VISION OVERVIEW DECK

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HRQoL, health-related quality of life; LBx, liquid biopsy; NSCLC, non-small cell lung cancer; TBx, tissue biopsy.

NSCLC DISEASE AND BACKGROUND

Lung Cancer: Key US 2024 Statistics

234,580 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]

234,580
New cases of lung cancer[1]

118,270 in women[3]

116,310 in men[3]

125,070
Deaths from lung cancer[1]

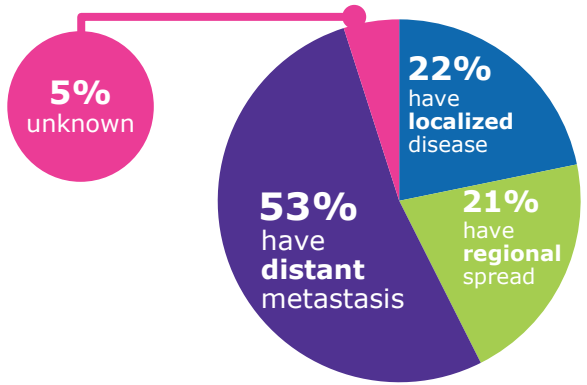
59,280 in women[3]

65,790 in men[3]

NSCLC accounts for 80%-85% of these:
~199,393 patients[3]

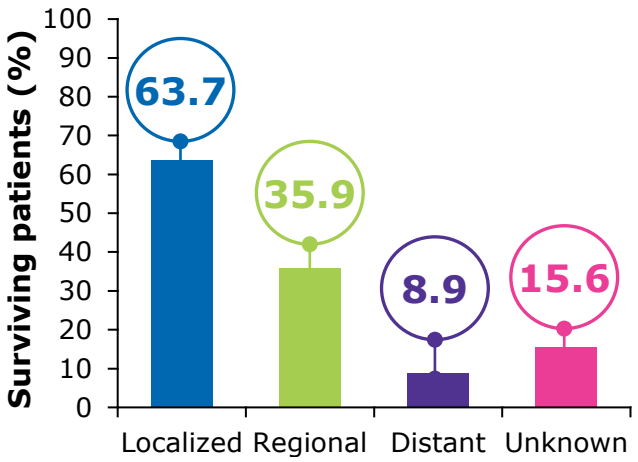
~3% of these patients have *MET*ex14 skipping NSCLC:
~5,982 patients[4]

Spread at diagnosis[1]



~53% of patients with lung cancer are diagnosed with advanced or metastatic disease with a 5-year survival rate of 8.9%[1]

5-year relative survival by spread at diagnosis (2014–2020)[1]



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

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

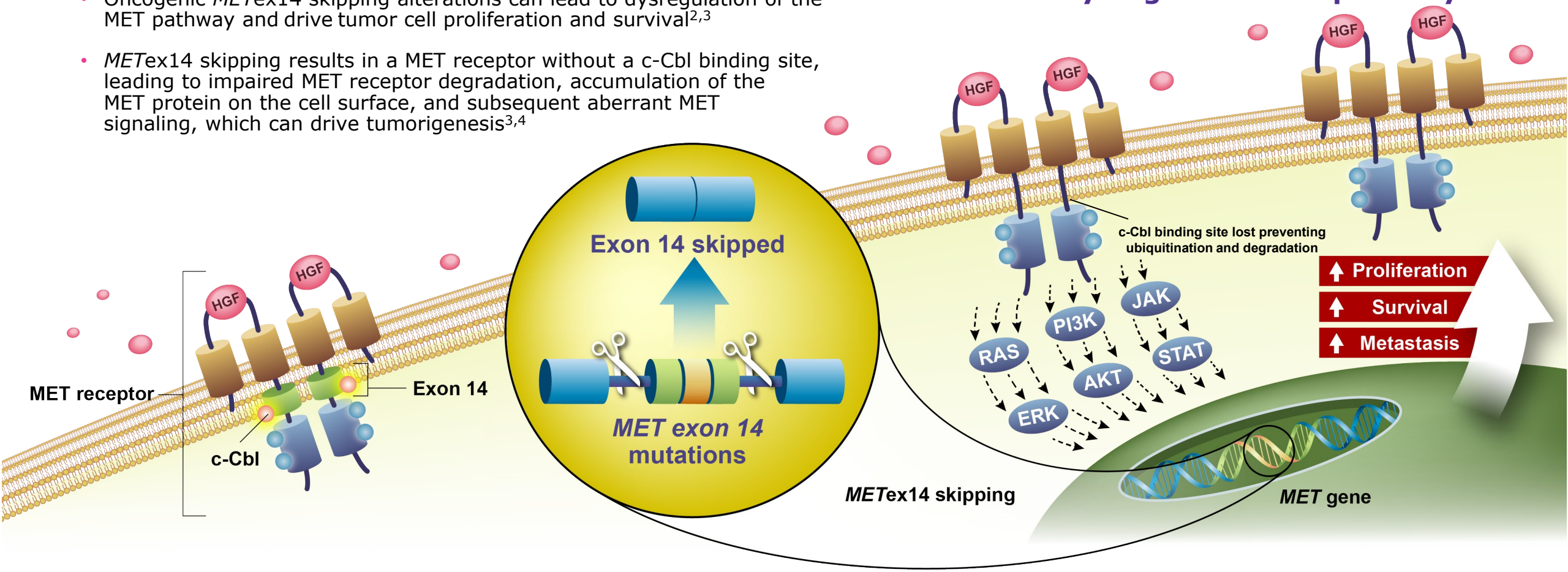
*Calculation: number of patients per year (5,966)/days in calendar year (365)=16.
MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer.

References: 1. Cancer Stat Facts: Lung and Bronchus Cancer. SEER Program, National Cancer Institute. https://seer.cancer.gov/statfacts/html/lungb.html (accessed September 2024); **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 September 2024); **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; RAS, rat sarcoma; 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]

METex14 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.

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
- The recommended dosage of tepotinib is 450 mg (two 225 mg tablets) orally once daily with food until disease progression or unacceptable toxicity

Please see the full TEPMETKO US Prescribing Information at https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

Reference: TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

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% of patients treated with tepotinib, with one patient experiencing Grade 3 or higher event; this event resulted in death

Pancreatic toxicity

- Tepotinib can cause **pancreatic toxicity** in form of elevations in amylase and lipase levels
- Increased amylase and/or lipase occurred in 13% of patients, with Grade 3 and 4 events occurring in 5% and 1.2% of patients, respectively
- Monitor amylase and lipase levels at baseline and regularly during treatment with tepotinib and temporarily withhold, dose reduce, or permanently discontinue based on severity of the adverse event

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 18% of patients treated with tepotinib. Grade 3 or 4 increased ALT/AST occurred in 4.7% 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 47 days (range 1–262)

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

Reference: TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

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 last dose

Drug interactions

- 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 (0.3%) due to pneumonitis, one patient (0.3%) due to hepatic failure, one patient (0.3%) due to dyspnea from fluid overload, one patient (0.3%) due to pneumonia, one patient (0.3%) due to sepsis, and one patient (0.3%) due to unknown cause

Serious adverse reactions

- **Serious adverse reactions** occurred in 51% of patients who received tepotinib. Serious adverse reactions in >2% of patients included pleural effusion (6%), pneumonia (6%), edema (5%), general health deterioration (3.8%), dyspnea (3.5%), musculoskeletal pain (2.9%), and pulmonary embolism (2.2%)

Most common adverse reactions

- **The most common adverse reactions (≥20%)** in patients who received tepotinib were edema (81%), nausea (31%), fatigue (30%), musculoskeletal pain (30%), diarrhea (29%), dyspnea (24%), rash (21%), and decreased appetite (21%)

Reference: TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

Important Safety Information (continued)

Clinically relevant adverse reactions

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

Selected laboratory abnormalities

- **Selected laboratory abnormalities (≥20%)** from baseline in patients receiving tepotinib in descending order were decreased albumin (81%), increased creatinine (60%), decreased lymphocytes (57%), increased ALP (52%), increased ALT (50%), increased AST (40%), decreased sodium (36%), decreased hemoglobin (31%), increased GGT (29%), increased potassium (26%), increased amylase (25%), decreased leukocytes (25%), decreased platelets (24%), and increased lipase (21%)

Most common Grade 3-4 laboratory abnormalities

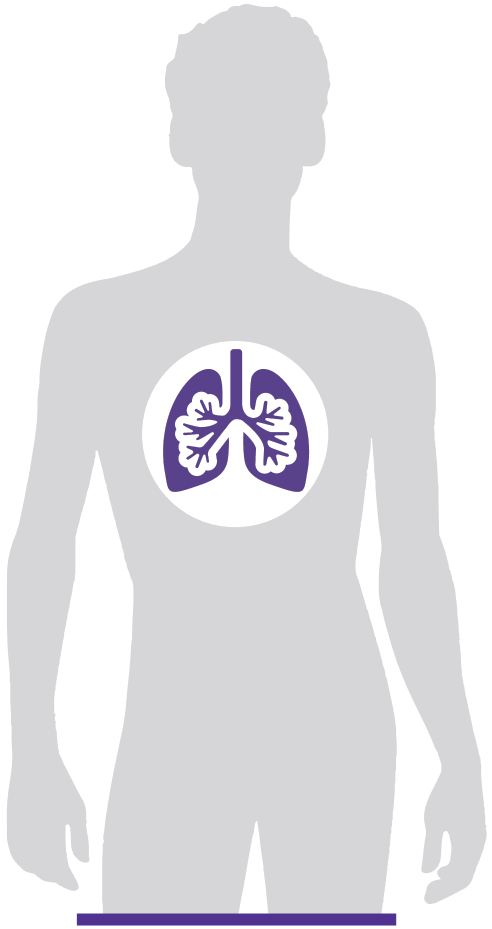
- **The most common Grade 3-4 laboratory abnormalities (≥2%)** in descending order were decreased lymphocytes (15%), decreased albumin (9%), decreased sodium (9%), increased GGT (6%), increased amylase (5%), increased lipase (5%), increased ALT (4.9%), increased AST (3.6%), and decreased hemoglobin (3.6%)

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

Reference: TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

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% 1 case; this event resulted in death
Discontinuation of tepotinib due to ILD/pneumonitis	1% (n=5)

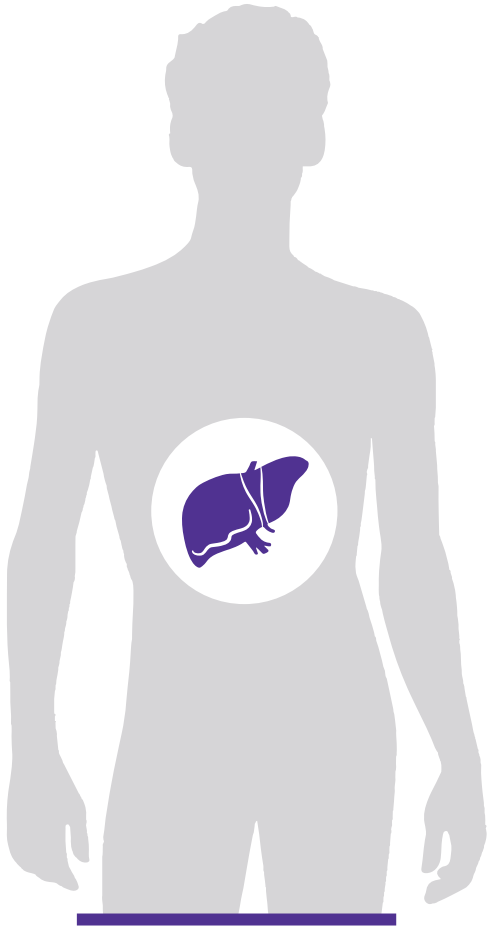
Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever)

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], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

Tepotinib Warnings and Precautions: Hepatotoxicity



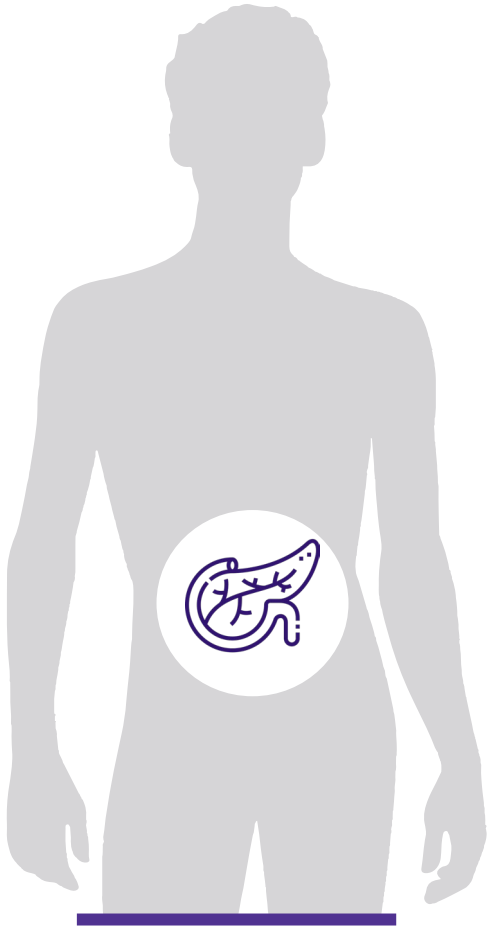
Hepatotoxicity occurred in patients treated with tepotinib	
Increased ALT/increased AST All grades Grade 3 or 4 increased ALT/AST	 18% 4.7%
Fatal AR of hepatic failure	0.2% (n=1)
Discontinuation of tepotinib due to increased ALT/AST	0.8% (n=4)
Median time to onset of Grade ≥3 increased ALT/AST	47 days (range: 1–262)

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], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

Tepotinib Warnings and Precautions: Pancreatic Toxicity



Elevations in amylase and lipase levels occurred in patients treated with tepotinib	
Increased amylase and/or lipase	
All grades	13%
Grade 3	5%
Grade 4	1.2%

Monitor amylase and lipase at baseline and regularly during treatment with tepotinib

Based on the severity of the adverse drug reaction, **temporarily withhold, dose reduce, or permanently discontinue** tepotinib

Reference: TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

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 last dose

AUC, area under the curve.

