periorbital edema	2 (0.8)	0	0
Scrotal edema	2 (0.8)	0	0
Peripheral swelling	1 (0.4)	0	0
Gastrointestinal AEs of clinical interest	–	–	–
Nausea	68 (26.7)	2 (0.8)	0
Diarrhea	67 (26.3)	1 (0.4)	0
Vomiting	33 (12.9)	3 (1.2)	0
Creatinine increase (composite term)	66 (25.9)	1 (0.4)	0
Blood creatinine increased	64 (25.1)	1 (0.4)	0
Hypercreatininemia	2 (0.8)	0	0

Tepotinib dosing recommendations for AEs of clinical interest:

- Grade 2: Maintain dose level. If intolerable, consider withholding tepotinib until resolved, then resume at a reduced dose
- Grade 3: Withhold tepotinib until resolved, then resume at a reduced dose
- Grade 4: Permanently discontinue tepotinib

AE, adverse event.

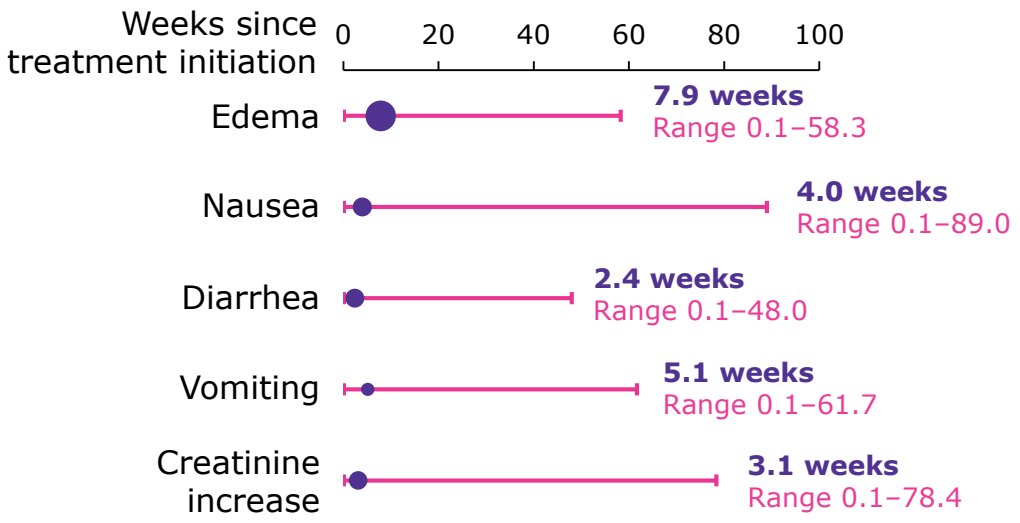
Reference: Veillon R, et al. Presented at WCLC, 2020, Abstract 821.

AEs of Clinical Interest: Time to First Onset and Resolution

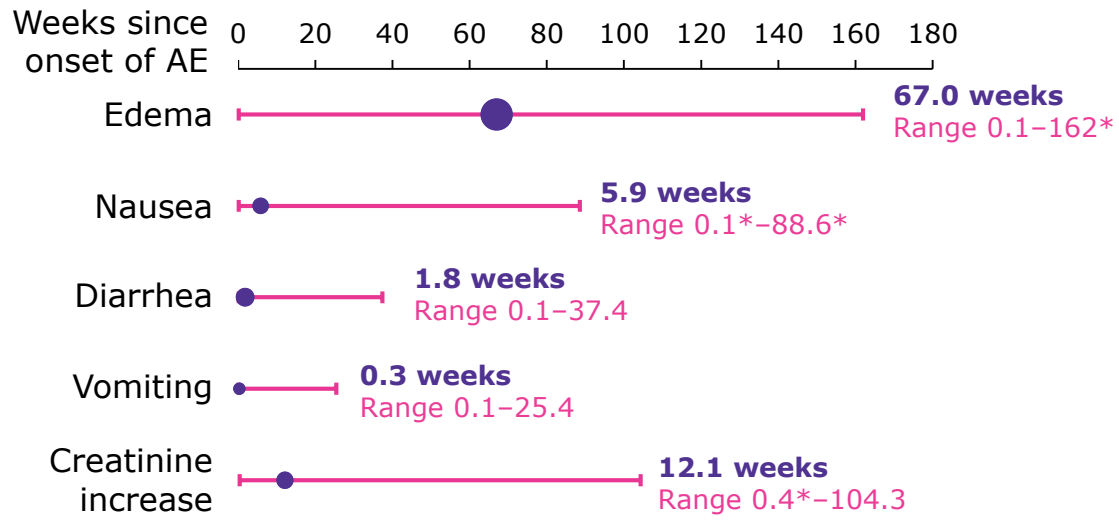
VISION Cohorts A + C

July 2020 cut-off

Median time to first onset



Median time to resolution



AE (patients with ≥1 event)	Edema (n=178)	Nausea (n=68)	Diarrhea (n=67)	Vomiting (n=33)	Creatinine increase (n=66)
Total events	337	87	112	47	96
Events resolved at time of analysis	115	67	102	44	67

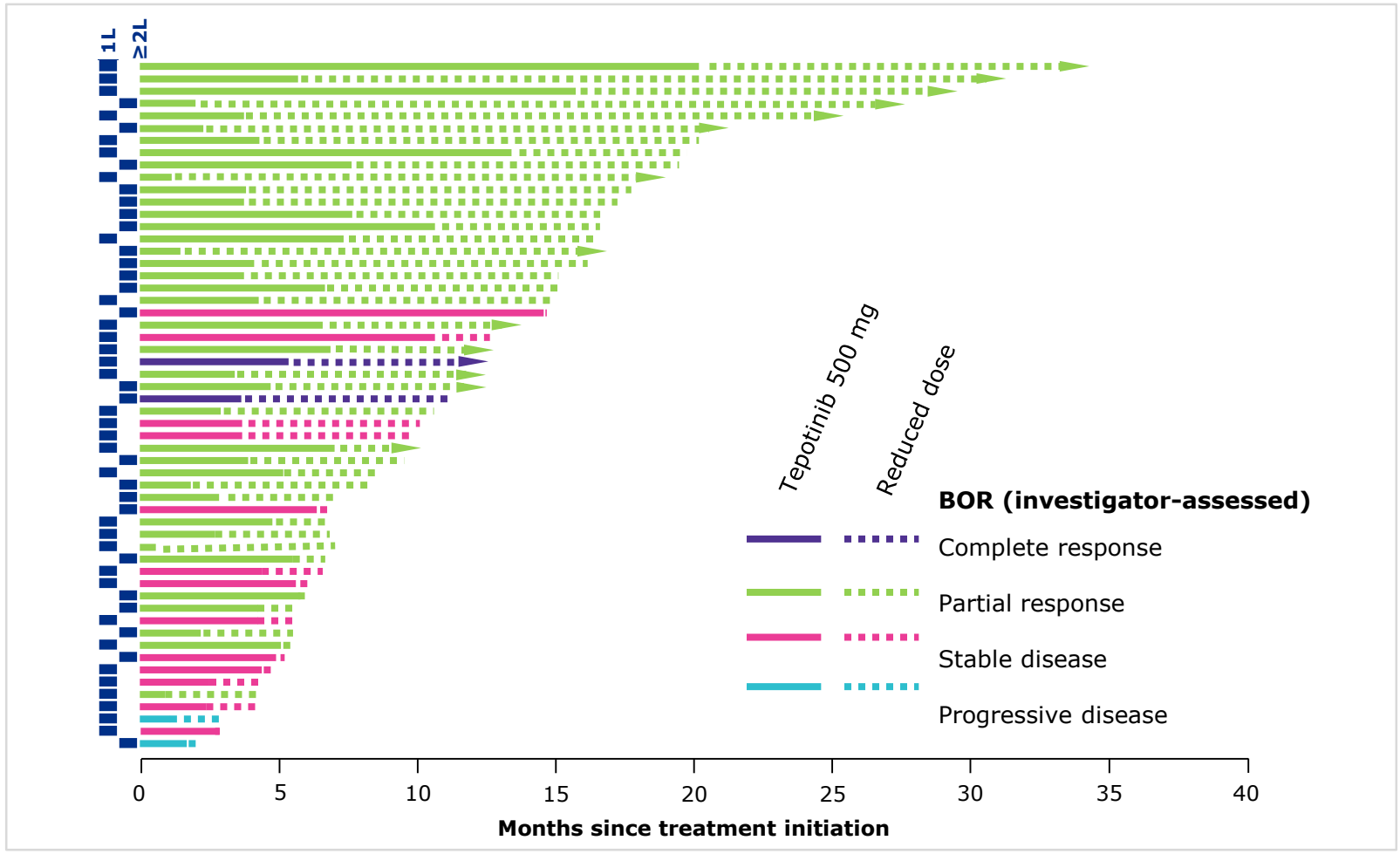
Analyses of time to first onset and time to resolution were carried out for AEs of clinical interest, including composite categories comprising preferred terms, and were analyzed irrespective of causal relation to study treatment. Time to first onset was described by median and range for observed AEs, not accounting for competing events. Time to resolution was analyzed using Kaplan–Meier methods in a descriptive manner, not accounting for the fact that one patient could contribute by more than one event of the respective AE.

*Denotes a censored value.

AE, adverse event.

Reference: Veillon R, et al. Presented at WCLC, 2020, Abstract 821.

Dose Reductions Yield Comparable Efficacy



Only patients with dose reductions are shown (n=56).
1L, first line; ≥2L, second line or greater; AE, adverse event; BOR, best objective response.
Reference: Le X, et al. Clin Cancer Res. 2022;28(6):1117–1126.

CONFIRMATORY COHORT C

Baseline Characteristics

- Patients in the confirmatory Cohort C had a median age of 71 years, about half were male, about half had smoking history, and most had adenocarcinoma histology

Baseline characteristics		Cohort C (N=161)	Cohort A (N=152)
Median age, years (range)		71.0 (42.0–91.0)	73.1 (41.0–94.0)
Sex, %	Male	46.6	52.0
Race, %	White/Asian	54.0/42.2	71.1/25.0
ECOG PS, %	0/1	24.8/74.5	27.0/73.0
Smoking history, %	Yes	43.5	52.0
Histology, %	Adenocarcinoma	75.2	86.2
Brain metastases at baseline, %	Yes	21.1	15.1
Line of therapy, %	Treatment-naive/previously treated	59.0/41.0	45.4/54.6
***MET*ex14 skipping detection,* %**	T+/L+	74.5/49.1	57.9/65.1

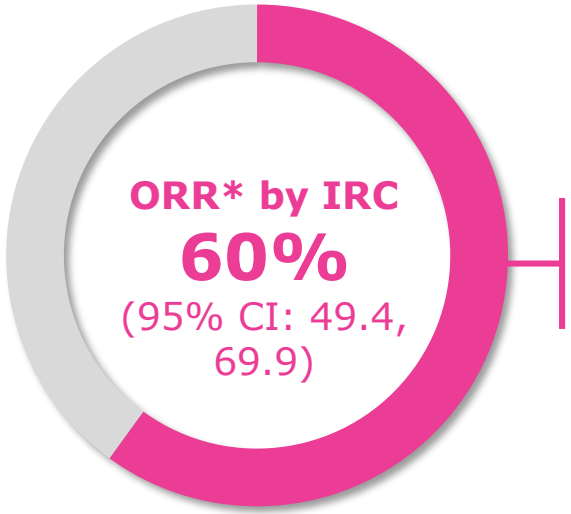
*Patients could have had *MET*ex14 skipping detected by both liquid and tissue biopsy and, as such, values do not add up to 100%; testing by both methods was not a requirement for study entry.
ECOG PS, Eastern Cooperative Oncology Group performance status; L+, *MET*ex14 skipping detected in liquid biopsy; *MET*ex14, *MET* exon 14; T+, *MET*ex14 skipping detected in tissue biopsy.
Reference: Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05.