Reference: TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

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, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer.

Reference: TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

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. Patients who have difficulty swallowing solids can disperse tablets in water
- 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
- 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], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

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
(450 mg active moiety)

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]

*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].

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.

References: 1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf; **2.** Smit EF, et al. Presented at ESMO, 2022, Abstract 985P; **3.** Thomas M, et al. Presented at WCLC, 2022. Abstract OA03.05.

*MET*ex14 Skipping Patient Populations in VISION

Main data cut-offs:

- January 2020 data cut-off (when 99/152 patients in Cohort A had ≥9 months of follow-up data)[1]: Primary efficacy analysis; not included in this deck
- July 2020 data cut-off[2,3] (Data submitted to FDA and included in USPI; full Cohort A and safety data for Cohorts A+C)
- February 2021[4,5] (not included in this deck) and February 2022[6-8] (see Backup section)
- November 2022 data cut-off[9-11] (Updated USPI after full approval; long-term follow-up based on full Cohorts A+C)

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 naïve n=69	2L+ n=83

February 2022 Data Cut-off[6-8]

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

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

Treatment naive n=95	2L+ n=66

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

Treatment naive n=164	2L+ n=149

November 2022 Data Cut-off[9-11]

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

Efficacy analysis set (N=313)
Full Cohort A + C

Treatment naïve n=164	2L+ n=149

2L+, second-or-later line; FDA, US Food and Drug Administration; MET, mesenchymal-epithelial transition; *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; **8.** Griesinger F, et al. Presented at ELCC, 2023, Poster 34P; **9.** Paik P, et al. Presented at ASCO Annual Meeting, 2023, Abstract 9060; **10.** Mazieres J, et al. *JAMA Oncol*. 2023;9(9):1260–1266; 11. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

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]

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

July 2020 data cut-off

USPI February 2021[3] (based on accelerated, conditional approval)

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]

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

February 2022 data cut-off

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

Griesinger F, et al. ELCC, 2023 (Cohorts A+C, N=313 [efficacy & safety])[8]

Paik P, et al. ASCO, 2023 (Cohorts A+C, N=313 [efficacy & safety])[9]

November 2022 data cut-off

Ahn M-J, et al. WCLC, 2023 (Cohorts A+C (Asian patients), N=106 [efficacy & safety])[10]

Rolfo C, et al. ESMO, 2023 (Cohorts A+C, N=313 [LBx and TBx])[11]

Viteri S, et al. ESMO, 2023 (Cohorts A+C, N=313 [2L+, 149; 2L, 92; 3L+, 57] [efficacy, prior and post tepotinib])[12]

Full USPI based on traditional approval in Feb 2024[13]: Mazieres J, et al. *JAMA Oncology*, 2023 (Cohorts A+C, N=313 [long-term follow-up])[14]

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; **8.** Griesinger F, et al. Presented at ELCC, 2023, Poster 34P; **9.** Paik P, et al. Presented at ASCO Annual Meeting, 2023, Abstract 9060; **10.** Ahn M-J, et al. Presented at WCLC 2023. Poster P2.11-02; **11.** Rolfo C, et al. Presented at ESMO, 2023, Poster 1382P; **12.** Viteri S, et al. Presented at ESMO 2023, Poster 1380P; 13. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf; 2024; 14. Mazieres J, et al. *JAMA Oncol*. 2023;9(9):1260–1266.

COHORTS A+C: UPDATED EFFICACY AND SAFETY DATA (NOVEMBER 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.

Patient Characteristics (N=313)[1,2]

Cohorts A + C

Nov 2022 cut-off

Age and ECOG PS*

- **Median age of 72 years** (range 41–94)
- **26%** had ECOG PS 0
- **74%** had ECOG PS 1

Disease characteristics‡

- **81%** had adenocarcinoma histology

Race† and gender

- **62%** White
- **34%** Asian
- **49%** male
- **51%** female

Smoking status§

- **49%** No smoking history

Line of therapy

- **52%** (n=164) treatment naïve (1L)
- **48%** (n=149) previously treated (2L+)

*MET*ex14 skipping detection

- **67%** of patients were enrolled by tissue (RNA-based) testing
- **57%** of patients were enrolled by plasma (ctDNA-based) testing

* One 1L patient was ECOG PS 2. †Nine patients had race reported as "other' or missing or not collected at the site. ‡Fifty-nine patients had histologies other than adenocarcinoma (32 in 1L and 27 in 2L+), and two had missing histology information (one each in 1L and 2L+). §Smoking history was missing in 10 patients (one in 1L and nine in 2L+).
1L, first line; 2L+, second-or-later line; ECOG PS, Eastern Cooperative Oncology Group performance status; LBx, liquid biopsy; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14.

Reference: 1. Paik P, et al. Presented at ASCO Annual Meeting, 2023, Abstract 9060; **2.** Mazieres J, et al. *JAMA Oncol*. 2023;9(9):1260–1266.

Baseline Characteristics by Line of Therapy[1,2]

Cohorts A + C

Nov 2022 cut-off

- Of 313 patients enrolled, median age was 72 years (range 41-94); the majority were T+

Baseline characteristics		Cohorts A+C		
		Overall (N=313)	1L (n=164)	2L+ (n=149)
Median age, years (range)		72.0 (41–94)	74.0 (47–94)	70.8 (41–89)
Sex, n (%)	Male	154 (49.2)	83 (50.6)	71 (47.7)
	Female	159 (50.8)	81 (49.4)	78 (52.3)
Race,* n (%)	White	195 (62.3)	112 (68.3)	83 (55.7)
	Asian	106 (33.9)	50 (30.5)	56 (37.6)
ECOG PS,† n (%)	0	81 (25.9)	45 (27.4)	36 (24.2)
	1	231 (73.8)	118 (72.0)	113 (75.8)
Smoking history,‡ n (%)	Yes	149 (47.6)	88 (53.7)	61 (40.9)
	No	154 (49.2)	75 (45.7)	79 (53.0)
Histology,§ adenocarcinoma, n (%)		252 (80.5)	131 (79.9)	121 (81.2)
***MET*ex14 skipping detection, n (%)**	TBx	208 (66.5)	111 (67.7)	97 (65.1)
	LBx	178 (56.9)	95 (57.9)	83 (55.7)

Note: 'T+' used here denotes 'known TBx positives'

*Nine patients had race reported as "other' or missing or not collected at the site. †One 1L patient was ECOG PS 2. ‡Smoking history was missing in 10 patients (one in 1L and nine in 2L+). §Fifty-nine patients had histologies other than adenocarcinoma (32 in 1L and 27 in 2L+), and two had missing histology information (one each in 1L and 2L+).
1L, first line; 2L+, second-or-later line; ECOG PS, Eastern Cooperative Oncology Group performance status; LBx, liquid biopsy; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; TBx, tissue biopsy; T+, known positive detection of *MET*ex14 skipping in tissue biopsy (TBx).
Reference: 1. Paik P, et al. Presented at ASCO Annual Meeting, 2023, Abstract 9060; **2.** Mazieres J, et al. *JAMA Oncol*. 2023;9(9):1260–1266.

Primary Endpoint: ORR*

Note: 'T+' used here denotes 'known TBx positives'

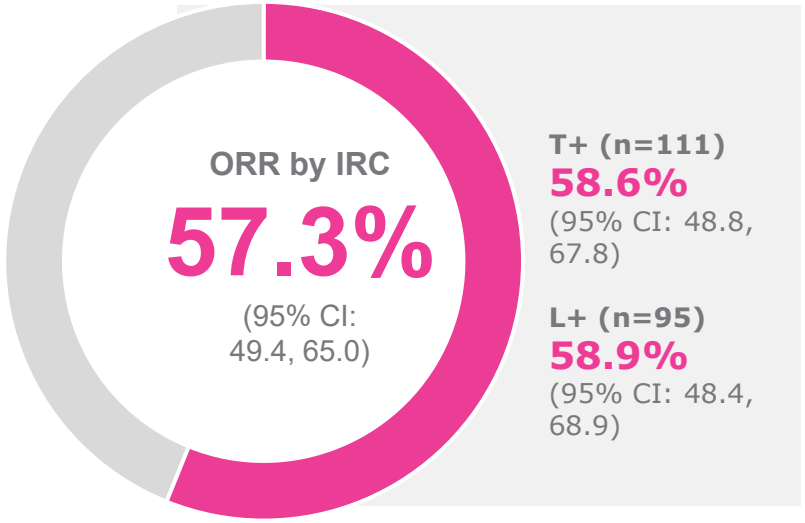
Cohorts A + C

Nov 2022 cut-off

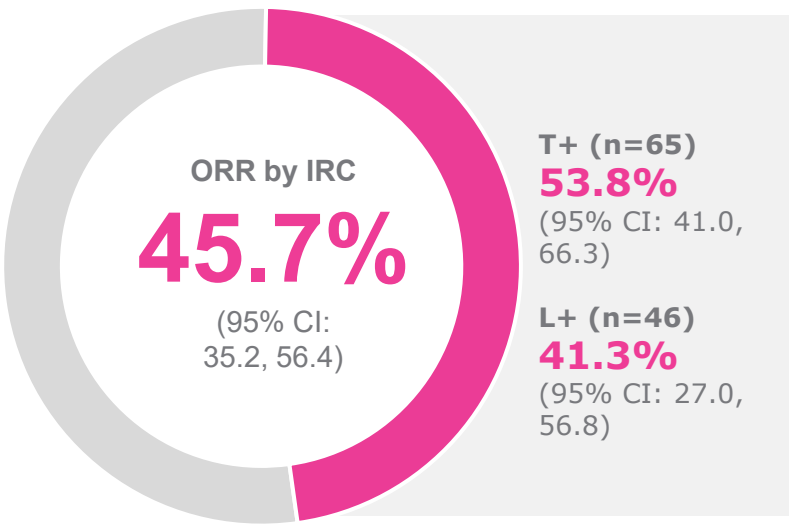
- Overall, ORR was 51.4% (95% CI: 45.8, 57.1). T+ ORR was 54.3% (95% CI: 47.3, 61.2) and L+ ORR was 51.7% (95% CI: 44.1, 59.2)

Previously treated

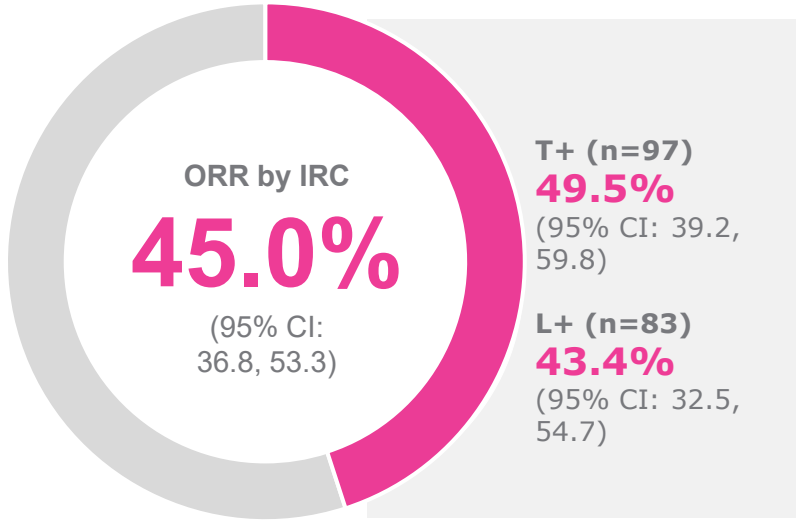
Treatment-naive (n=164)



Second-line tepotinib (1 previous treatment) (n=92)



Second-line+ tepotinib (1 or more previous treatment) (n=149)



Limitation: ORR by biopsy type was a predefined exploratory analysis and should be interpreted with caution

*One treatment-naïve patient had a complete response; all other objective responses were partial responses.
CI, confidence interval; IRC, Independent Review Committee; L+, positive for *MET*ex14 skipping in liquid biopsy; MET, mesenchymal-epithelial transition; *MET*ex14, MET exon 14; ORR, objective response rate; T+, known positive for *MET*ex14 skipping in tissue biopsy; TBx, tissue biopsy.

References: 1. Mazieres J, et al. *JAMA Oncol*. 2023;9(9):1260–1266.

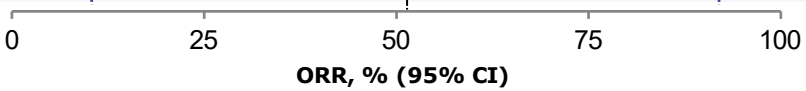
ORR by Baseline Characteristics[1-2]

Cohorts A + C

Nov 2022 cut-off

- ORR was consistent across subgroups irrespective of age, sex, smoking history, and ECOG PS

Subgroup		n	ORR (95% CI)
Overall		313	51.4 (45.8, 57.1)
Sex	Male	154	51.3 (43.1, 59.4)
	Female	159	51.6 (43.5, 59.6)
Age	<75 years	184	54.9 (47.4, 62.2)
	≥75 years	129	46.5 (37.7, 55.5)
Smoking history*	Yes	149	55.7 (47.3, 63.8)
	No	154	47.4 (39.3, 55.6)
Histology†	Adenocarcinoma	252	53.6 (47.2, 59.9)
	Squamous	28	35.7 (18.6, 55.9)
ECOG PS‡	0	81	58.0 (46.5, 68.9)
	1	231	49.4 (42.7, 56.0)
Presence of brain metastases at baseline§	Yes	57	56.1 (42.4, 69.3)
	No	256	50.4 (44.1, 56.7)
Line of therapy	1L	164	57.3 (49.4, 65.0)
	2L	92	45.7 (35.2, 56.4)
	2L+	149	45.0 (36.8, 53.3)



*Smoking history was missing for 10 patients. †Thirty-three patients had histology other than squamous and adenocarcinoma. ‡One patient had ECOG PS 2. §Identified at baseline (investigator or independent review).
1L, first line; 2L, second line; 2L+, second-or-later line; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, objective response rate.

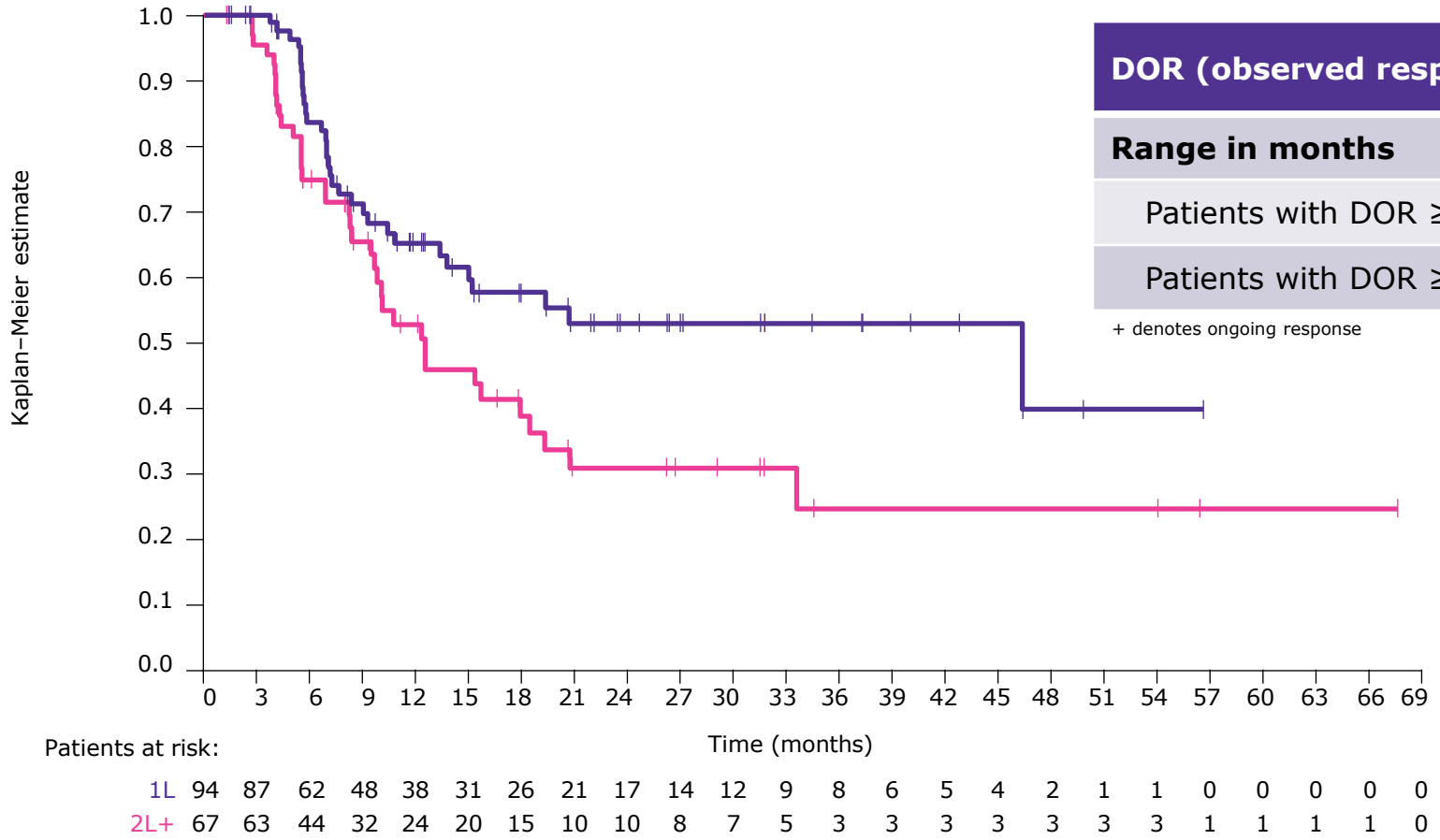
Reference: 1. Paik P, et al. Presented at ASCO Annual Meeting, 2023, Abstract 9060, Supplement; **2.** Mazieres J, et al. *JAMA Oncol*. 2023;9(9):1260–1266.

Secondary Endpoint: DOR

Cohorts A + C

Nov 2022 cut-off

DOR[1,2]*



DOR (observed responses)[3]	1L (n=164)	2L+ (n=149)
Range in months	**1.3+, 56.6+**	**1.4+, 67.6+**
Patients with DOR ≥6 months	66%	66%
Patients with DOR ≥12 months	40%	36%

+ denotes ongoing response

*Only patients with a response were included in Kaplan–Meier analyses.
1L, first line; 2L+, second-or-later line; DOR, duration of response.

Reference: 1. Paik P, et al. Presented at ASCO Annual Meeting, 2023, Abstract 9060, Supplement; **2.** Mazieres J, et al. *JAMA Oncol*. 2023;9(9):1260–1266. **3.** TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

Efficacy with Prior Treatments and Tepotinib[1]

- Outcomes were similar across prior regimens, including platinum-based CT without IO, IO monotherapy, and IO + platinum-based CT
- Compared with prior regimens, outcomes with tepotinib were greatly improved, with an ORR of 45.0% (95% CI: 36.8, 53.3)[2]
  - Tepotinib outcomes were similar between patients treated in 2L and 3L+

Efficacy outcomes	Patients, n	ORR, % (95% CI)*
All prior regimens	149	28.9
Platinum-based CT without IO	99	29.3
IO monotherapy	59	22.0
IO + platinum- based CT	22	22.7
2L+[2]	149	45.0 (36.8, 53.3)
2L[2]	92	45.7 (35.2, 56.4)
3L+	57	43.9 (30.7, 57.6)

Limitation: Efficacy outcomes in prior treatment regimens was not a prespecified endpoint in the VISION trial and this retrospective ad hoc analysis should be interpreted with caution

*95% confidence intervals for ORR calculated only for tepotinib.
2L, second line; 2L+, second-or-later line; 3L+, third-or-later line; CI, confidence interval; CT, chemotherapy; IO, immunotherapy; ORR, objective response rate.
Reference: 1. Viteri S, et al. Presented at ESMO 2023, Poster 1380P; **2**. Mazieres J, et al. *JAMA Oncol*. 2023;9(9):1260–1266.

Overall Safety Profile of Tepotinib

Cohorts A + C

Nov 2022 cut-off

Summary of ARs per prescribing information[1]

- **Fatal ARs** occurred in 1.9% of patients who received tepotinib, including pneumonitis (0.3%), hepatic failure (0.3%), dyspnea from fluid overload (0.3%), pneumonia (0.3%), sepsis (0.3%), and death due to unknown cause (0.3%)
- **Serious ARs** occurred in 51% of patients who received tepotinib
  - Serious ARs in >2% of patients included pleural effusion (6%), pneumonia (6%), edema (5%), general health deterioration (3.8%), dyspnea (3.5%), musculoskeletal pain (2.9%), and pulmonary embolism (2.2%)
- **The most common ARs** (≥20%) in patients who received tepotinib were: edema (81%), nausea (31%), fatigue (30%), musculoskeletal pain (30%), diarrhea (29%), dyspnea (24%), decreased appetite (21%), and rash (21%)
- **The most common Grade 3–4 laboratory abnormalities** (≥2%) were: decreased lymphocytes (15%), decreased albumin (9%), decreased sodium (9%), increased GGT (6%), increased amylase (5%), increased lipase (5%), increased ALT (4.9%), increased AST (3.6%), and decreased hemoglobin (3.6%)

Summary of AEs per VISION study[2]

AEs, n (%)	*MET*ex14 skipping (N=313)	
	All-cause[2]	TRAEs[3]
All grades	310 (99.0)	287 (91.7)
Serious AEs	159 (50.8)	49 (15.7)
Grade ≥3	203 (64.9)	109 (34.8)
Grade ≥4	57 (18.2)	12 (3.8)
Leading to dose reduction	113 (36.1)	105 (33.5)
Leading to treatment interruption	165 (52.7)	135 (43.1)
Leading to permanent discontinuation	78 (24.9)	46 (14.7)
Leading to death*	41 (13.1)	3 (1.0)

*Of the three patients with treatment-related AEs leading to death, two patients were detailed in Le X et al. *Clin Cancer Res*. 2022;28(6):1117-1126, and the third patient had progressive disease or a lung cancer-related condition leading to multiple organ failure, which was considered treatment-related due to a missing causality report

Safety population comprised all patients from VISION Cohorts A and C who received at least one dose of tepotinib (data cut-off: November 20, 2022).

AE, adverse event; ALT, alanine aminotransferase; AR, adverse reaction; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; TRAE, treatment-related adverse event.