VISION Cohort C

Feb 2022 cut-off

Efficacy by Previous Treatment Status

Treatment naive (n=95)



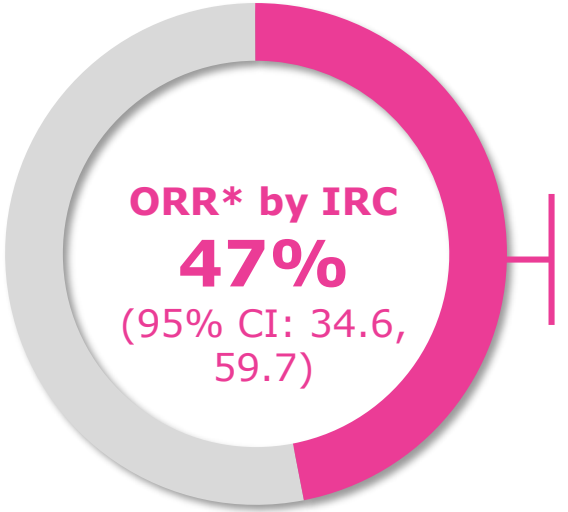
ORR* by IRC
60%
(95% CI: 49.4, 69.9)

mDOR† by BIRC
NE
(95% CI: 13.4, NE)

mPFS
15.9 mo
(95% CI: 10.4, NE)

mOS
21.1 mo
(95% CI: 12.7, NE)

Previously treated (n=66)



ORR* by IRC
47%
(95% CI: 34.6, 59.7)

mDOR† by BIRC
12.6 mo
(95% CI: 5.1, NE)

mPFS
12.1 mo
(95% CI: 6.9, NE)

mOS
18.8 mo
(95% CI: 13.5, NE)

*Confirmed responses. †Product-limit (Kaplan-Meier) estimates, 95% CI for the median using the Brookmeyer and Crowley method.
IRC, Independent Review Committee; CI, confidence interval; DOR, duration of response; mDOR, median duration of response; mo, months; NE, not estimable; ORR, objective response rate.
Reference: Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05.

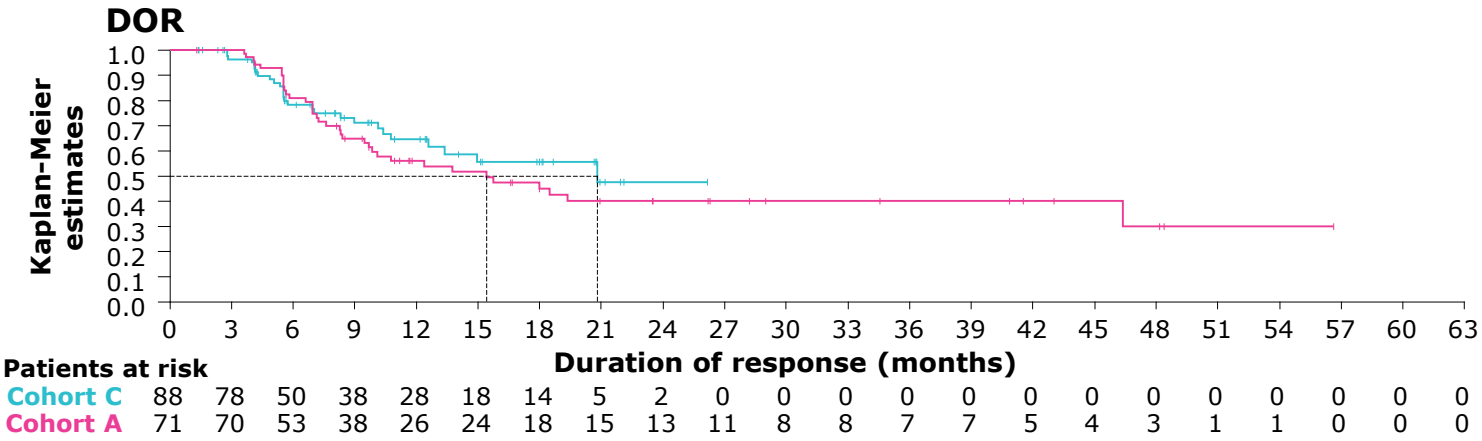
Overall Efficacy in Confirmatory Cohort

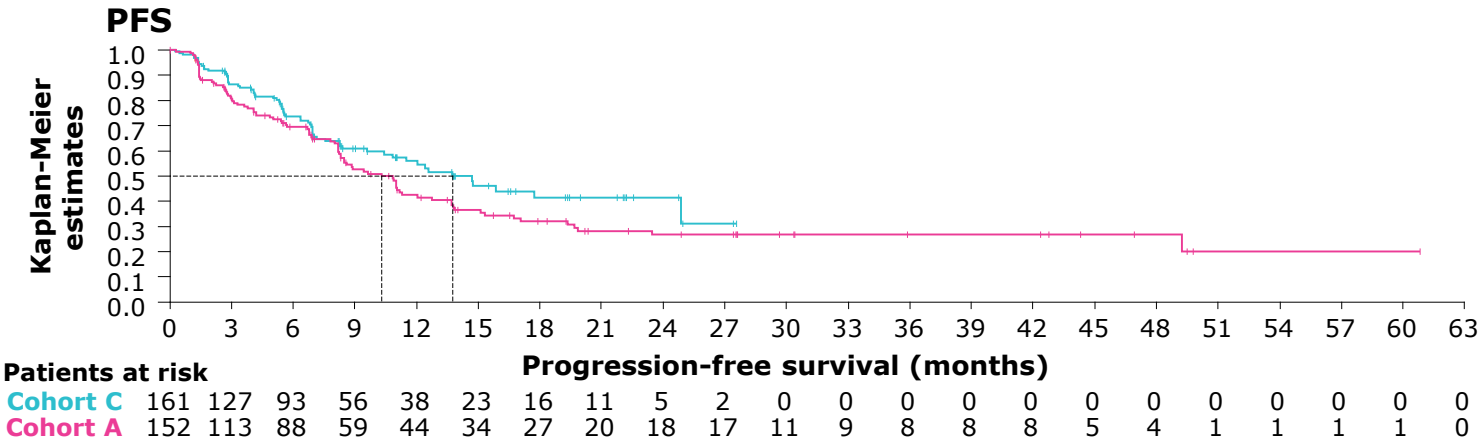
VISION Cohort C

Feb 2022 cut-off

- Cohort C primary analysis provided independent confirmation of efficacy for tepotinib

	Cohort C (N=161)	Cohort A (N=152)
ORR, % (95% CI)	54.7 (46.6, 62.5)	46.7 (38.6, 55.0)
DCR, % (95% CI)	80.1 (73.1, 86.0)	72.4 (64.5, 79.3)
mDOR, months (95% CI)	20.8 (12.6, NE)	15.4 (9.7, 46.4)
mPFS, months (95% CI)	13.8 (10.4, NE)	10.3 (8.2, 12.7)
mOS, months (95% CI)	18.8 (14.4, 25.5)	19.8 (15.2, 22.9)





CI, confidence interval; DCR, disease control rate; DOR, duration of response; m, median; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

Reference: Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05.

Efficacy by Line of Therapy

- Cohort C demonstrated efficacy across therapy lines

	1L* (T+ and/or L+)		2L+ (T+ and/or L+)	
	Cohort C (n=95)	Cohort A (n=69)	Cohort C (n=66)	Cohort A (n=83)
ORR, % (95% CI)	60.0 (49.4, 69.9)	50.7 (38.4, 63.0)	47.0 (34.6, 59.7)	43.4 (32.5, 54.7)
mDOR, months (95% CI)	NE (13.4, NE)	46.4 (7.2, NE)	12.6 (5.1, NE)	12.4 (8.4, 18.5)
mPFS, months (95% CI)	15.9 (10.4, NE)	10.3 (8.0, 15.3)	12.1 (6.9, NE)	10.9 (8.2, 12.7)
mOS, months (95% CI)	21.1 (12.7, NE)	19.1 (9.9, 25.9)	18.8 (13.5, NE)	19.8 (15.0, 22.3)

*1L enrollment began approximately 8 months later than 2L+.
1L, first line; 2L+, second-or-later line; CI, confidence interval; DOR, duration of response; L+, *MET*ex14 skipping detected in liquid biopsy; m, median; *MET*ex14, *MET* exon 14; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; T+, *MET*ex14 skipping detected in tissue biopsy.

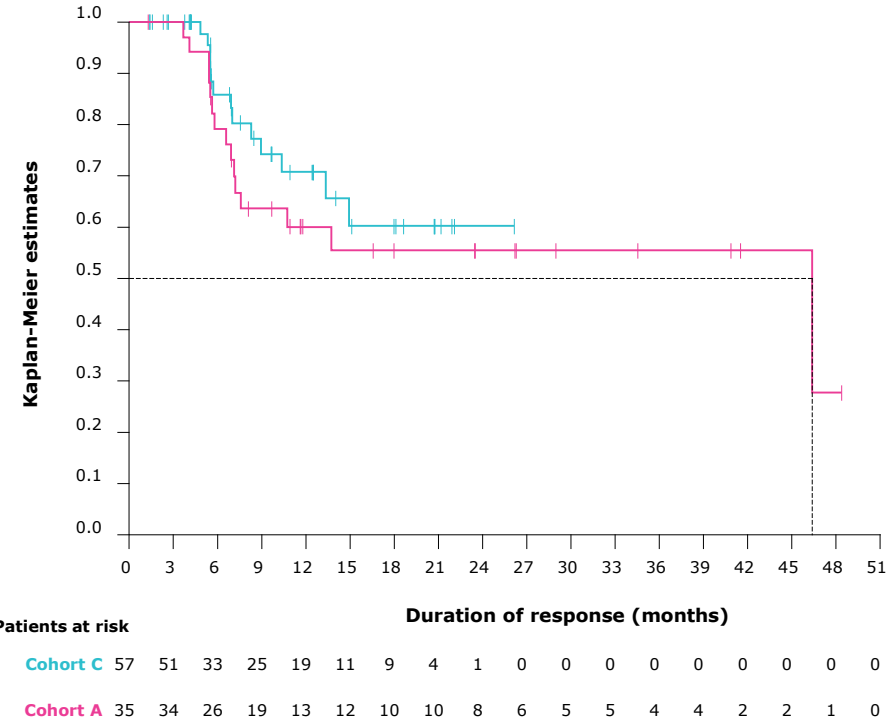
Reference: Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05.

Efficacy by Line of Therapy (DOR)

- Cohort C demonstrated efficacy across therapy lines

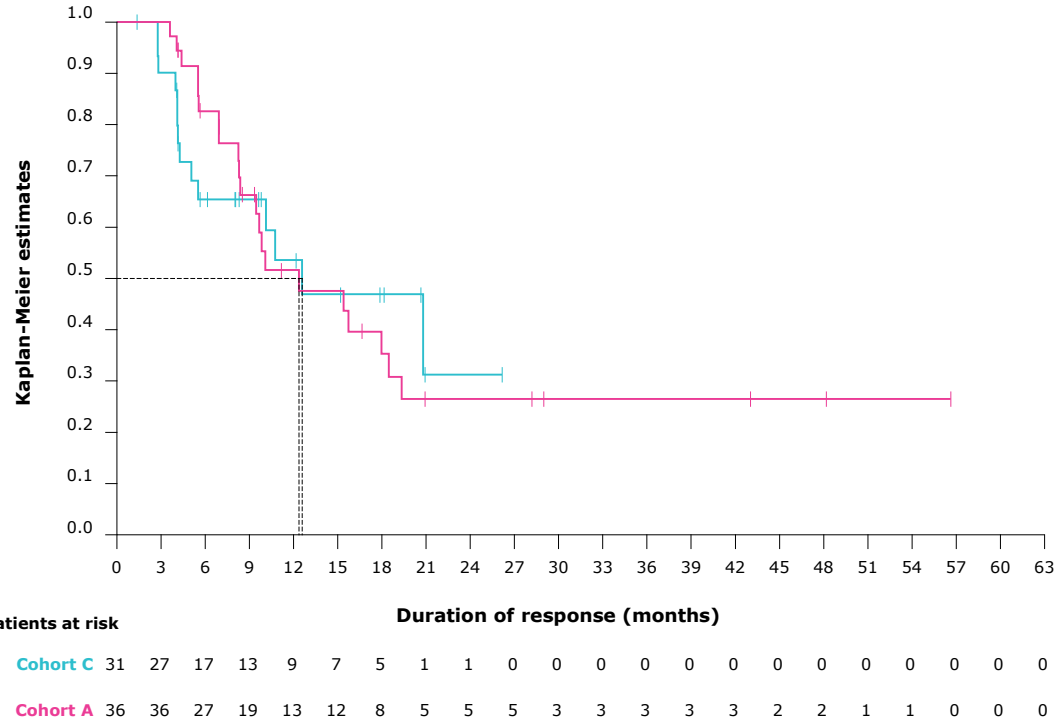
DOR

1L*



Patients at risk																		
Cohort C	57	51	33	25	19	11	9	4	1	0	0	0	0	0	0	0	0	0
Cohort A	35	34	26	19	13	12	10	10	8	6	5	5	4	4	2	2	1	0

2L+



Patients at risk																						
Cohort C	31	27	17	13	9	7	5	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Cohort A	36	36	27	19	13	12	8	5	5	5	3	3	3	3	3	2	2	1	1	0	0	0