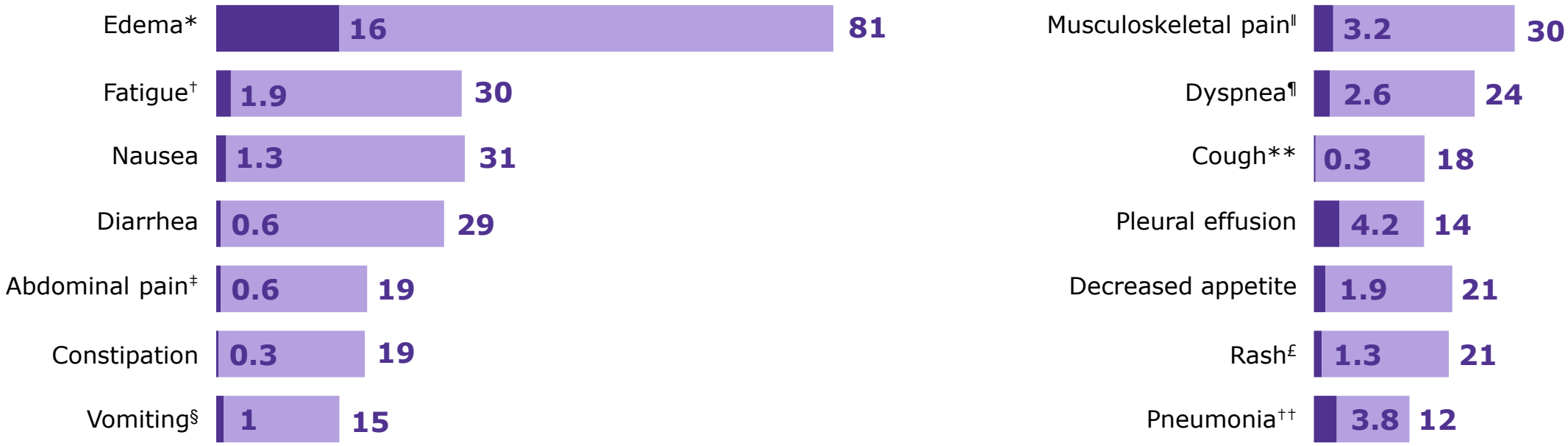
Reference: 1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf; **2.** Mazieres J, et al. *JAMA Oncology*. 2023;9(9):1260-1266.

ARs

Cohorts A + C

Nov 2022 cut-off

- Adverse reactions in ≥10% of patients with NSCLC with *MET*ex14 skipping alterations who received tepotinib in VISION[1]



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

*Includes eye edema, face edema, generalized edema, localized edema, edema, genital edema, peripheral edema, peripheral swelling, periorbital edema, and scrotal edema; †Includes asthenia and fatigue; ‡Includes abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper, gastrointestinal pain, and hepatic pain; §Vomiting includes retching and vomiting; ‖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; ¶Includes dyspnea, dyspnea at rest, and dyspnea exertional; **Includes cough and productive cough; £Includes rash, palmar-plantar erythrodysaesthesia syndrome, rash maculo-papular, eczema, exfoliative rash, rash erythematous, rash pustular, skin exfoliation, dermatitis acneiform, drug eruption, dermatitis, rash pruritic, dermatitis bullous, toxic skin eruption; ††Includes pneumonia, pneumonia aspiration, and pneumonia bacterial. AR, adverse reaction; ILD, interstitial lung disease; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer.

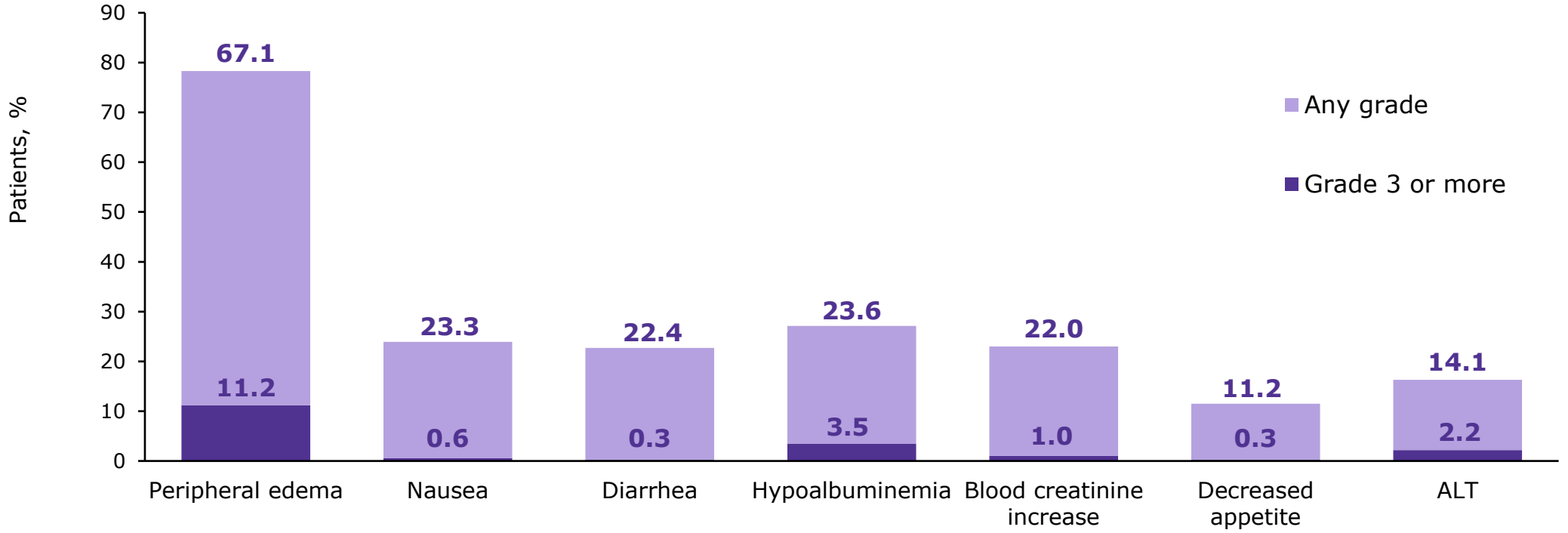
Reference: 1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

TRAEs

Cohorts A + C

Nov 2022 cut-off

- TRAEs occurring in ≥10% of patients with *MET*ex14 skipping NSCLC who received tepotinib in VISION[1]



- Peripheral edema was the most commonly occurring TRAE

ALT, Alanine transaminase increase; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer; TRAE, treatment-related adverse event.

Reference: 1. Mazieres J, et al. *JAMA Oncology*. 2023;9(9):1260-1266.

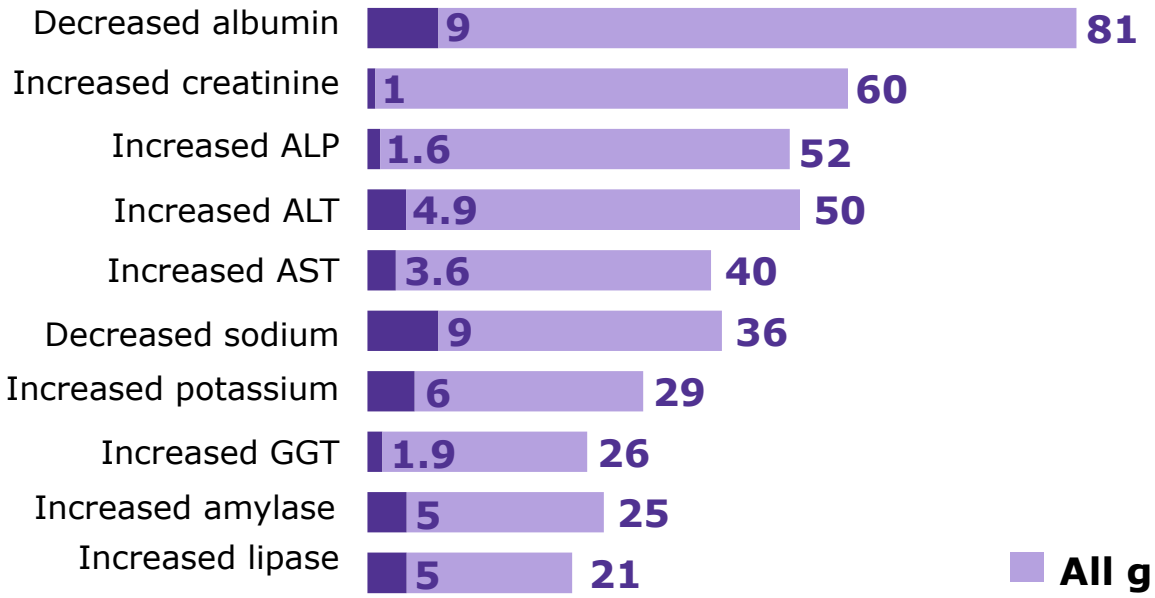
Laboratory Abnormalities

Cohorts A + C

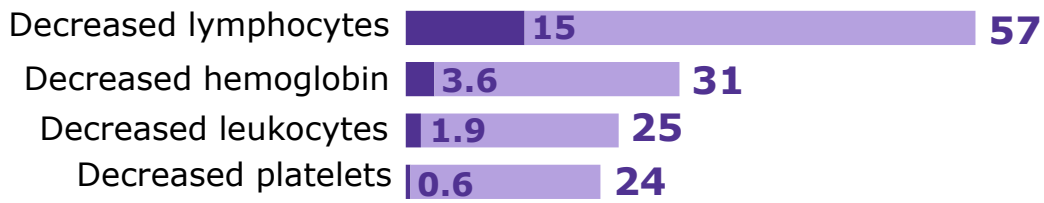
Nov 2022 cut-off

- Select laboratory abnormalities (≥20%) that worsened from baseline in patients who received tepotinib in VISION*[1]

Chemistry



Hematology



All grades (%) Grades 3–4 (%)

- Decreased albumin was the most commonly occurring laboratory abnormality

*The denominator used to calculate the rate varied from 268 to 309 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: 1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

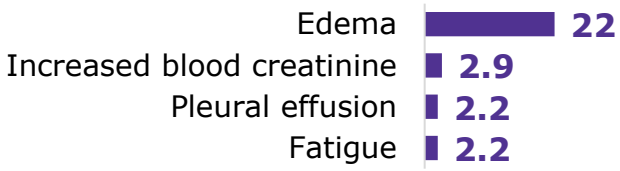
Permanent discontinuations, dosage interruptions, dose reductions, and dose modifications for ARs[1]

Cohorts A + C

Nov 2022 cut-off

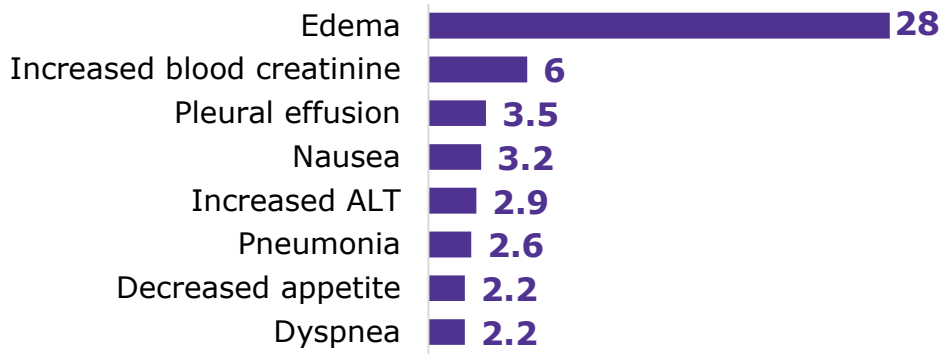
Dose reductions (Overall 36%)

ARs that required dose reductions in >2% of patients who received tepotinib (%)



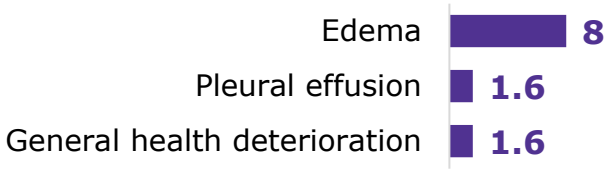
Dosage interruptions (Overall 53%)

ARs that required dosage interruption in >2% of patients who received tepotinib (%)



Permanent discontinuation (Overall 25%)

Most frequent ARs (>1%) leading to permanent discontinuation of tepotinib (%)



Dose modifications for ARs[1]

- Management of some ARs may require temporary withhold, dose reduction, or permanent discontinuation
- 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
- See the full prescribing information for recommended dosage modifications of tepotinib

Data cut-off: Nov 20, 2022 (N=313).

AR, adverse reaction; ALT, alanine aminotransferase.

Reference: 1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

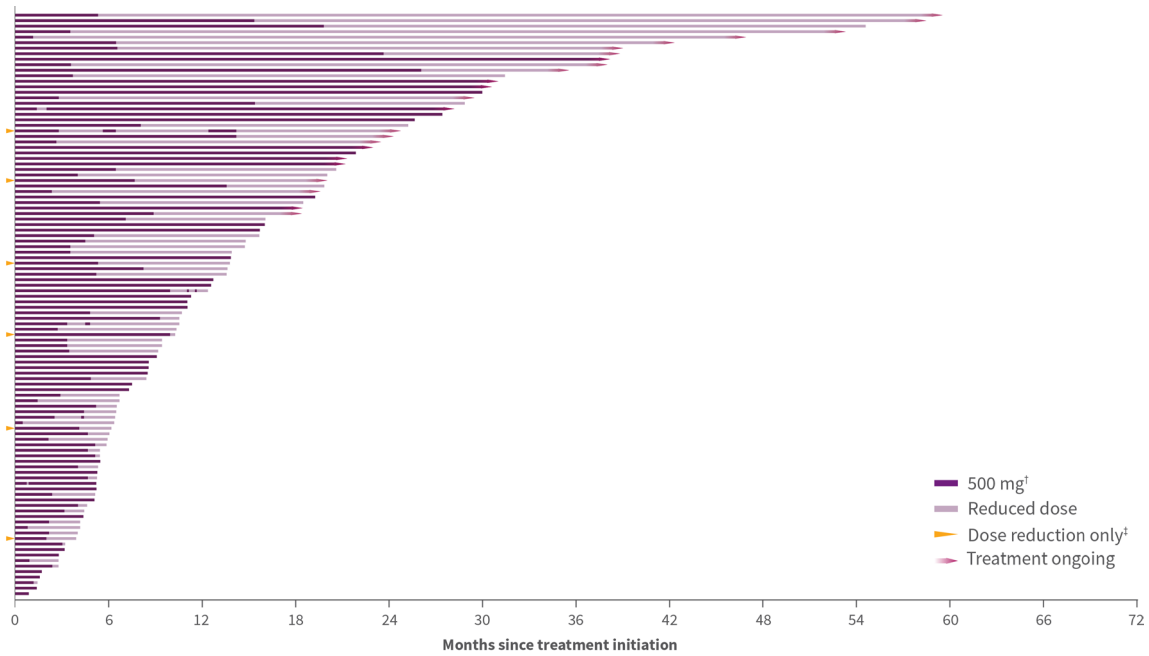
Safety

Cohorts A + C

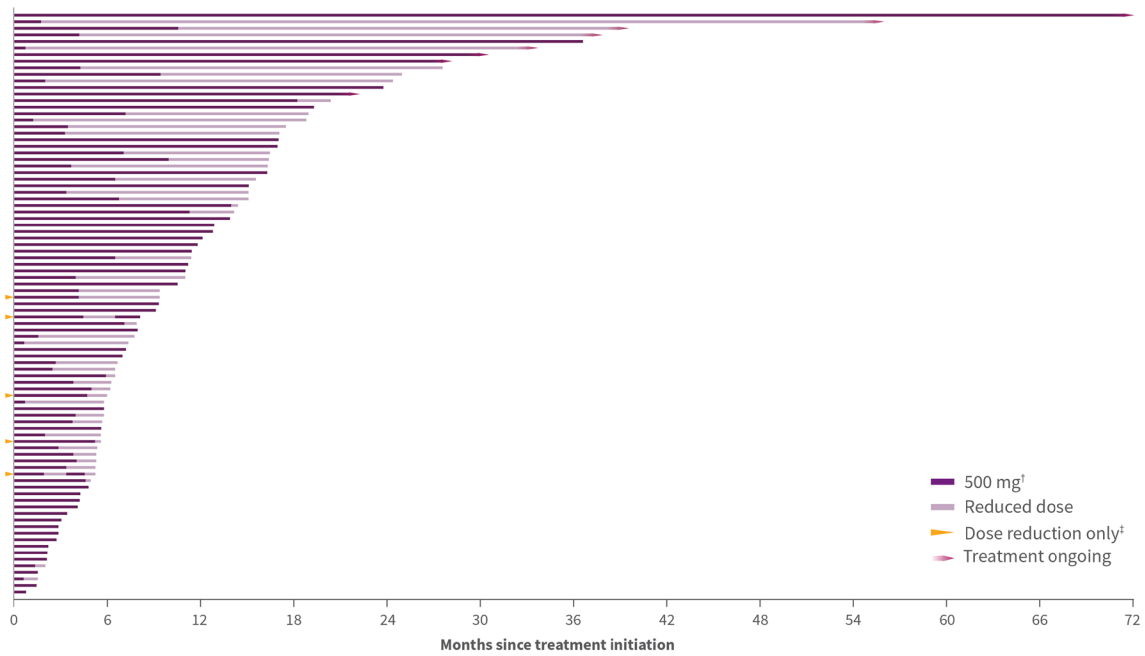
Nov 2022 cut-off

- Patients requiring treatment interruptions and dose reductions were able to continue treatment with tepotinib[1]

Time on treatment in treatment-naïve patients with dose reductions and/or interruptions (n=106)*



Time on treatment in previously treated patients with dose reductions and/or interruptions (n=89)*



Median duration of treatment

- 7.5 months (range: 0.03-71.9) across all treatment-naïve and previously treated patients (N=313)
- 10.7 months (range: 0.7-71.9) in both treatment-naïve and previously treated patients with dose reductions and/or interruptions (n=195)

*Of total patients, 116 patients (37.1%) had dose reductions, and 184 patients (58.8%) had treatment interruptions. †450 mg active moiety. ‡All other patients had ≥1 treatment interruptions.

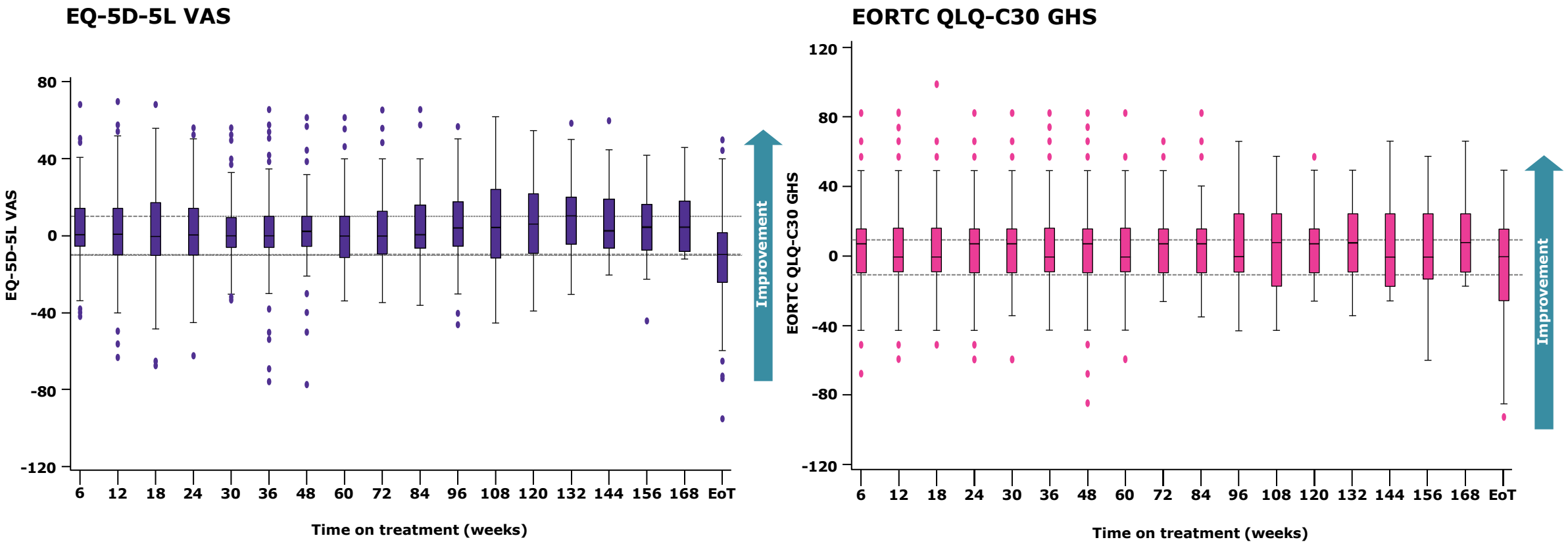
Reference: 1. Paik P, et al. ASCO 2023 | June 2–6, 2023 | Chicago, Illinois. Abstract 9060.

Overall HRQoL

Cohorts A + C

Nov 2022 cut-off

- EQ-5D-5L VAS and EORTC QLQ-C30 GHS scores over time*



Limitation: QoL was a predefined exploratory analysis and should be interpreted with caution in a single-arm study

*Visits with <10 patients are not presented, with the exception of the EoT/30-day safety follow-up. Dashed lines show minimal clinically important difference of +/– 10 points.
EORTC, European Organization for Research and Treatment of Cancer; EoT, end of treatment; EQ-5D-5L VAS, EuroQol Five-Dimension Five-Level Visual Analogue Scale; GHS, global health status; HRQoL, health-related quality of life; QLQ-C30, Quality of Life Questionnaire Core 30; QoL, quality of life.
Reference: Paik P, et al. Presented at ASCO Annual Meeting, 2023, Abstract 9060, Supplement.

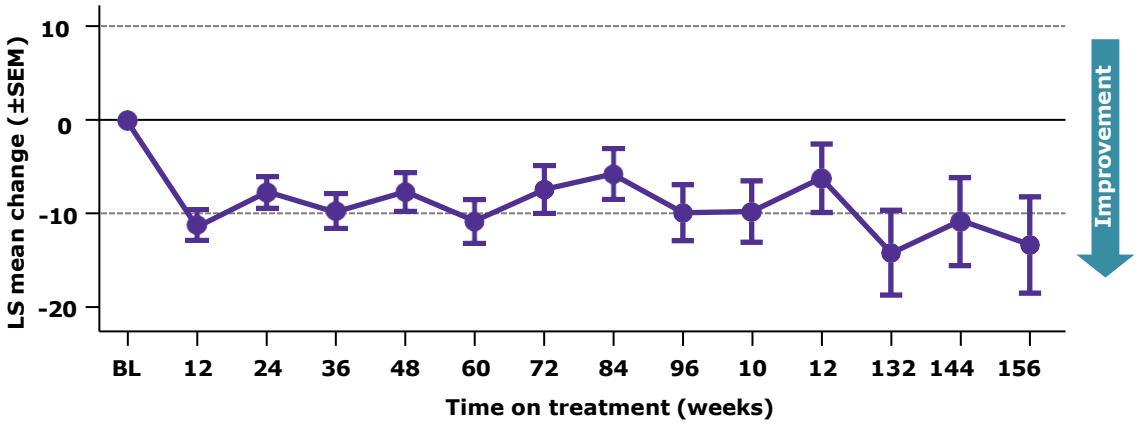
HRQoL by Symptom Scale

Cohorts A + C

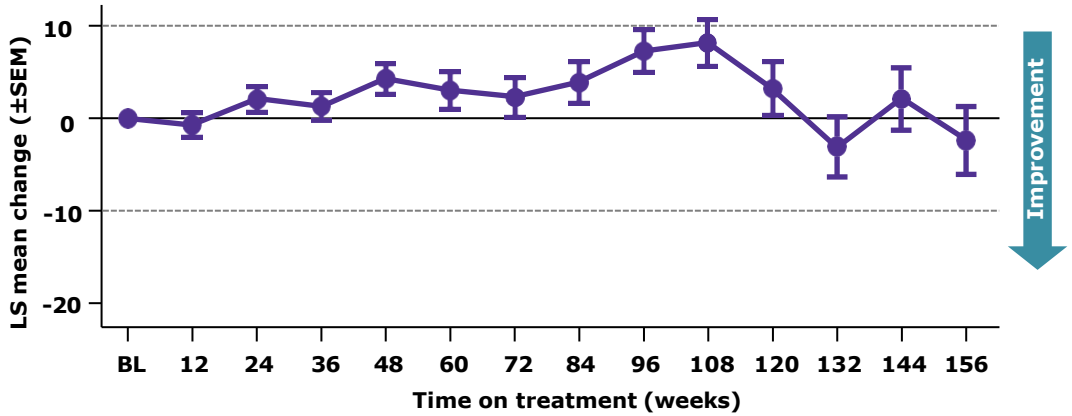
Nov 2022 cut-off

- LS mean change from baseline in EORTC QLQ LC-13 symptom scales†

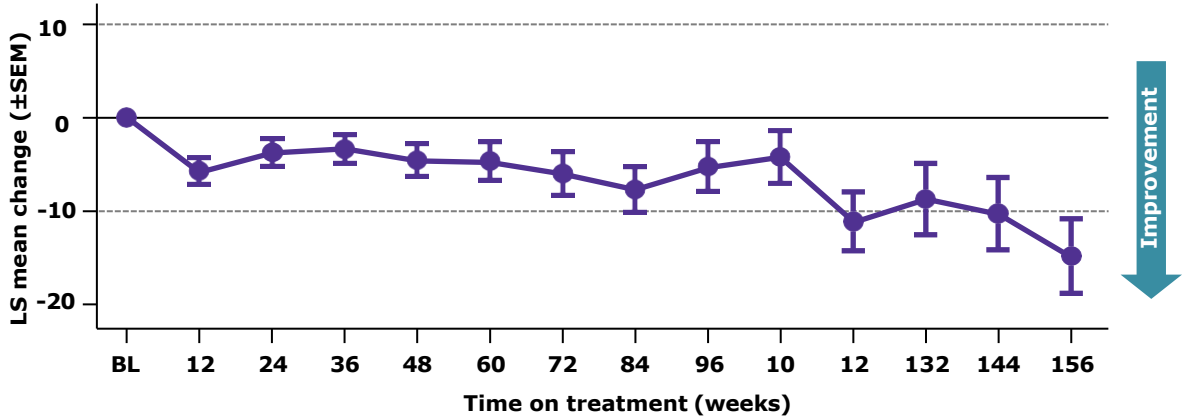
Cough



Dyspnea



Chest pain



Limitation: QoL was a predefined exploratory analysis and should be interpreted with caution in a single-arm study