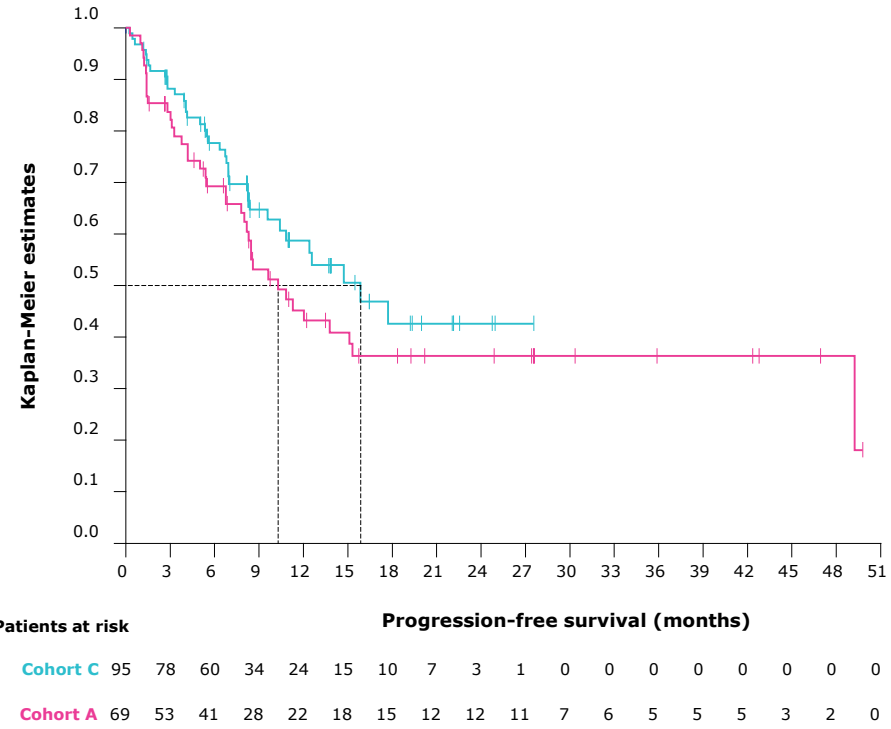
*1L enrollment began approximately 8 months later than 2L+.
1L, first line; 2L+, second-or-later line; DOR, duration of response.
Reference: Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05.

Efficacy by Line of Therapy (PFS)

- Cohort C demonstrated efficacy across therapy lines

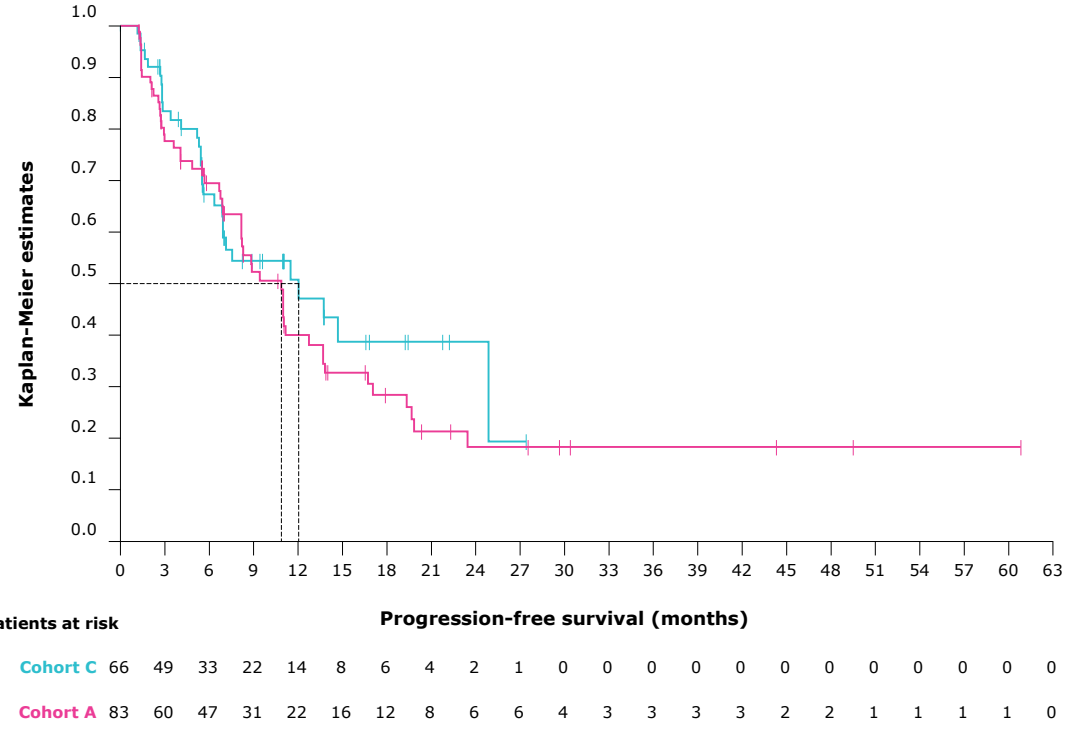
PFS

1L*



Patients at risk																		
Cohort C	95	78	60	34	24	15	10	7	3	1	0	0	0	0	0	0	0	0
Cohort A	69	53	41	28	22	18	15	12	12	11	7	6	5	5	5	3	2	0

2L+



Patients at risk																							
Cohort C	66	49	33	22	14	8	6	4	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Cohort A	83	60	47	31	22	16	12	8	6	6	4	3	3	3	3	2	2	1	1	1	1	1	0

*1L enrollment began approximately 8 months later than 2L+.
1L, first line; 2L+, second-or-later line; PFS, progression-free survival.
Reference: Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05.

COHORTS A+C: UPDATED EFFICACY AND SAFETY DATA (FEBRUARY 2022)

Due to the single-arm design of the VISION Trial for TEPMETKO, no formal statistical comparisons were conducted, and data, including PFS and OS, were analyzed in a descriptive manner. For these reasons, results from this analysis should be interpreted with caution.

Baseline Characteristics

- VISION comprises a large population of elderly patients with NSCLC harboring *MET*ex14 skipping

Baseline characteristics		Treatment-naive (n=164)	Previously treated (n=149)
Median age, years (range)		74.0 (47–94)	70.8 (41–89)
Sex, %	Male	50.6	47.7
	Female	49.4	52.3
Race*, %	White	68.3	55.7
	Asian	30.5	37.6
ECOG PS, %	0	27.4	24.2
	1	72.0	75.8
Smoking history†, %	Yes	53.7	40.9
	No	45.7	53.0
Histology, adenocarcinoma, %		79.9	81.2
Enrolled in Europe, %		53.7	43.0
***MET*ex14 skipping detection, %**	TBx	67.7	65.1
	LBx	57.9	55.7

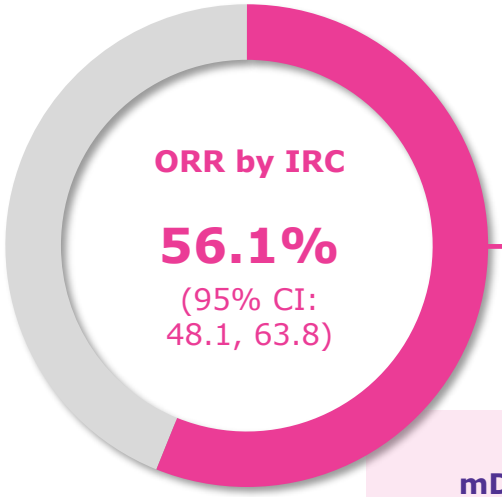
*Race was missing/not collected at the study site for eight patients, three patients were Black/African American, and one patient was recorded as 'other'. †Smoking history was missing in 10 patients.
ECOG PS, Eastern Cooperative Oncology Group performance status; *MET*, mesenchymal-epithelial transition factor; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer.
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Efficacy by Previous Treatment Status

VISION Cohorts A + C

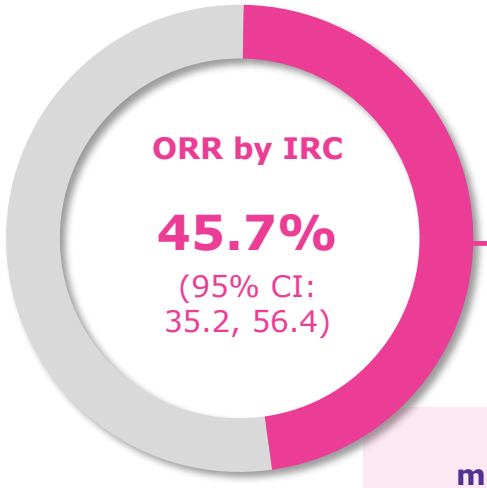
Feb 2022 cut-off

Treatment naive (n=164)



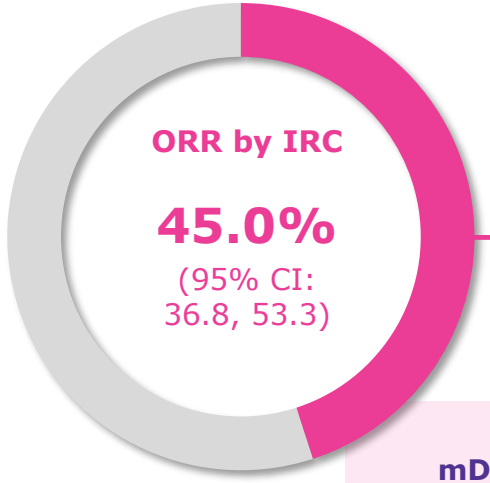
mDOR by IRC
46.4 mo
(95% CI: 13.8, NE)
mPFS
12.6 mo
(95% CI: 9.6, 17.7)
mOS
19.1 mo
(95% CI: 13.7, 23.7)

Previously treated, 2L only (n=92)



mDOR by IRC
12.6 mo
(95% CI: 8.3, 20.8)
mPFS
10.9 mo
(95% CI: 8.2, 13.8)
mOS
20.0 mo
(95% CI: 15.8, 23.7)

Previously treated (n=149)



mDOR by IRC
12.4 mo
(95% CI: 9.5, 18.5)
mPFS
11.0 mo
(95% CI: 8.2, 13.7)
mOS
19.6 mo
(95% CI: 15.2, 22.3)

1L, first line; 2L, second line; 2L+, second-or-later line; CI, confidence interval; DOR, duration of response; IRC, Independent Review Committee; m, median; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

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

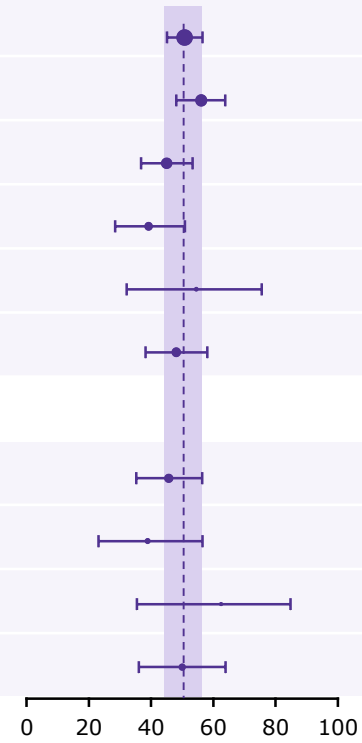
Efficacy by Prior Therapy in Previously Treated Patients (ORR)

VISION Cohorts A + C

Feb 2022 cut-off

- ORR for 2L patients who received CT alone as 1L was 50.0% (95% CI: 36.1, 63.9), IO + CT was 62.5% (35.4, 84.8) and IO was 38.9% (23.1, 56.5)

Tepotinib efficacy		Overall (N=313)	
		n	ORR, % (95% CI)
Overall		313	50.8 (45.1, 56.5)
Treatment-naive		164	56.1 (48.1, 63.8)
Previously treated: 2L+		149	45.0 (36.8, 53.3)
Prior therapy	IO*	79	39.2 (28.4, 50.9)
	IO + CT	22	54.5 (32.2, 75.6)
	CT	104	48.1 (38.2, 58.1)
Previously treated: 2L only		92	45.7 (35.2, 56.4)
Prior therapy	IO*	36	38.9 (23.1, 56.5)
	IO + CT	16	62.5 (35.4, 84.8)
	CT	54	50.0 (36.1, 63.9)