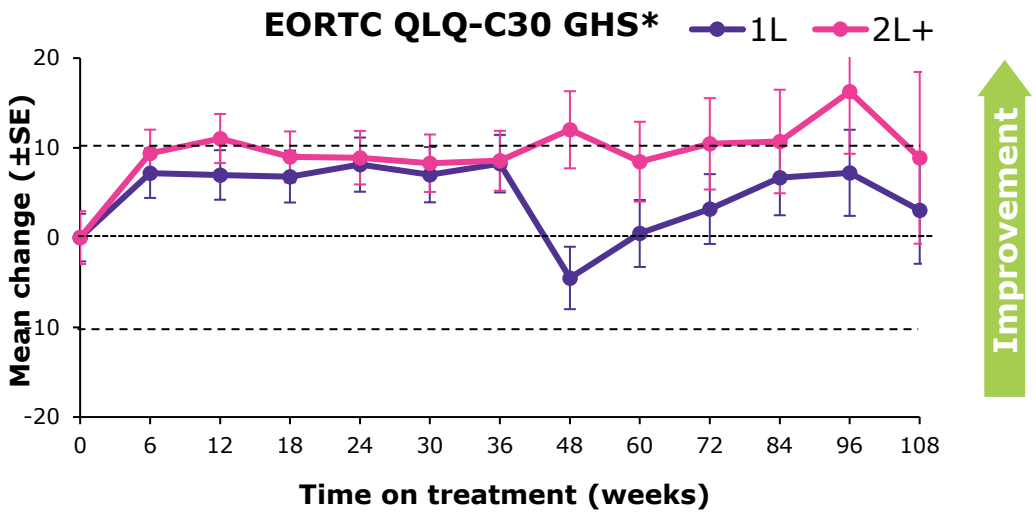
†Visits with <10 patients are not presented. Dashed lines show minimal clinically important difference of +/− 10 points.
EORTC, European Organization for Research and Treatment of Cancer; HRQoL, health-related quality of life; LS, least square; QLQ-LC13, Quality of Life Questionnaire–Lung Cancer 13; QoL, quality of life; SEM, standard error of the mean.
Reference: Paik P, et al. Presented at ASCO Annual Meeting, 2023, Abstract 9060, Supplement.

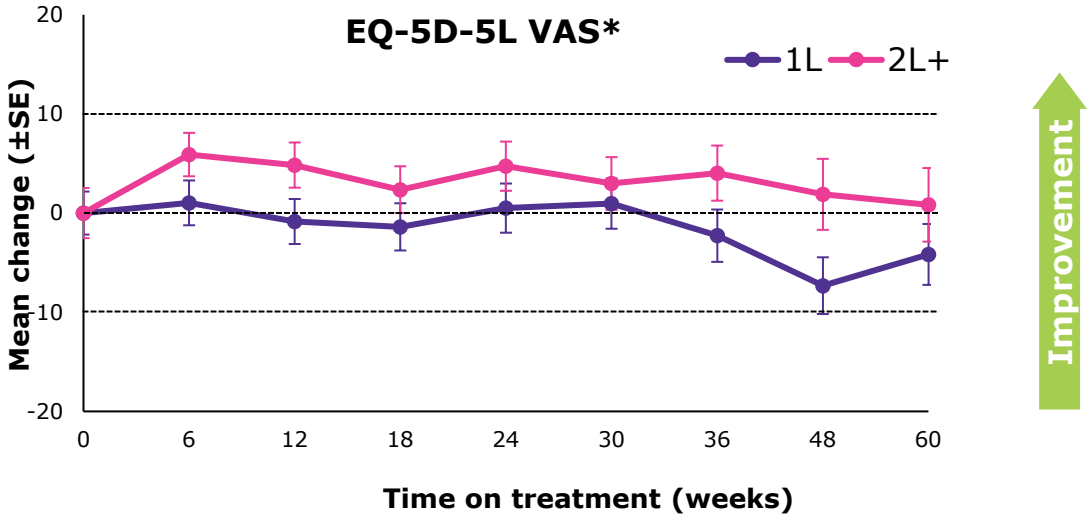
Overall HRQoL in Asian Patients

Cohorts A + C

Nov 2022 cut-off

- EORTC QLQ-C30 GHS[1] and EQ-5D-5L VAS[2] scores during treatment





Limitation: QoL was a predefined exploratory analysis and should be interpreted with caution in a single-arm study

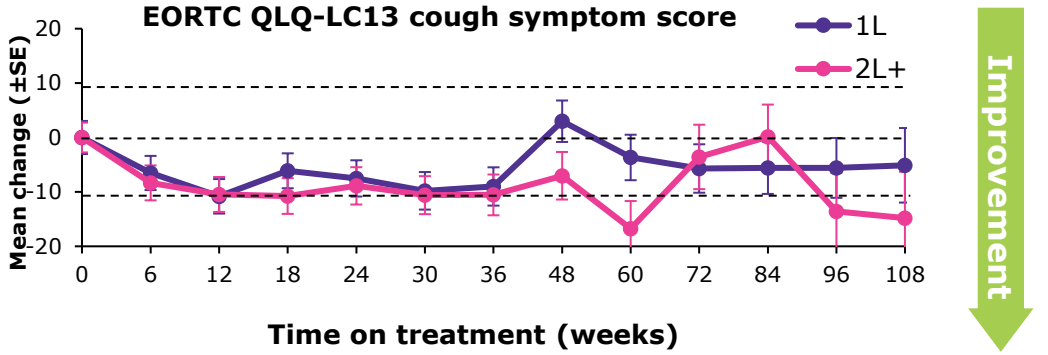
*Higher scores indicate greater function (scale 0–100). †Overall, 100 Asian patients across treatment completed the EORTC QLQ-C30 GHS and EQ-5D-5L VAS; however, there were no baseline PRO score observations for one patient. Dashed lines show minimal clinically important difference of +/– 10 points.
1L, first line; 2L+, second-or-later line; EORTC, European Organization for Research and Treatment of Cancer; EQ-5D-5L VAS, EuroQol Five-Dimension Five-Level Visual Analogue Scale; GHS, global health status; HRQoL, health-related quality of life; QLQ-C30, quality of Life Questionnaire Core 30; QoL, quality of life; SE, standard error.
Reference: 1. Ahn M-J, et al. Presented at WCLC 2023. Poster P2.11-02. **2.** Ahn M-J, et al. Presented at WCLC 2023. Poster P2.11-02, Supplement.

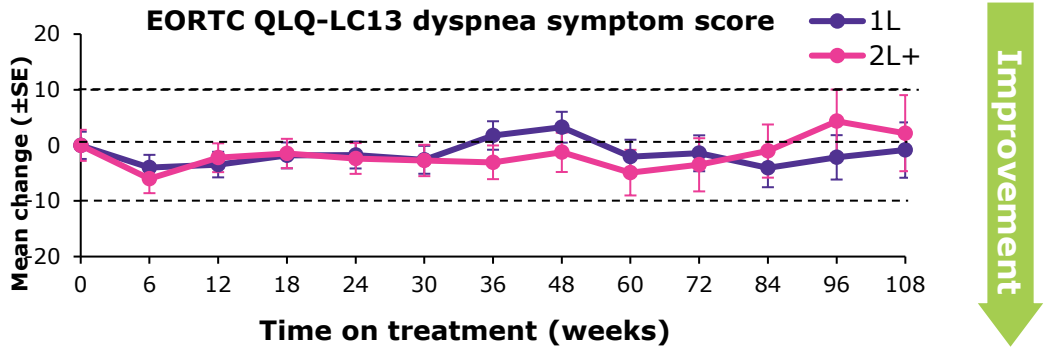
HRQoL by Symptom Scale in Asian Patients

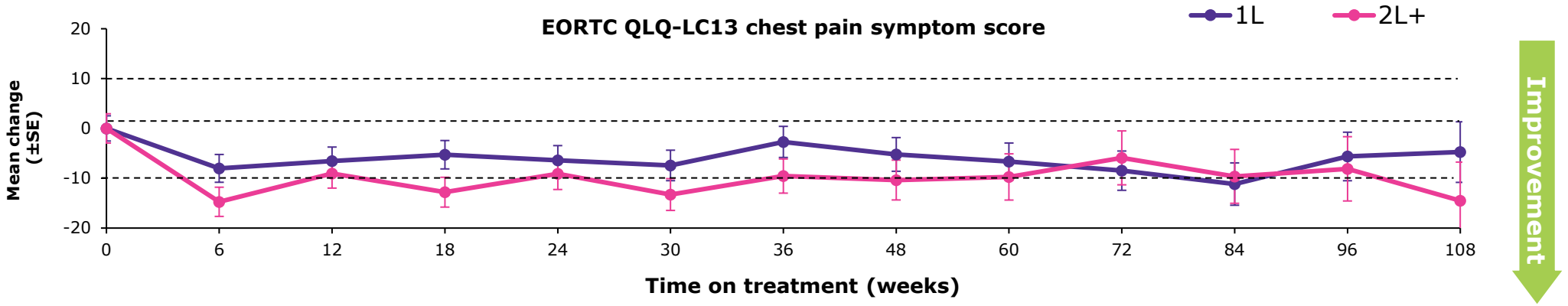
Cohorts A + C

Nov 2022 cut-off

- EORTC QLQ-LC13* symptom scores in cough, dyspnea, and chest pain







Limitation: QoL was a predefined exploratory analysis and should be interpreted with caution in a single-arm study

*EORTC QLQ LC13 symptom score - lower scores indicate milder symptoms (scale 0–100). †Overall, 100 Asian patients across treatment completed the EORTC QLQ LC13 symptom score; however, there were no baseline PRO score observations for one patient. Dashed lines show minimal clinically important difference of +/– 10 points.
1L, first line; 2L+, second-or-later line; EORTC, European Organization for Research and Treatment of Cancer; HRQoL, health-related quality of life; LS, least square; QLQ-LC13, Quality of Life Questionnaire–Lung Cancer 13; QoL, quality of life; SE, standard error.
Reference: Ahn M-J, et al. Presented at WCLC 2023. Poster P2.11-02.