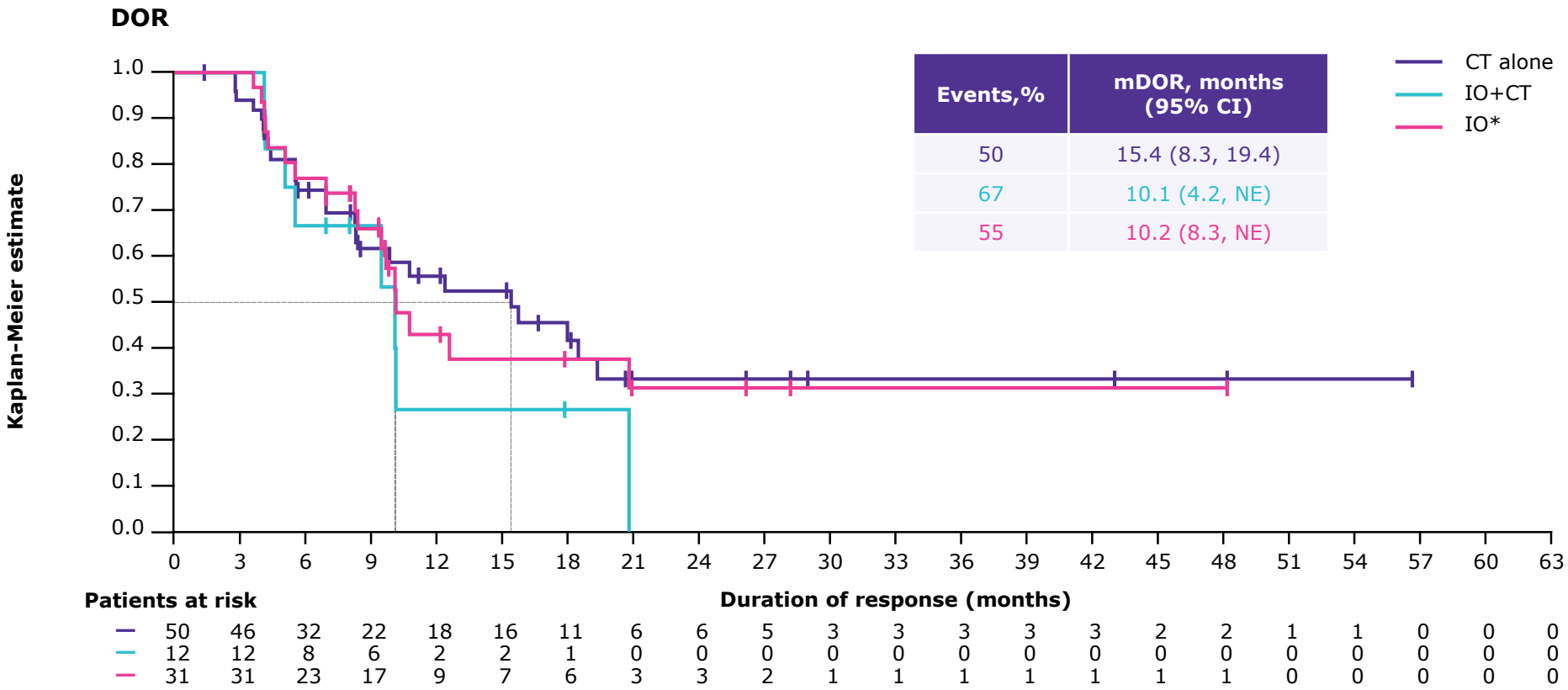
*Patients received IO monotherapy or IO + platinum-based CT.
1L, first line; 2L, second line; 2L+, second-or-later line; CI, confidence interval; CT, chemotherapy; IO, immunotherapy; ORR, objective response rate.
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Efficacy by Prior Therapy in Previously Treated Patients (DOR)

VISION Cohorts A + C

Feb 2022 cut-off

- In patients with prior CT alone, mDOR was 15.4 months; in patients with prior IO + CT, mDOR was 10.1 months



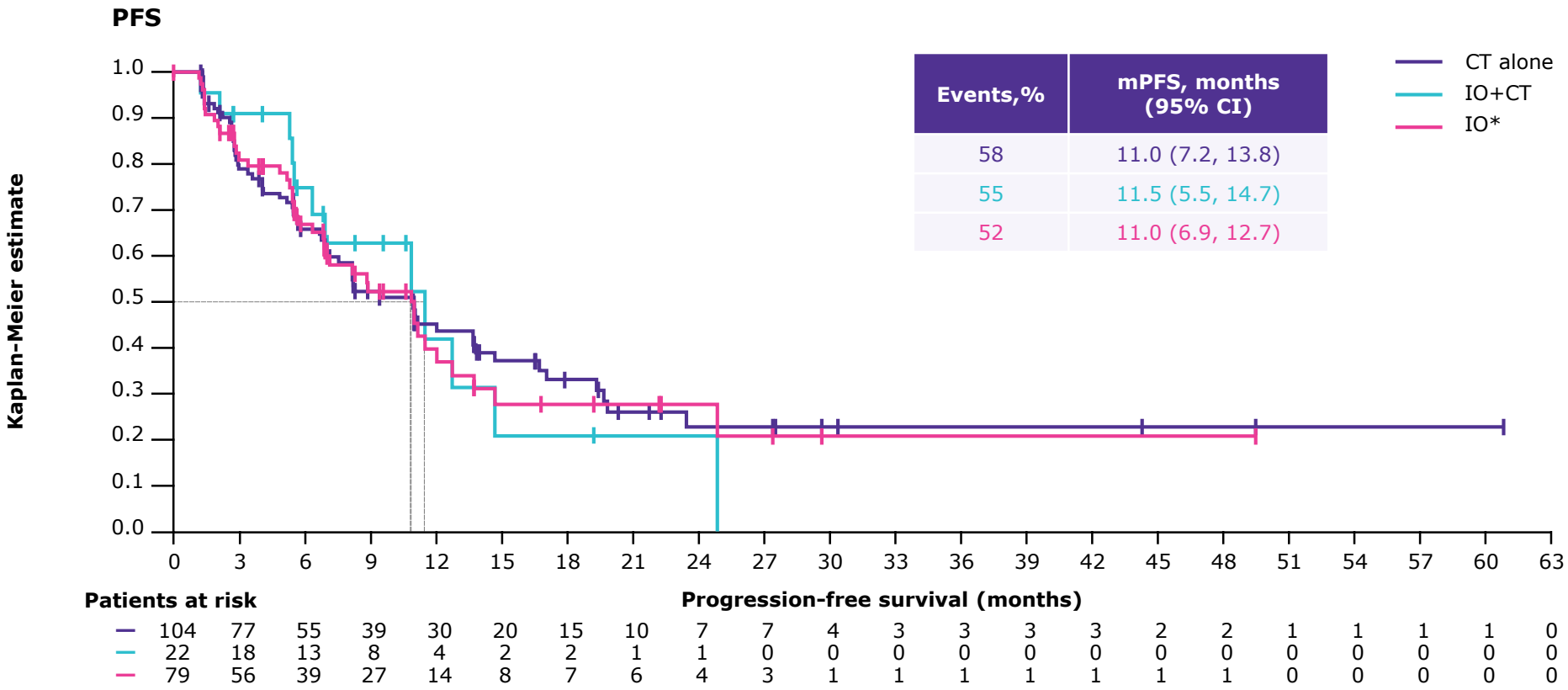
*Patients received IO monotherapy or IO + platinum-based CT.
CI, confidence interval; CT, chemotherapy; DOR, duration of response; IO, immunotherapy; m, median; NE, not estimable.
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Efficacy by Prior Therapy in Previously Treated Patients (PFS)

VISION Cohorts A + C

Feb 2022 cut-off

- In patients with prior CT alone, mPFS was 11.0 months; in patients with prior IO + CT, mPFS was 11.5 months.



Events,%	mPFS, months (95% CI)
58	11.0 (7.2, 13.8)
55	11.5 (5.5, 14.7)
52	11.0 (6.9, 12.7)

Patients at risk

104	77	55	39	30	20	15	10	7	7	4	3	3	3	3	2	2	1	1	1	1	0
22	18	13	8	4	2	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
79	56	39	27	14	8	7	6	4	3	1	1	1	1	1	1	1	0	0	0	0	0

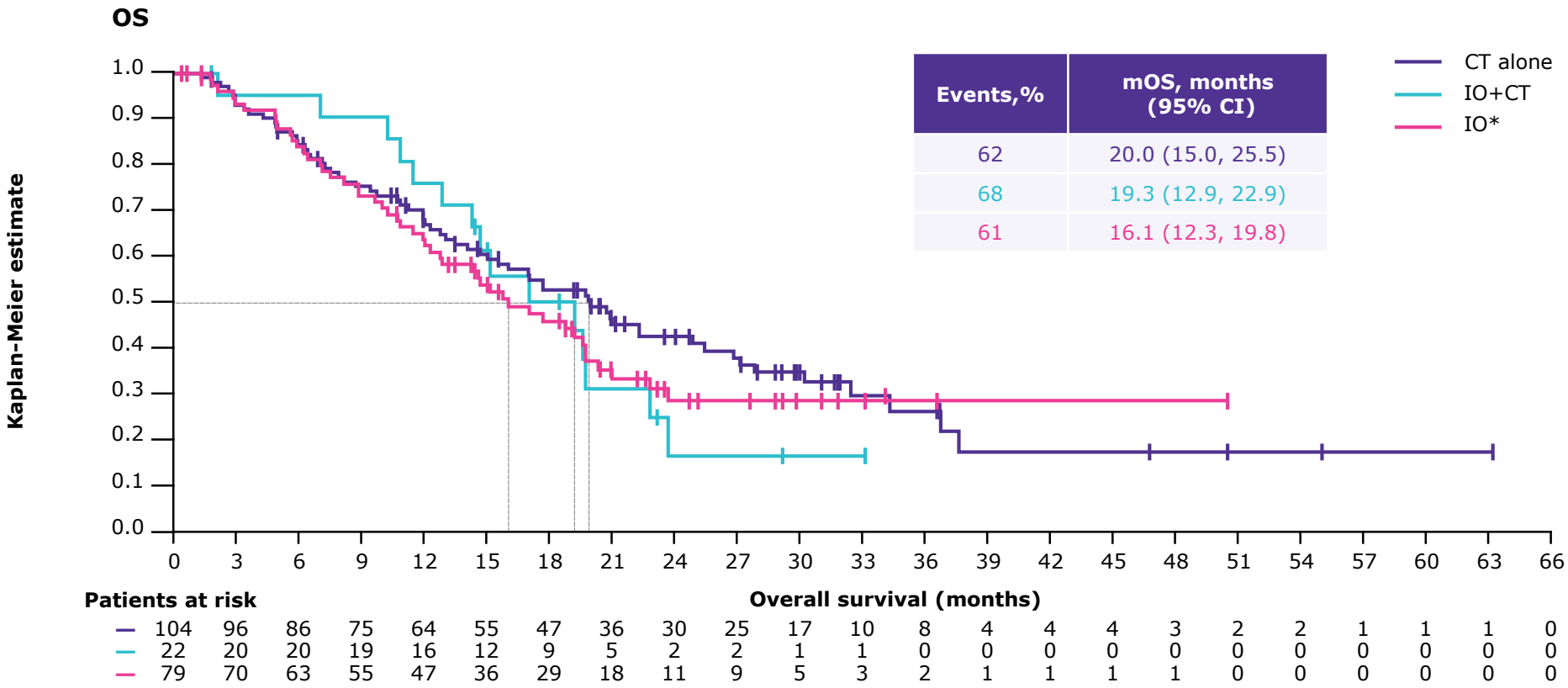
*Patients received IO monotherapy or IO + platinum-based CT.
CI, confidence interval; CT, chemotherapy; IO, immunotherapy; m, median; PFS, progression-free survival.
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Efficacy by Prior Therapy in Previously Treated Patients (OS)

VISION Cohorts A + C

Feb 2022 cut-off

- In patients with prior CT alone, mOS was 20.0 months; in patients with prior IO + CT, mOS was 19.3 months

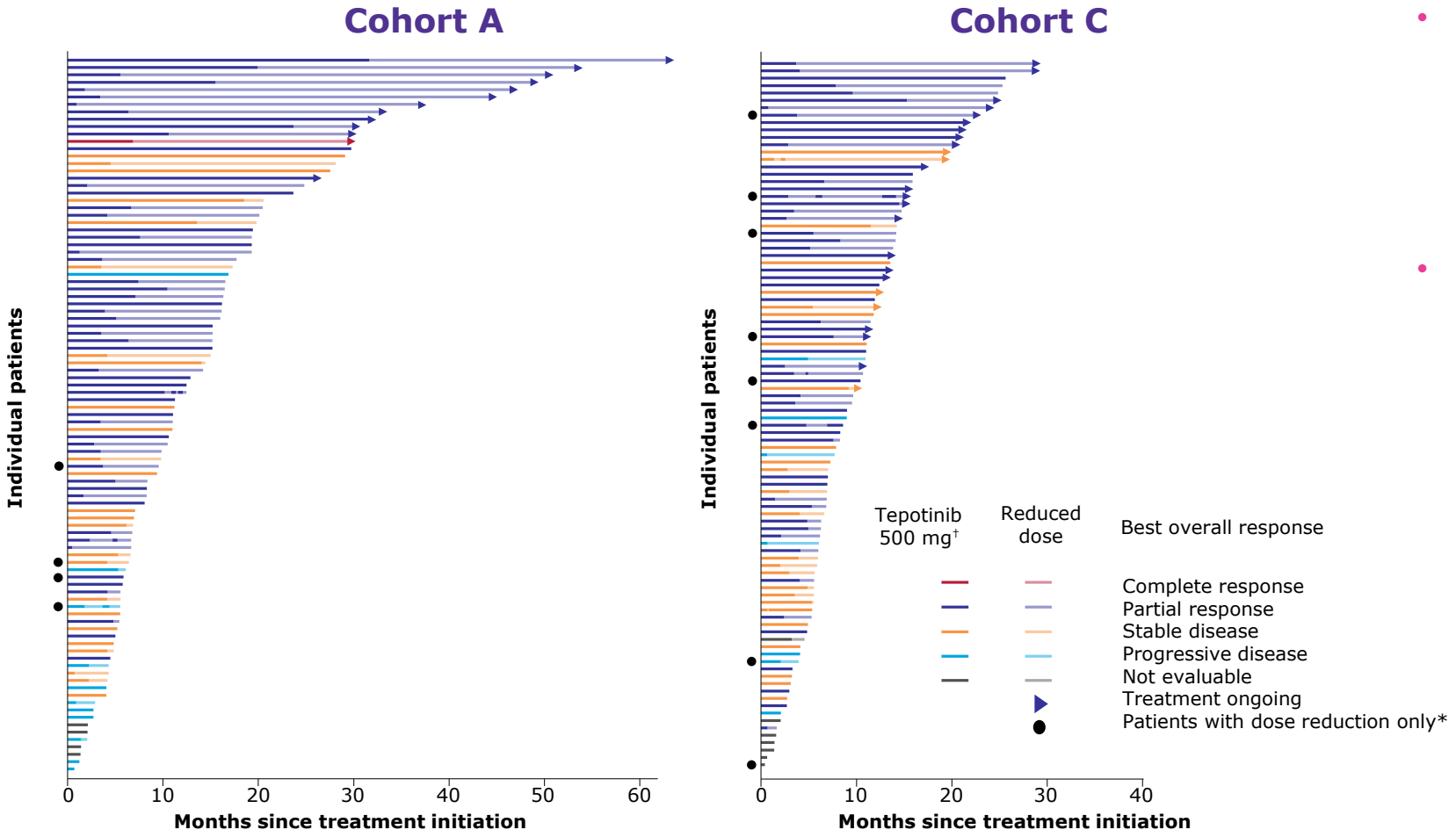


*Patients received IO monotherapy or IO + platinum-based CT.
CI, confidence interval; CT, chemotherapy; IO, immunotherapy; m, median; OS, overall survival.
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Time on Treatment in Patients With Dose Reductions or Interruptions

VISION Cohorts A + C

Feb 2022 cut-off



- Duration of tepotinib treatment across all patients in Cohort A+C (N=313) was:
  - Mean ± SD: 10.35 months ± 9.64
  - Median (range): 7.5 months (0.03–63.2)
  - 48 patients (15.3%) were still receiving treatment
- Duration of tepotinib treatment in patients across Cohort A+C with dose reductions and/or interruption (n=192) was:
  - Mean ± SD: 12.78 months ± 10.46
  - Median (range): 10.5 months (0.7–63.2)
  - 39 patients (20.3%) were still receiving treatment

*Patients indicated with a black circle had no treatment interruptions, patients indicated with solid lines only had no dose reductions, and all other patients had both treatment interruptions and dose reductions. †450 mg active moiety.
SD, standard deviation.

Reference: Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05.

Most Common TRAEs and AEs of Clinical Interest

VISION Cohorts A + C

Feb 2022 cut-off

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

*Safety population comprised all patients from VISION Cohorts A and C.
AE, adverse event; ALT, alanine transaminase; TRAE, treatment-related adverse event.
Reference: Thomas M, et al. Presented at WCLC, 2022, Abstract OA03.05.

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TRAE by Line 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)

- Overall (N=313), TRAEs occurred in 91.7% of patients, 34.2% had Grade ≥3 TRAEs, and 14.7% discontinued due to TRAEs
- 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

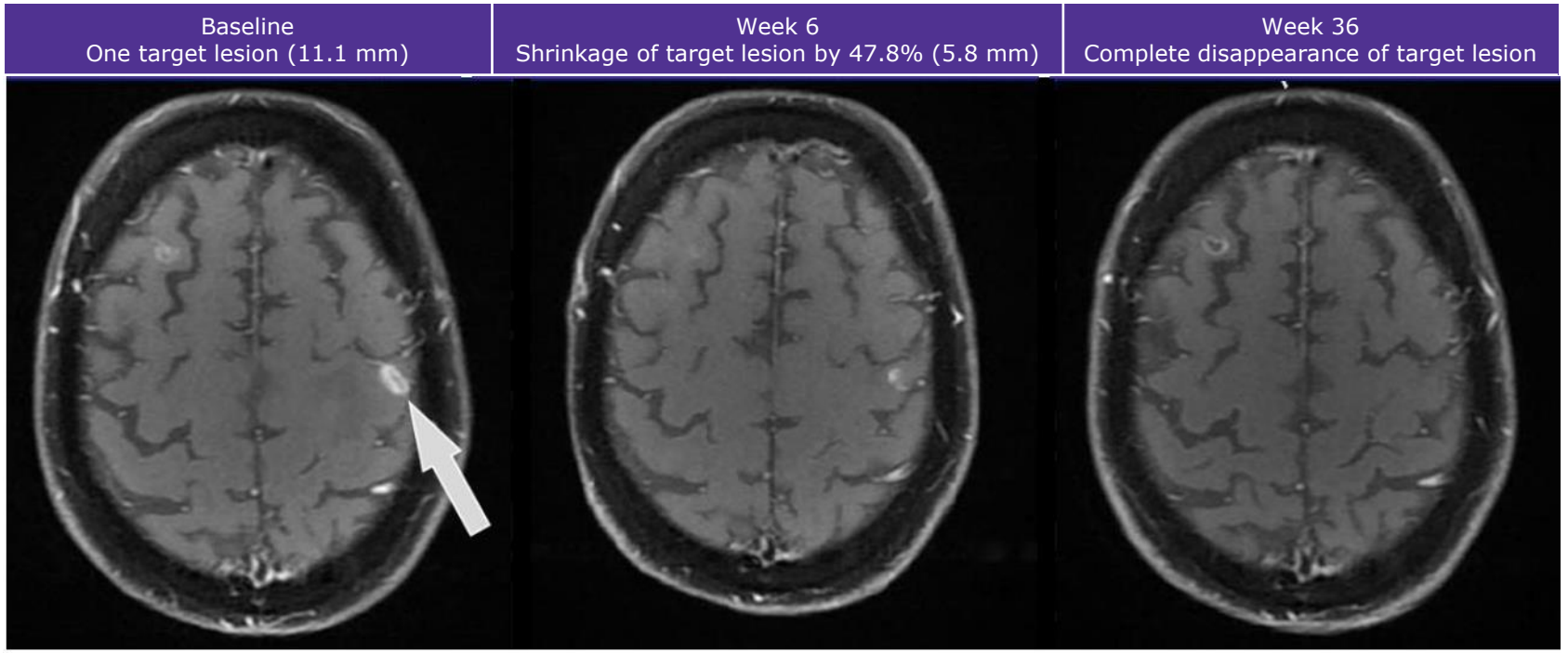
AE, adverse event; IO, immunotherapy; TRAE, treatment-related adverse event.

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

ACTIVITY IN PATIENTS WITH BRAIN METASTASES

Analyses in Patients With Brain Metastases

- An explorative ad hoc retrospective analysis was conducted using RANO-BM criteria on Cohort A (n=23 patients enrolled with brain metastases)



MRI* images showing intracranial response to tepotinib in target lesion per RANO-BM criteria

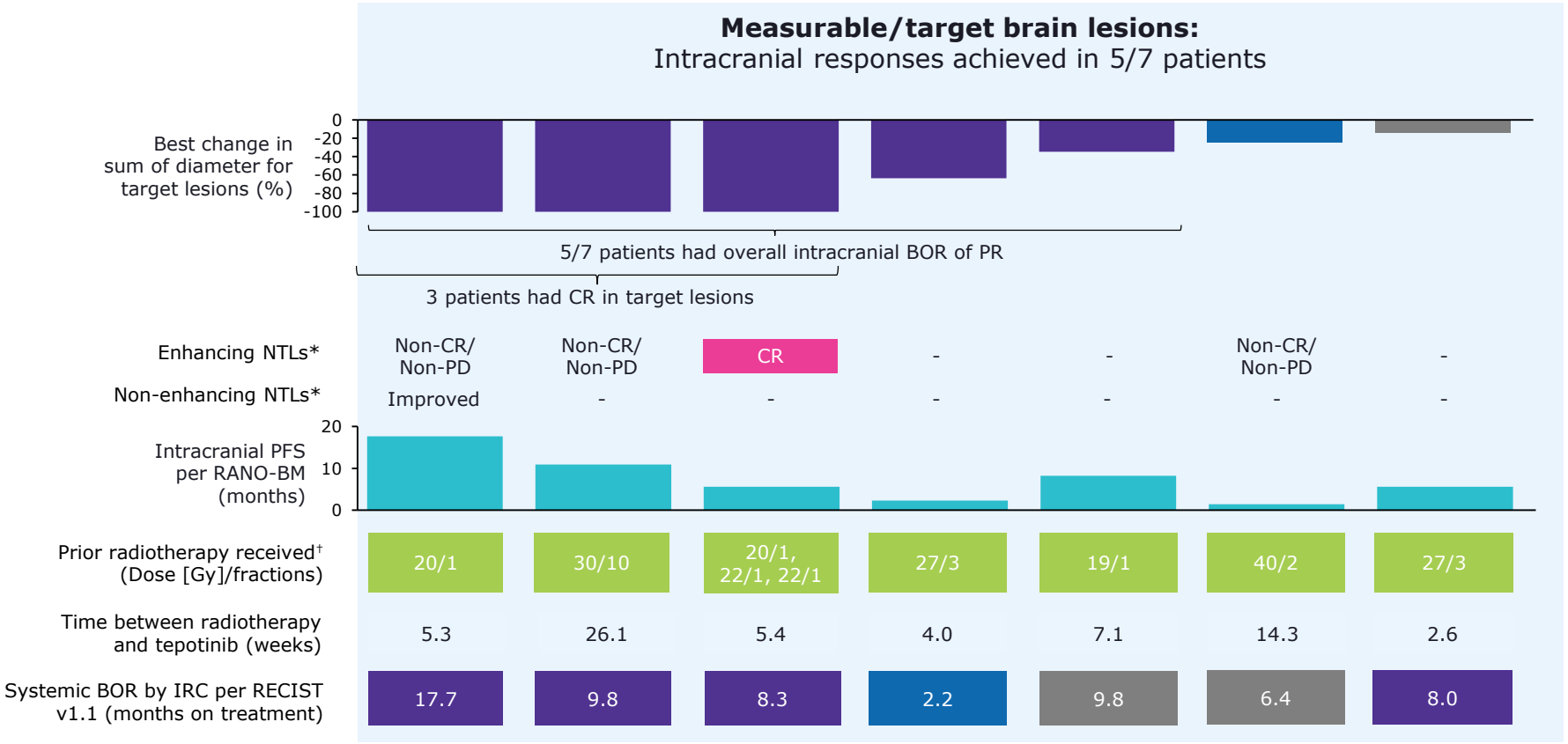
Due to the single-arm design of the VISION Trial, no formal statistical comparisons were conducted; data were analyzed in a descriptive manner. For analysis of intracranial activity, brain imaging had no mandatory schedule and, as such, data for this retrospective ad hoc analysis were incomplete, and 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.

*T1-weighted, gadolinium-enhanced.
MRI, magnetic resonance imaging; RANO-BM, Response Assessment in Neuro-Oncology Brain Metastases.
Reference: Patel JD, et al. J Clin Oncol. 2021;39(no. 15_suppl):9084–9084.