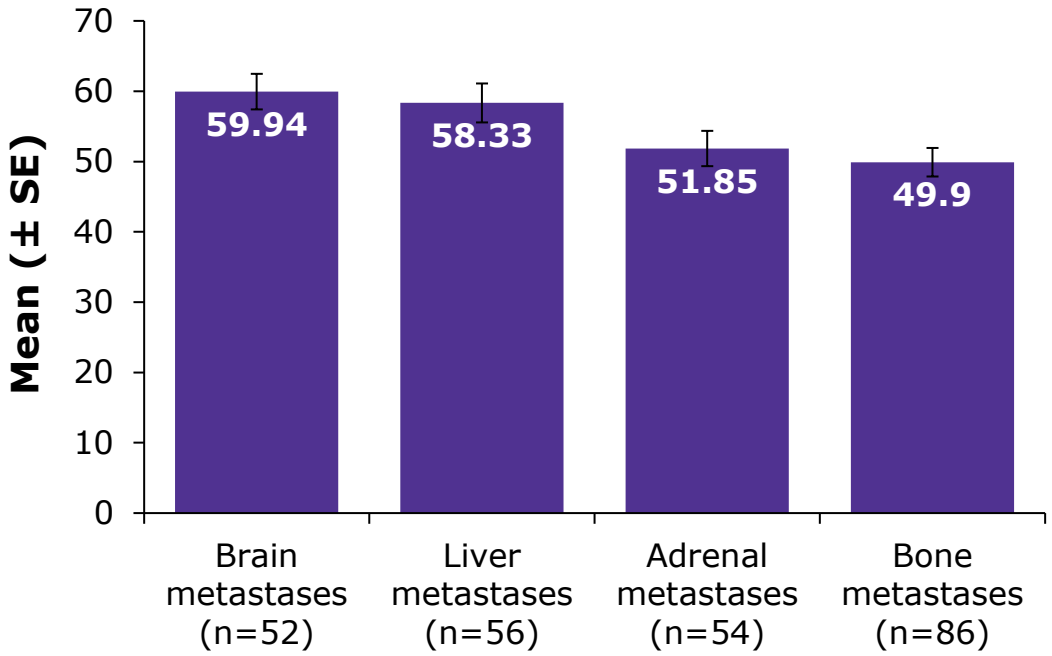
Baseline HRQoL by Metastatic site

Cohorts A + C

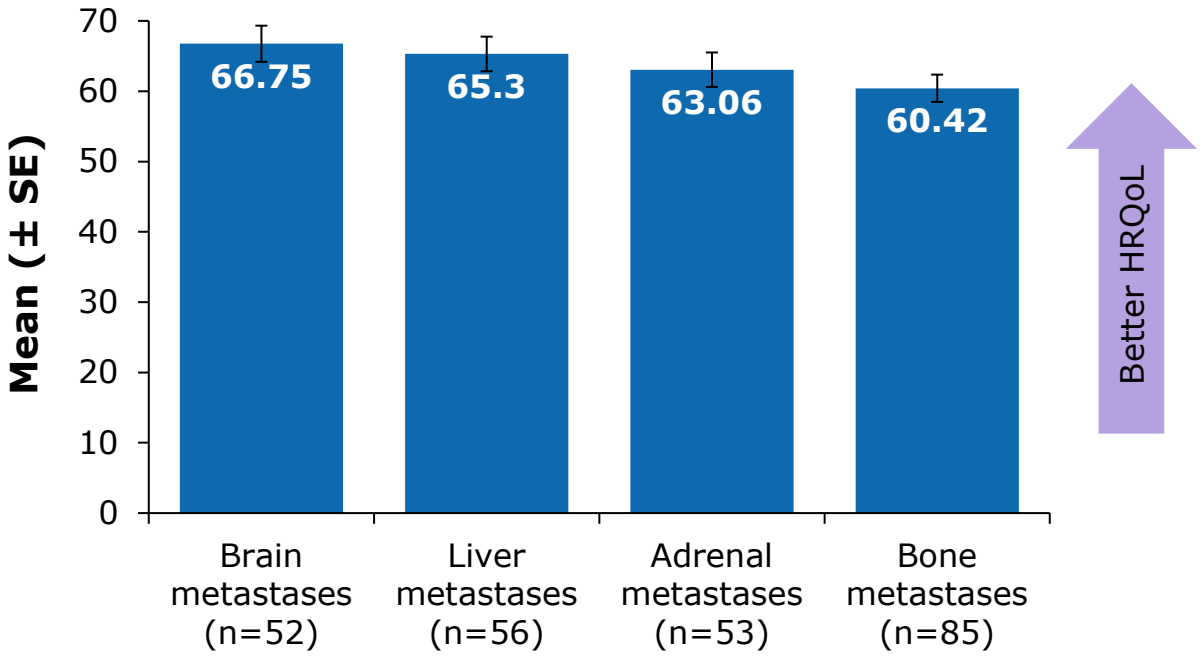
Nov 2022 cut-off

- Baseline HRQoL scores were available for 52 patients with brain metastases, 56 with liver metastases, 54 with adrenal metastases (53 for EQ-5D-5L VAS), and 86 with bone metastases (85 for EQ-5D-5L VAS)

A. EORTC QLQ-C30 GHS



B. EQ-5D-5L VAS



Limitation: QoL was a predefined exploratory analysis and should be interpreted with caution in a single-arm study

EORTC, European Organization for Research and Treatment of Cancer; EQ-5D-5L, European Quality of Life five-dimension five-level; GHS, Global Health Status; HRQoL, health-related quality of life; QLQ-C30, Quality of Life Questionnaire Core 30; QoL, quality of life; SE, standard error; VAS, visual analog scale

Reference: Reinmuth N, et al. Presented at ASCO 2024. Abstract 8575.

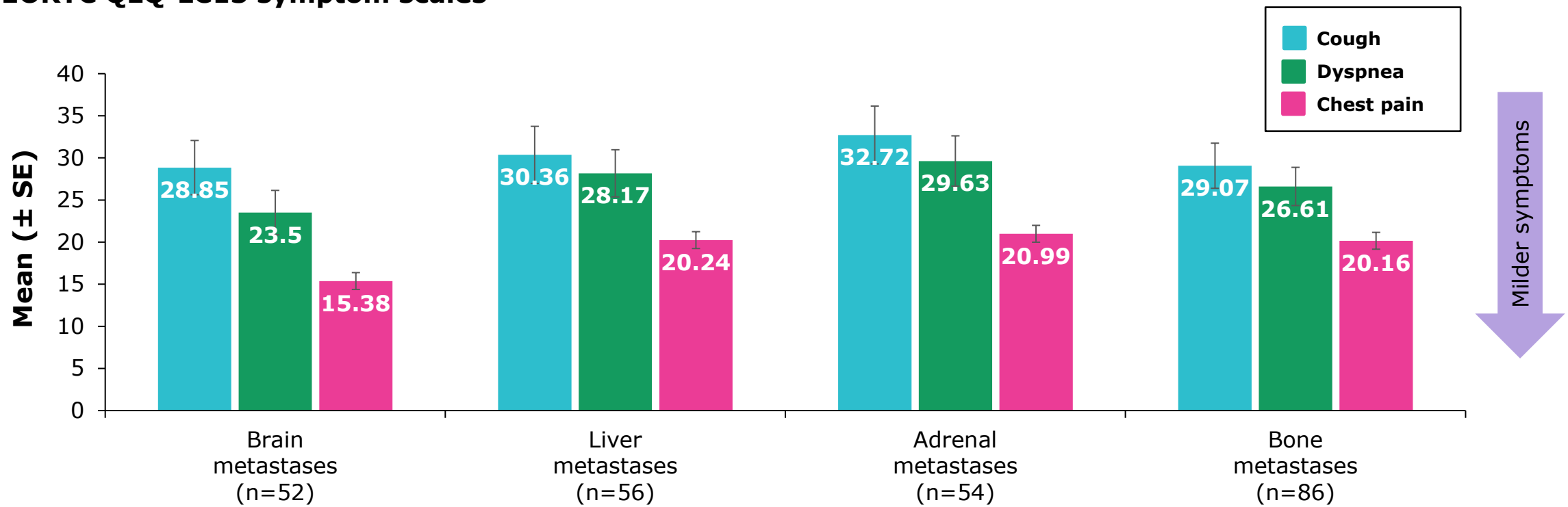
Baseline HRQoL by Metastatic site

Cohorts A + C

Nov 2022 cut-off

- Cough, dyspnea, and chest pain were most severe in patients with adrenal metastases, followed by patients with liver, bone, and brain metastases

EORTC QLQ-LC13 symptom scales



Limitation: QoL was a predefined exploratory analysis and should be interpreted with caution in a single-arm study

EORTC, European Organization for Research and Treatment of Cancer; HRQoL, health-related quality of life; QLQ-LC13, Quality of Life-Lung Cancer 13; QoL, quality of life; SE, standard error.

Reference: Reinmuth N, et al. Presented at ASCO 2024. Abstract 8575.

Change from Baseline in HRQoL Scores

Cohorts A + C

Nov 2022 cut-off

- Mean change from baseline across all visits in overall HRQoL in patients with brain, liver, adrenal, or bone metastases during tepotinib treatment

Mean ± SE change from baseline in HRQoL scores across all visits

	EORTC QLQ-C30 GHS	EQ-5D-5L VAS	EORTC QLQ-LC13		
			Cough	Dyspnea	Chest pain
Brain metastases (n=52)	0.91 ± 2.41	−1.38 ± 1.95	−8.34 ± 2.62	−3.20 ± 2.04	−4.52 ± 2.12
Liver metastases (n=56)	2.10 ± 2.27	−0.18 ± 2.11	−6.73 ± 2.31	−0.32 ± 1.92	−5.02 ± 1.84
Adrenal metastases (n=54)*	3.69 ± 2.60	−0.48 ± 2.25	−7.33 ± 2.90	−1.27 ± 1.77	−8.07 ± 2.70
Bone metastases (n=86)†	6.92 ± 2.11	0.09 ± 1.69	−7.10 ± 2.04	−0.12 ± 1.66	−4.76 ± 1.88

Limitation: QoL was a predefined exploratory analysis and should be interpreted with caution in a single-arm study

*Baseline HRQoL scores were available for 53 patients for EQ-5D-5L VAS. †Baseline HRQoL scores were available for 85 patients for EQ-5D-5L VAS
EORTC, European Organization for Research and Treatment of Cancer; EQ-5D-5L, European Quality of Life five-dimension five-level; GHS, Global Health Status; HRQoL, health-related quality of life; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-LC13, Quality of Life-Lung Cancer 13; QoL, quality of life; SE, standard error; VAS, visual analog scale
Reference: Reinmuth N, et al. Presented at ASCO 2024. Abstract 8575.

SUMMARY

Summary

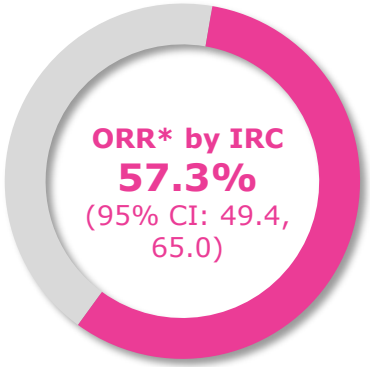
Cohorts A + C

Nov 2022 cut-off

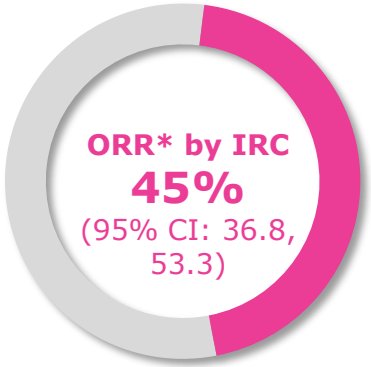
VISION: A single-arm, open-label, multicenter, non-randomized, multicohort study[1]

Response by previous treatment status (N=313)[2-4]

Treatment naive (n=164)



Previously treated (n=149)



DOR (observed responses)[1]	Treatment naive (n=164)	Previously treated (n=149)
Range in months	**1.3+, 56.6+**	**1.4+, 67.6+**
Patients with DOR ≥6 months	66%	66%
Patients with DOR ≥12 months	40%	36%

\+ denotes ongoing response

- The most common ARs (≥10%) in patients who received tepotinib were edema, hypoalbuminemia, nausea, diarrhea, increased blood creatinine, increased ALT, and decreased appetite[3,4]

- TEPMETKO® (tepotinib) is indicated for the treatment of adult patients with metastatic NSCLC harboring *MET*ex14 skipping alterations[1]
- The recommended dosage of tepotinib is 450 mg (two 225 mg tablets) orally once daily with food until disease progression or unacceptable toxicity

*One treatment-naïve patient had a complete response; all other objective responses were partial responses.
ALT, alanine aminotransferase; AR, adverse reaction; CI, confidence interval; DOR, duration of response; IRC, Independent Review Committee; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer; ORR, objective response rate.

References: 1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf; **2.** Paik P, et al. Presented at ASCO Annual Meeting, 2023, Abstract 9060; **3.** Paik P, et al. Presented at ASCO Annual Meeting, 2023, Abstract 9060, Supplement; **4.** Mazieres J, et al. *JAMA Oncol*. 2023;9(9):1260–1266.

APPENDIX

EFFICACY BY KNOWN T+ AND/OR L+ STATUS AND ctDNA BURDEN (NOVEMBER 2022 & 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.