Assessment of Intracranial Response to Tepotinib by IRC

VISION Cohort A

July 2020 cut-off



- Of 7 patients with measurable/target brain lesions per RANO-BM, intracranial BOR was:
  - PR (n=5; including 3 cases of CR in target lesions
  - SD (n=1)
  - PD (n=1)

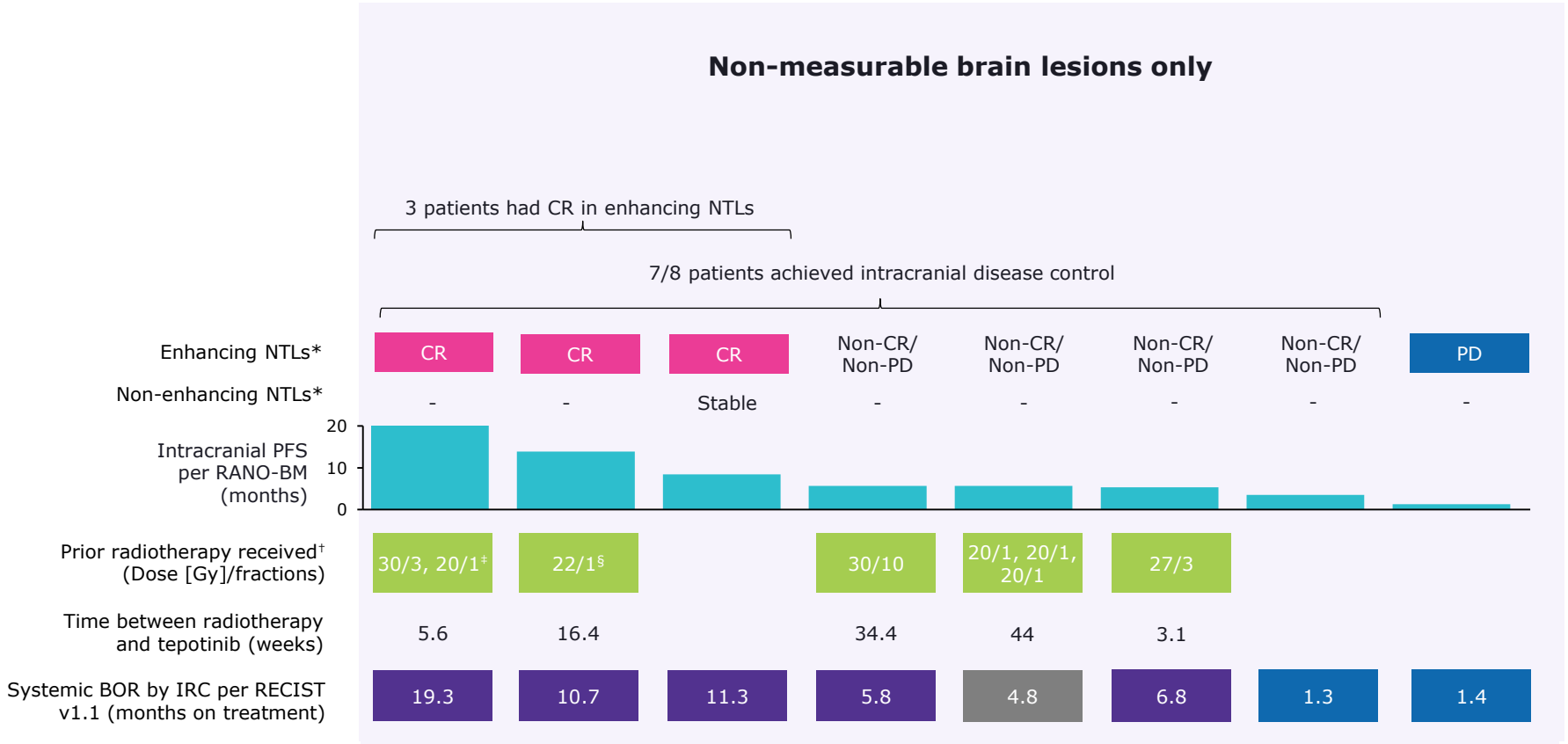
Tepotinib demonstrated intracranial activity in evaluable patients with baseline brain metastases (per RANO-BM)
Intracranial disease control was observed in 13/15 patients

Data cut-off: July 1, 2020.
*Dashes (-) indicate NTLs were not recorded. †Radiotherapy for brain lesions.
BOR, best objective response; CR, complete response; IRC, Independent Review Committee; NTL, non-target lesion; PD, progressive disease; PR, partial response; RANO-BM, Response Assessment in Neuro-Oncology Brain Metastases; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.
Reference: Patel JD, et al. ASCO 2021 (Poster 9084).

Assessment of Intracranial Response to Tepotinib by IRC

VISION Cohort A

July 2020 cut-off



- Of 8 patients with non-measurable/non-target brain lesions (NTLs), **7 patients achieved intracranial disease control** and 1 patient had PD
- Three of 7 patients with disease control had CR of the enhancing NTL

Tepotinib demonstrated intracranial activity in evaluable patients with baseline brain metastases (per RANO-BM)
Intracranial disease control was observed in 13/15 patients

Data cut-off: July 1, 2020.
*Dashes (-) indicate NTLs were not recorded. †Radiotherapy for brain lesions. ‡20 Gy in one fraction was reported during the same time period as 30 Gy in 3 fractions. §GammaKnife was also received 31.4 weeks prior to the start of tepotinib treatment.
BOR, best objective response; CR, complete response; IRC, Independent Review Committee; NTL, non-target lesion; PD, progressive disease; PR, partial response; RANO-BM, Response Assessment in Neuro-Oncology Brain Metastases; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.
Reference: Patel JD, et al. ASCO 2021 (Poster 9084).

Systemic Response in Patients With Brain Metastases

VISION Cohorts A + C

Feb 2021 cut-off

- At baseline, 51 patients (18.5%) had brain metastases (lesions identified according to RECIST v1.1)
- Systemic ORR was 52.9% (95% CI: 38.5, 67.1), and median DOR was 9.0 months (95% CI: 5.6, NE) in patients with brain metastases

Systemic objective response (IRC)*		Patients with brain metastases (n=51)
ORR (95% CI), %		52.9 (38.5, 67.1)
BOR, n (%)	CR	0
	PR	27 (52.9)
	SD	12 (23.5)
	PD	7 (13.7)
	NE	5 (9.8)
DCR (95% CI), %		76.5 (62.5, 87.2)

*T1-weighted, gadolinium-enhanced.
BOR, best objective response; CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; IRC, Independent Review Committee; MRI, magnetic resonance imaging; NE, not estimable; ORR, objective response rate; PD, progressive disease; PR, partial response; RANO-BM, Response Assessment in Neuro-Oncology Brain Metastases; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.
Reference: Thomas M, et al. Presented at DGHO Annual Meeting 2021, Abstract 52.

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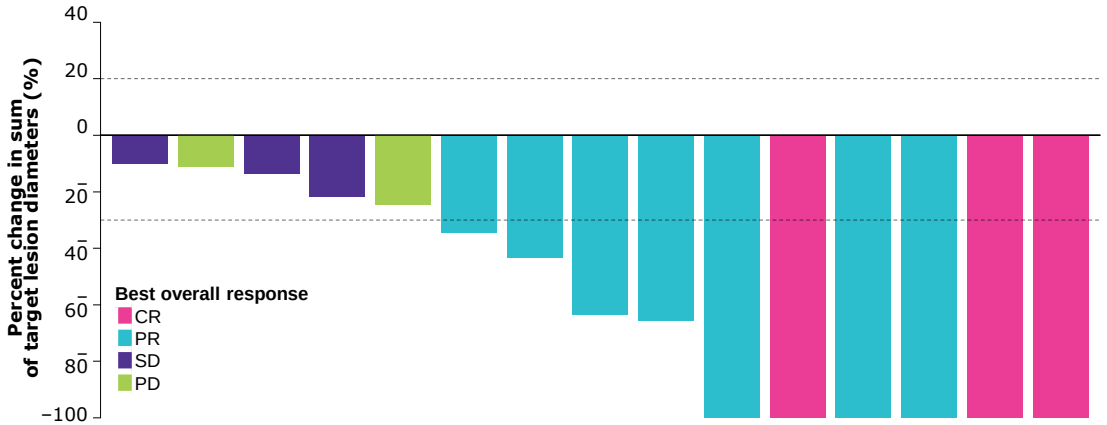
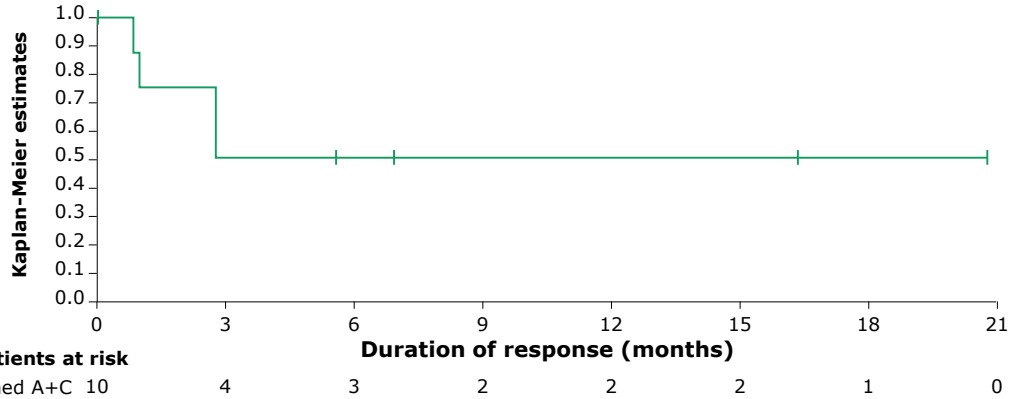
Analysis of Patients With Brain Metastases

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)

1L, first line; 2L+, second-or-later line; CI, confidence interval; CNS, central nervous system; CR, complete response; DOR, duration of response; $Kp_{u,u}$, unbound partition coefficient; m, median; 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.

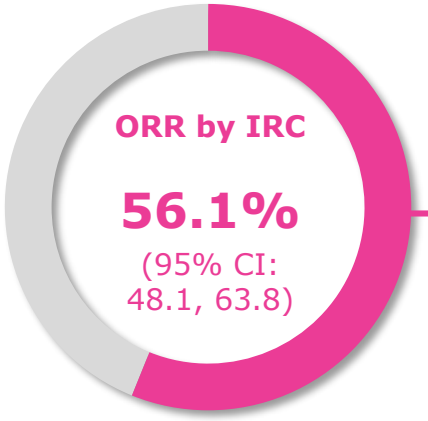
SUMMARY

Summary

VISION: A single-arm, open-label, multicenter, non-randomized, multicohort study[1]

Response by previous treatment status (N=313)[2]

Treatment naive (n=164)

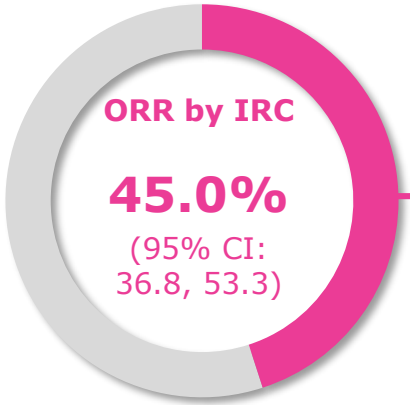


mDOR by IRC
46.4 mo
(95% CI: 13.8, NE)

mPFS
12.6 mo
(95% CI: 9.6, 17.7)

mOS
19.1 mo
(95% CI: 13.7, 23.7)

Previously treated (n=149)



mDOR by IRC
12.4 mo
(95% CI: 9.5, 18.5)

mPFS
11.0 mo
(95% CI: 8.2, 13.7)

mOS
19.6 mo
(95% CI: 15.2, 22.3)

- The most common ARs (≥20%) in patients who received tepotinib were edema, nausea, diarrhea, hypoalbuminemia, blood creatinine increase, dyspnea, and decreased apetite[2]

- TEPMETKO® (tepotinib) is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (*MET*) exon 14 skipping alterations[1]
- This indication is approved under accelerated approval based on ORR and duration of the response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials[1]

1L, first line; 2L, second line; 2L+, second-or-later line; AR, adverse reaction; CI, confidence interval; DOR, duration of response; IRC, Independent Review Committee; m, median; *MET*, mesenchymal-epithelial transition factor; *MET*ex14, *MET* exon 14; NE, not estimable; SCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

References: 1. TEPMETKO® (tepotinib) [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021; **2.** Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

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BACKUP: UPDATED EFFICACY AND SAFETY DATA FEBRUARY 2021

Patient Characteristics

VISION Cohorts A + C

Feb 2021 cut-off

Disease Characteristics[1,2]

- **80%** had adenocarcinoma histology
- **19%** had CNS metastases

Smoking Status[1,*]

- **47%** former smokers
- **50%** never smokers

Age, ECOG PS[1,2]

- **Median age of 72 years** (range 41 to 94)
  - **80%** were ≥65 years of age
- **28%** had ECOG PS 0 and **72%** had ECOG PS 1

Race and Gender[1]

- **67%** White
- **29%** Asian
- **49%** male
- **51%** female

Line of Therapy[1]

- **50%** (n=137) treatment naive
- **50%** (n=138) previously treated[†]

*MET*ex14 skipping alterations were identified through PCR or NGS testing[3,‡]

- **63%** of patients were enrolled by tissue (RNA-based) testing
- **58%** of patients were enrolled by plasma (ctDNA-based) testing

*Smoking history was missing in 10 patients.[1] †Had progressed on up to 2 lines of prior systemic therapies.[1] ‡Some patients tested positive using both methodologies.[3]
ctDNA, circulating tumor DNA; ECOG PS, Eastern Cooperative Oncology Group performance status; *MET*ex14, *MET* exon 14.
References: 1. Thomas M, et al. Presented at DGHO Annual Meeting 2021, Abstract 52; **2.** Garassino M, et al. Presented at ESMO Annual Meeting 2021, Poster 1254P; **3.**.Felip E, et al. Presented at WCLC 2021, Abstract 170.

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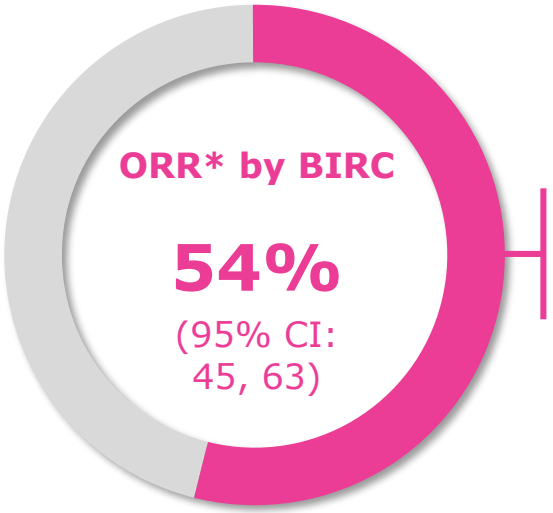
Efficacy by Previous Treatment Status

VISION Cohorts A + C

Feb 2021 cut-off

Treatment Naive (n=137)

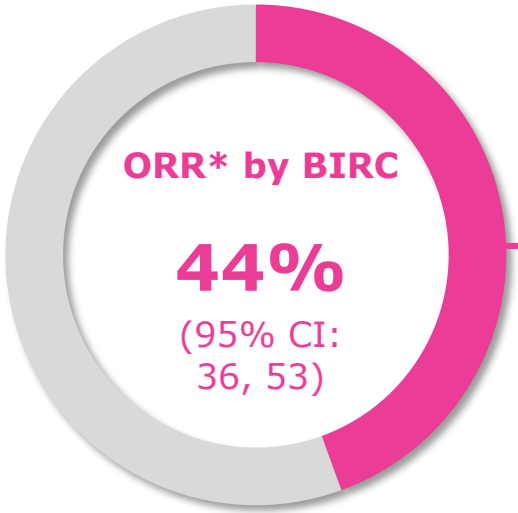


mDOR† by BIRC

32.7 mo

(95% CI: 9.0, NE)

Previously Treated (n=138)



mDOR† by BIRC

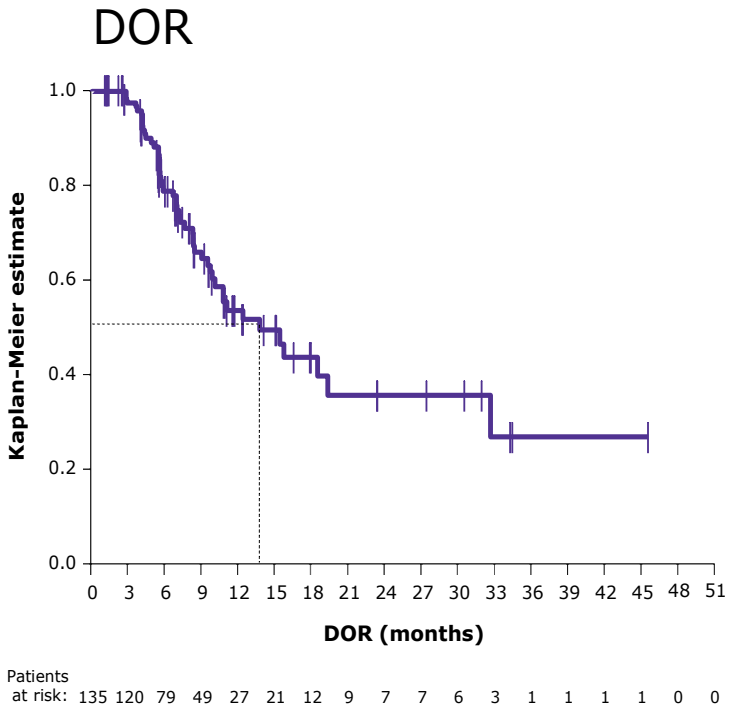
11.1 mo

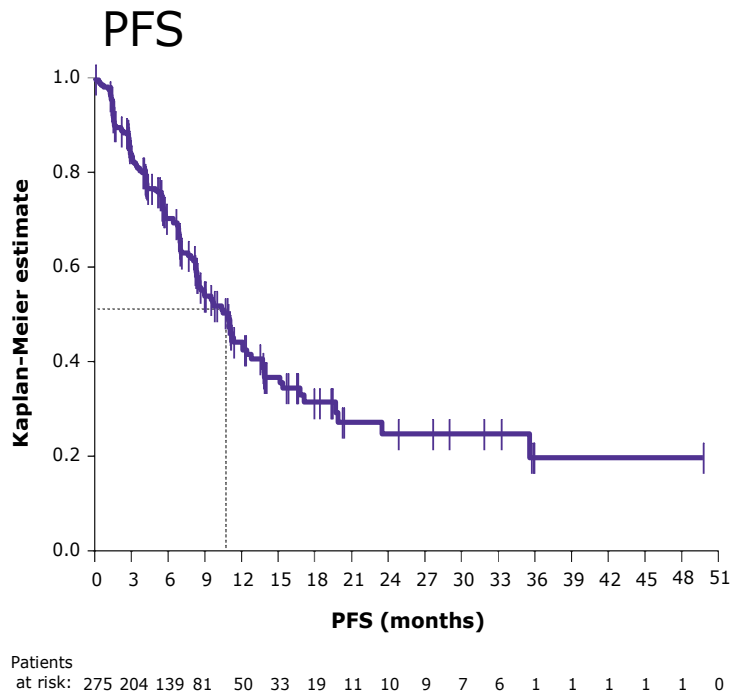
(95% CI: 8.4, 18.5)

*Confirmed responses. †Product-limit (Kaplan-Meier) estimates, 95% CI for the median using the Brookmeyer and Crowley method.
BIRC, Blinded Independent Review Committee; mo, months; mDOR, median duration of response; NE, not estimable; ORR, objective response rate.
Reference: Thomas M, et al. Presented at DGHO Annual Meeting 2021, Abstract 52.

Overall Activity

Efficacy (IRC)		Overall (N=275)
ORR (95% CI), %		49.1 (43.0, 55.2)
BOR, n (%)	CR	0
	PR	135 (49.1)
	SD	71 (25.8)
	PD	34 (12.4)
	NE	35 (12.7)
DCR, (95% CI), %		74.9 (69.4, 79.9)
DOR, median (95% CI), months *Events*		13.8 (9.9, 19.4) *37.0%*
PFS, median (95% CI), months *Events*		10.8 (8.5, 12.4) *47.6%*





Overall, ORR was 49.1% (95% CI: 43.0, 55.2), 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)

BOR, best objective response; CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; IRC, Independent Review Committee; NE, not estimable; ORR, objective response rate; 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.

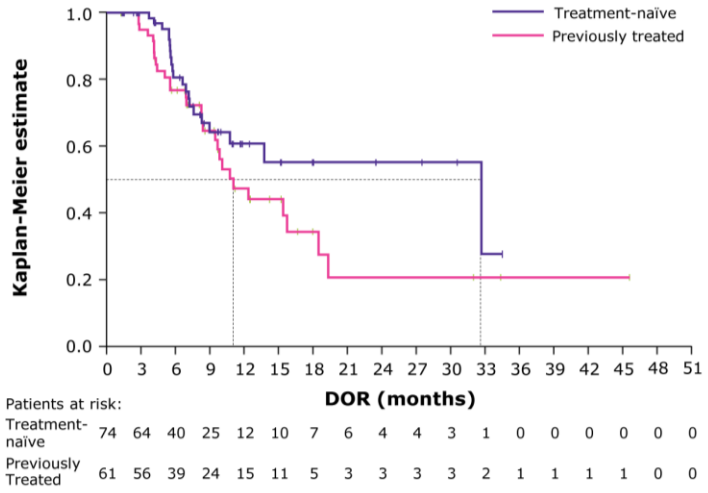
Duration of Response/Progression-Free Survival

VISION Cohorts A + C

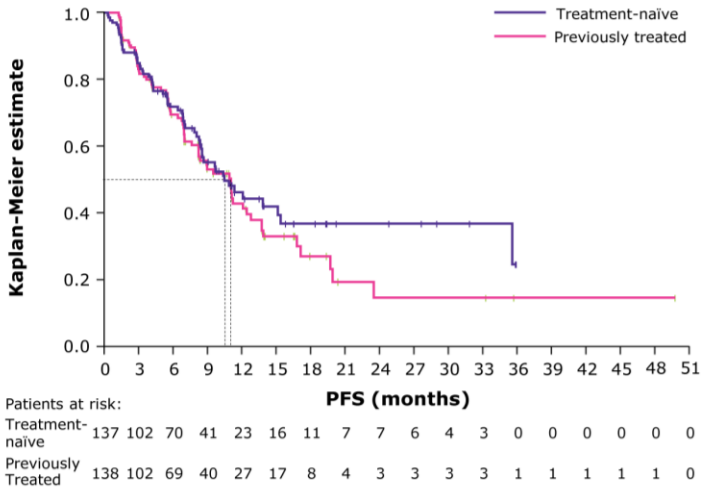
Feb 2021 cut-off

Efficacy according to IRC		Treatment naive (n=137)	Previously treated (n=138)
ORR (95% CI), %		54.0 (45.3, 62.6)	44.2 (35.8, 52.9)
BOR, n (%)	CR	0	0
	PR	74 (54.0)	61 (44.2)
	SD	28 (20.4)	43 (31.2)
	PD	16 (11.7)	18 (13.0)
	NE	19 (13.9)	16 (11.6)
DCR (95% CI), %		74.5 (66.3, 81.5)	75.4 (67.3, 82.3)

	Events	mDOR, months (95% CI)
Treatment-naïve	28.4%	32.7 (9.0, ne)
Previously treated	47.5%	11.1 (8.4, 18.5)



	Events	mPFS, months (95% CI)
Treatment-naïve	43.8%	10.4 (8.4, 15.3)
Previously treated	51.4%	11.0 (8.2, 12.4)



- In treatment-naive patients (n=137), ORR was 54.0% (95% CI: 45.3, 62.6), DOR was 32.7 months (95% CI: 9.0, NE), and PFS was 10.4 months (95% CI: 8.4, 15.3)
- In previously treated patients (n=138), ORR was 44.2% (95% CI: 35.8, 52.9), DOR was 11.1 months (95% CI: 8.4, 18.5), and PFS was 11 months (95% CI: 8.2, 12.4)

BOR, best objective response; CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; IRC, Independent Review Committee; NE, not estimable; ORR, objective response rate; 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.

TRAEs (Any Grade) Occurring in ≥10% of All Patients

VISION Cohorts A + C

Feb 2021 cut-off

TRAE, n (%)	Overall (N=291)
Peripheral edema	175 (60.1)
Nausea	66 (22.7)
Diarrhea	62 (21.3)
Blood creatinine increased	57 (19.6)
Hypoalbuminemia	55 (18.9)

The most common TRAE was peripheral edema (60% any grade, 10% Grade ≥3)

TRAE, treatment-related adverse event.

Reference: Thomas M, et al. Presented at DGHO Annual Meeting 2021, Abstract 52.

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TRAE Summary Across Age Subgroups and Most Common All-Cause AEs by Age

VISION Cohorts A + C

Feb 2021 cut-off

TRAE, n (%)	Overall (N=291)	Age subgroup, years			
		<65 (n=64)	≥65–<75 (n=107)	≥75–<85 (n=96)	≥85 (n=24)
Any grade Grade ≥3	264 (90.7) 86 (29.6)	52 (81.3) 9 (14.1)	105 (98.1) 28 (26.2)	84 (87.5) 39 (40.6)	23 (95.8) 10 (41.7)
Leading to dose reduction	90 (30.9)	10 (15.6)	36 (33.6)	36 (37.5)	8 (33.3)
Leading to temporary interruption	114 (39.2)	14 (21.9)	39 (36.4)	46 (47.9)	15 (62.5)
Leading to permanent discontinuation	41 (14.1)	4 (6.3)	14 (13.1)	17 (17.7)	6 (25.0)

Most common all-cause AEs, n(%)	Overall (N=291)	Age subgroup, years			
		<65 (n=64)	≥65–<75 (n=107)	≥75–<85 (n=96)	≥85 (n=24)
Peripheral edema	191 (65.6)	35 (54.7)	75 (70.1)	61 (63.5)	20 (83.3)
Nausea	87 (29.9)	16 (25.0)	35 (32.7)	32 (33.3)	5 (20.8)
Diarrhea	81 (27.8)	17 (26.6)	27 (25.2)	30 (31.3)	7 (29.2)
Hypoalbuminemia	81 (27.8)	15 (23.4)	27 (25.2)	31 (32.3)	8 (33.3)
Blood creatinine increase	76 (26.1)	13 (20.3)	30 (28.0)	29 (30.2)	4 (16.7)
Dyspnea	60 (20.6)	9 (14.1)	21 (19.6)	22 (22.9)	8 (33.3)
Decreased appetite	48 (16.5)	3 (4.7)	21 (19.6)	22 (22.9)	2 (8.3)
Constipation	46 (15.8)	9 (14.1)	17 (15.9)	19 (19.8)	1 (4.2)
Fatigue	45 (15.5)	8 (12.5)	16 (15.0)	20 (20.8)	1 (4.2)

- Tepotinib was generally well tolerated with low proportion of TRAEs leading to discontinuation
- Grade ≥3 TRAEs occurred in 29.6% of patients, 30.9% of patients had TRAEs leading to dose reduction, 39.2% temporary interruption, and 14.1% permanent discontinuation
- The most common AE was peripheral edema, occurring in 66% of patients, which was considered treatment related in 60% of patients

Reference: Garassino M, et al. Presented at ESMO 2021, Poster 1254P.

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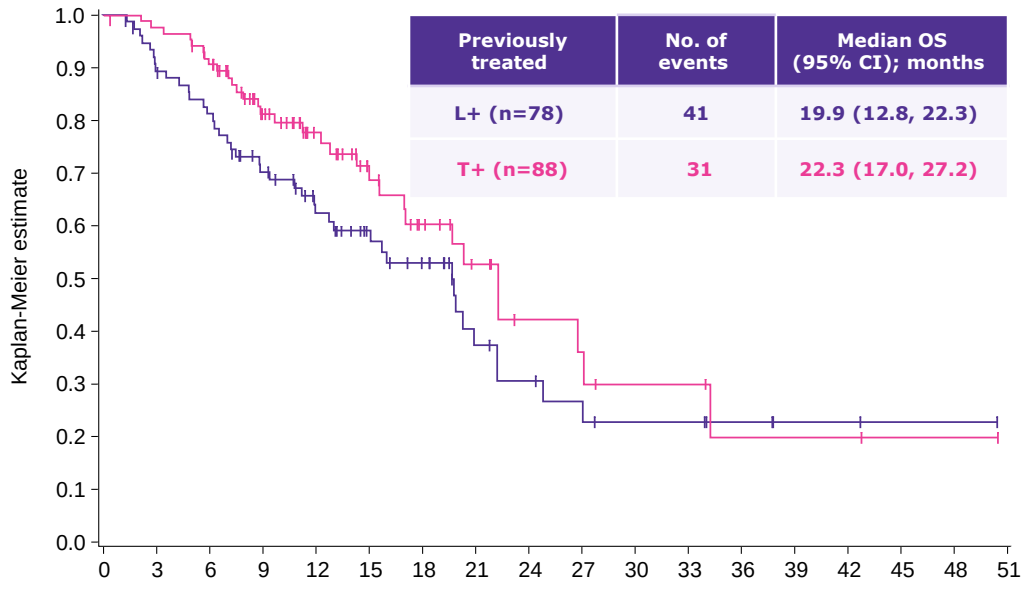
BACKUP: RESULTS BY BIOPSY LIQUID VS TISSUE

Overall Survival by Biopsy

VISION Cohorts A + C

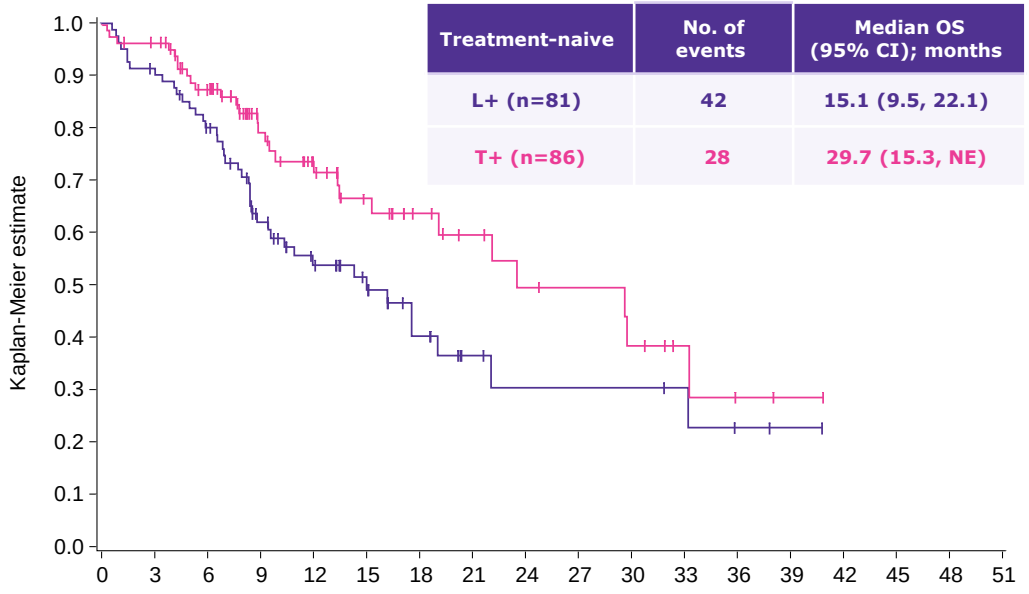
Feb 2021 cut-off



Previously treated	No. of events	Median OS (95% CI); months
L+ (n=78)	41	19.9 (12.8, 22.3)
T+ (n=88)	31	22.3 (17.0, 27.2)

Patients at risk:

L+	78	67	60	49	39	29	24	13	9	7	5	5	3	2	2	1	1	0
T+	88	85	76	55	38	27	19	13	7	6	4	4	2	2	2	1	1	0



Treatment-naive	No. of events	Median OS (95% CI); months
L+ (n=81)	42	15.1 (9.5, 22.1)
T+ (n=86)	28	29.7 (15.3, NE)

Patients at risk:

L+	81	73	63	41	31	22	13	7	5	5	5	4	2	1	0	0	0	0
T+	86	81	67	44	35	24	17	13	10	9	7	4	2	1	0	0	0	0

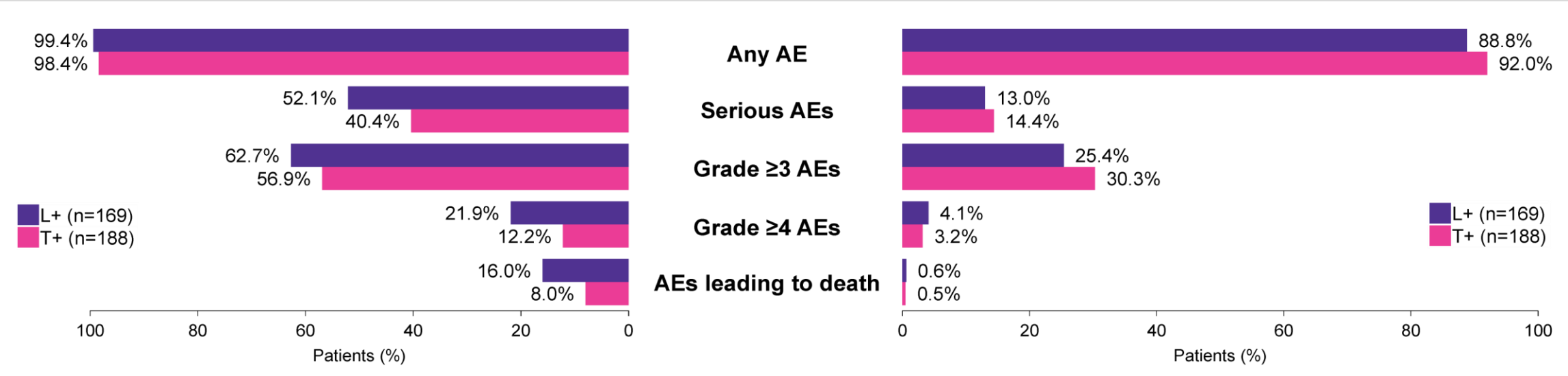
Time-dependent endpoints showed a trend for improvement in the tissue biopsy population, despite having comparable ORRs in both treatment-naive and previously treated patients

CI, confidence interval; L+, positive detection of *MET*ex14 skipping in liquid biopsy sample; *MET*, mesenchymal epithelial transition factor; *MET*ex14, *MET* exon 14; NE, not estimable; ORR, objective response rate; T+, positive detection of *MET*ex14 skipping in tissue biopsy sample.

Reference: Felip E, et al. Presented at WCLC 2021, Abstract 170.

All-Cause and TRAEs by Biopsy

- Across Cohorts A and C, 291 patients received at least one dose of tepotinib and were analyzed for safety*
- Incidences of serious and Grade ≥3 TRAEs were similar across the L+ and T+ populations, but any-cause AEs were reported in a larger proportion of L+ patients, suggesting a population with a higher disease burden



*Patients analyzed for safety include and additional 16 patients with <3 months' follow up in Cohort C that were excluded from efficacy analyses. AEs were defined as events that start within the day of first dose of trial treatment until 30 days after last dose of treatment, or started prior to first dose but worsened during the treatment period, and were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events v4.03.
AE, adverse event; L+, positive detection of *MET*ex14 skipping in liquid biopsy sample; *MET*, mesenchymal epithelial transition factor; *MET*ex14, *MET* exon 14; T+, positive detection of *MET*ex14 skipping in tissue biopsy sample; TRAE, treatment-related adverse event.

Reference: Felip E, et al. Presented at WCLC 2021, Abstract 170.

Efficacy by Line of Therapy and Biopsy

Efficacy (IRC)	L+ (N=178)*			T+ (N=208)*		
	1L (n=95)	2L (n=46)	2L+ (n=83)	1L (n=111)	2L (n=65)	2L+ (n=97)
ORR, % (95% CI)	57.9 (47.3, 68.0)	41.3 (27.0, 56.8)	43.4 (32.5, 54.7)	56.8 (47.0, 66.1)	53.8 (41.0, 66.3)	49.5 (39.2, 59.8)
mDOR, months (95% CI)	46.4 (8.3, NE)	9.7 (5.6, ne)	12.4 (8.4, NE)	46.4 (13.4, NE)	12.4 (7.0, 20.8)	10.2 (8.3, 18.0)
mPFS, months (95% CI)	9.7 (8.0, 15.1)	6.9 (5.5, 9.5)	8.2 (5.7, 11.0)	15.3 (11.3, NE)	13.7 (8.2, 19.4)	11.5 (8.2, 16.8)
mOS, months (95% CI)	16.3 (10.4, 22.9)	18.8 (10.9, 22.3)	18.8 (12.0, 22.3)	25.9 (17.5, 36.6)	20.9 (17.7, 32.5)	20.4 (17.0, 26.8)

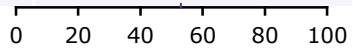
*Some patients in the VISION trial had a positive detection of *MET*ex14 skipping in both tissue and liquid biopsy samples.
1L, first line; 2L, second line; 2L+, second-or-later line; CI, confidence interval; DOR, duration of response; IRC, Independent Review Committee; L+, positive detection of *MET*ex14 skipping in liquid biopsy sample; m, median; *MET*, mesenchymal epithelial transition factor; *MET*ex14, *MET* exon 14; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; T+, positive detection of *MET*ex14 skipping in tissue biopsy sample;
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Efficacy by Prior Therapy in Previously Treated Patients Confirmed With Tissue Biopsy (ORR)

VISION Cohorts A + C

Feb 2022 cut-off

Tepotinib efficacy		T+ patients (N=208)	
		n	ORR, % (95% CI)
Overall		208	53.4 (46.3, 60.3)
Treatment-naive		111	56.8 (47.0, 66.1)
Previously treated: 2L+		97	49.5 (39.2, 59.8)
Prior therapy	IO*	47	38.3 (24.5, 53.6)
	IO + CT	16	56.3 (29.9, 80.2)
	CT	64	53.1 (40.2, 65.7)
Previously treated: 2L only		65	53.8 (41.0, 66.3)
Prior therapy	IO*	25	44.0 (24.4, 65.1)
	IO + CT	11	63.6 (30.8, 89.1)
	CT	38	60.5 (43.4, 76.0)



*Patients received IO monotherapy or IO + platinum-based CT.
1L, first line; 2L, second line; 2L+, second-or-later line; CI, confidence interval; CT, chemotherapy; IO, immunotherapy; ORR, objective response rate.
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.