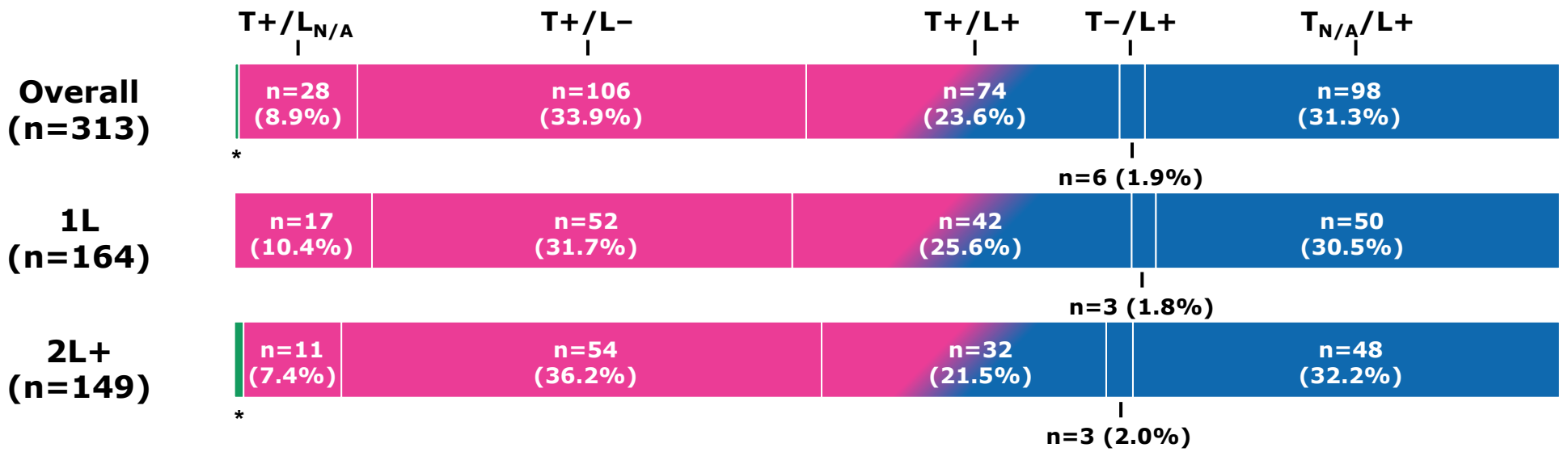
For these reasons, results from this analysis should be interpreted with caution.

Detection of *MET*ex14 Skipping in TBx and LBx Patients

Cohorts A + C

Nov 2022 cut-off

- Of 313 patients enrolled, 208 (66.5%) were T+ and 178 (56.9%) were L+
- A total of 186 patients (59.4%) had matched TBx and LBx results; 106 were T+/L– (33.9%), 74 were T+/L+ (23.6%), and six were T–/L+ (1.9%)



Note: 'T+' used here denotes 'known TBx positives'

*One patient (0.3%) was enrolled based on local testing (without central confirmation) in a protocol violation.
1L, first line; 2L+, second-or-later line; L–, negative for *MET*ex14 skipping in liquid biopsy; L+, positive for *MET*ex14 skipping in liquid biopsy; LBx, liquid biopsy; $L_{N/A}$, *MET*ex14 skipping result from liquid biopsy not available; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; T–, negative for *MET*ex14 skipping in tissue biopsy; T+, known positive for *MET*ex14 skipping in tissue biopsy; TBx, tissue biopsy; $T_{N/A}$, *MET*ex14 skipping result from tissue biopsy not available.
Reference: Rolfo C, et al. Presented at ESMO, 2023, Poster 1382P.

Baseline Characteristics in T+ and L+ Patients

Cohorts A + C

Nov 2022 cut-off

- Overall, baseline demographics were broadly comparable between T+ and L+ patients

		T+ (n=208)	L+ (n=178)
Median age, years (range)		72.7 (41–94)	71.2 (47–89)
Female, n (%)		100 (48.1)	95 (53.4)
Race, n (%)*	White Asian	120 (57.7) 83 (39.9)	123 (69.1) 48 (27.0)
Geographic region, n (%)	North America Europe Asia	33 (15.9) 88 (42.3) 87 (41.8)	37 (20.8) 93 (52.2) 48 (27.0)
Current/former smokers, n (%)†		98 (47.1)	84 (47.2)
ECOG PS, n (%)‡	0 1	57 (27.4) 150 (72.1)	42 (23.6) 136 (76.4)
Adenocarcinoma, n (%)§		170 (81.7)	143 (80.3)
Median time since diagnosis, years (range)‖		0.25 (0.01–25.26)	0.24 (−0.02¶–4.44)

Note: 'T+' used here denotes 'known TBx positives'

*Race was Black or African American in three patients, 'other' in one patient and missing in eight patients. †Smoking history was missing in 10 patients. ‡ECOG PS was 2 in one patient. §Histology was missing in two patients. ‖Median time since initial cancer diagnosis. ¶One patient provided informed consent for prescreening shortly before formal NSCLC diagnosis.
ECOG PS, Eastern Cooperative Oncology Group performance status; L+, positive for *MET*ex14 skipping in liquid biopsy; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer; T+, known positive for *MET*ex14 skipping in tissue biopsy (TBx).
Reference: Rolfo C, et al. Presented at ESMO, 2023, Poster 1382P.

Baseline Characteristics in T+ and L+ by Line of Therapy

Cohorts A + C

Nov 2022 cut-off

- Baseline demographics were broadly comparable between 1L and 2L+ subgroups

		1L (n=164)		2L+ (n=149)	
		T+ (n=111)	L+ (n=95)	T+ (n=97)	L+ (n=83)
Median age, years (range)		75.0 (47–94)	71.6 (47–88)	70.3 (41–89)	70.8 (49–89)
Female, n (%)		52 (46.8)	49 (51.6)	48 (49.5)	46 (55.4)
Race, n (%)*	White Asian	68 (61.3) 42 (37.8)	73 (76.8) 21 (22.1)	52 (53.6) 41 (42.3)	50 (60.2) 27 (32.5)
Geographic region, n (%)	North America Europe Asia	16 (14.4) 49 (44.1) 46 (41.4)	19 (20.0) 54 (56.8) 22 (23.2)	17 (17.5) 39 (40.2) 41 (42.3)	18 (21.7) 39 (47.0) 26 (31.3)
Current/former smokers, n (%)†		58 (52.3)	50 (52.6)	40 (41.2)	34 (41.0)
ECOG PS, n (%)‡	0 1	32 (28.8) 78 (70.3)	23 (24.2) 72 (75.8)	25 (25.8) 72 (74.2)	19 (22.9) 64 (77.1)
Adenocarcinoma, n (%)§		90 (81.1)	77 (81.1)	80 (82.5)	66 (79.5)
Median time since diagnosis, years (range)‖		0.10 (0.02–25.26)	0.10 (−0.02¶– 4.38)	0.78 (0.01–15.59)	0.76 (0.02–4.44)

Note: 'T+' used here denotes 'known TBx positives'

*Race was Black or African American in three patients, 'other' in one patient and missing in eight patients. †Smoking history was missing in 10 patients. ‡ECOG PS was 2 in one patient. §Histology was missing in two patients. ‖Median time since initial cancer diagnosis. ¶One patient provided informed consent for prescreening shortly before formal NSCLC diagnosis.
1L, first line; 2L+, second-or-later line; ECOG PS, Eastern Cooperative Oncology Group performance status; L+, positive for *MET*ex14 skipping in liquid biopsy; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer; T+, known positive for *MET*ex14 skipping in tissue biopsy (TBx).
Reference: Rolfo C, et al. Presented at ESMO, 2023, Poster 1382P, Supplement.

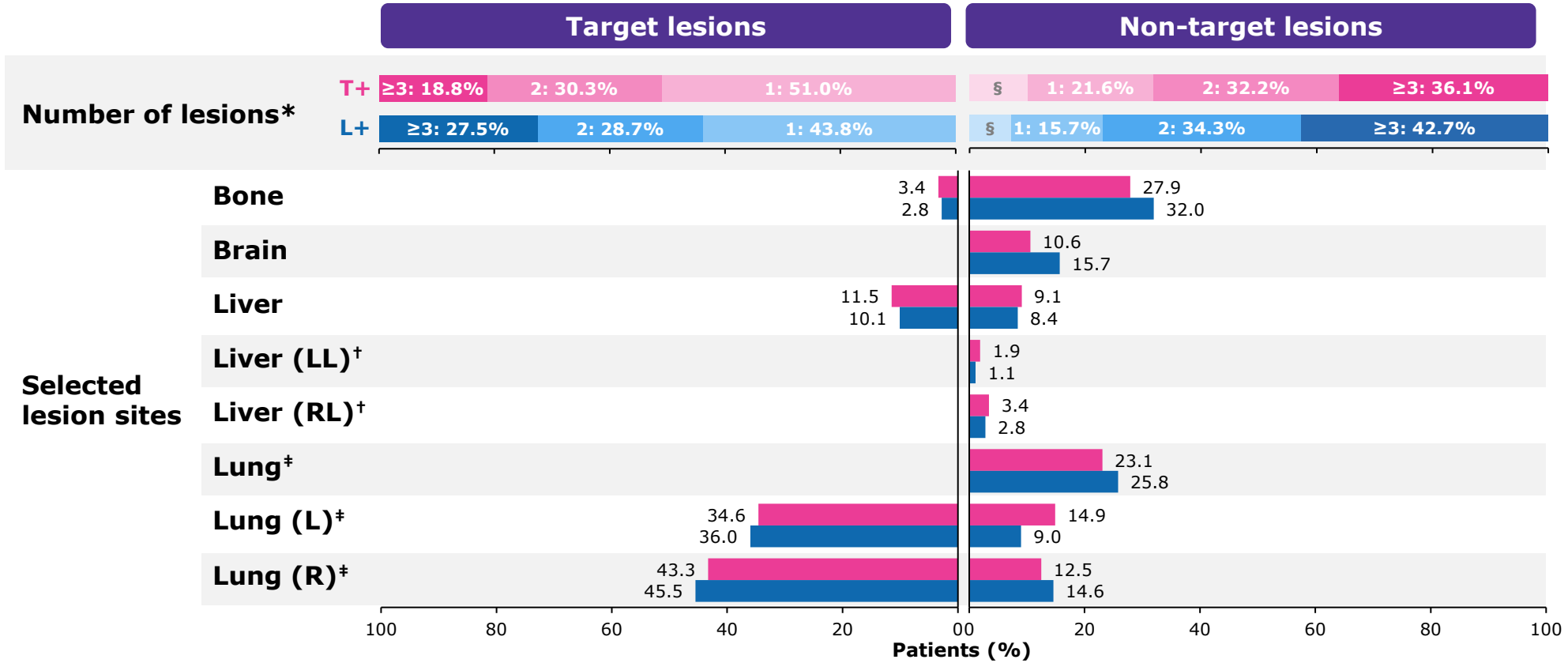
Disease Burden at Baseline in T+ and L+ Patients

Cohorts A + C

Nov 2022 cut-off

- T+ patients had a lower disease burden than L+ patients with lower median SOLD per RECIST v1.1, and fewer patients with ≥3 target lesions or ≥3 non-target lesions

	Median SOLD per RECIST v1.1, mm (range)
T+ (n=208)	55.2 (10.2–267.5)
L+ (n=178)	67.1 (11.6–227.8)



Note: 'T+' used here denotes 'known TBx positives'

*Target and non-target lesions by IRC. †'Liver (LL)' and 'liver (RL)' categories were not included for target lesions. ‡Lung lesion site was categorized as 'lung', 'lung (L)', or 'lung (R)' for target and non-target lesions, but no target lesions were reported in the overall 'lung' category. §No non-target lesions were reported for 10.1% of T+ patients and 7.3% of L+ patients.
L+, positive for *MET*ex14 skipping in liquid biopsy; RECIST, Response Evaluation Criteria in Solid Tumors; SOLD, sum of lesion diameters; T+, known positive for *MET*ex14 skipping in tissue biopsy (TBx).
Reference: Rolfo C, et al. Presented at ESMO, 2023, Poster 1382P.

Baseline HRQoL in T+ and L+ Patients

Cohorts A + C

Nov 2022 cut-off

- At baseline, T+ patients had better HRQoL than L+ patients with higher EORTC QLQ-C30 GHS and EQ-5D-5L VAS scores, and milder cough and dyspnea symptoms on the EORTC QLQ-LC13

Mean (SD)	T+ (n=208)	L+ (n=178)
EORTC QLQ-C30 patient functioning scales*		
GHS	60.1 (22.49)	53.9 (24.07)
Physical	72.1 (23.02)	69.0 (25.62)
Role	71.7 (30.02)	65.3 (32.14)
Emotional	75.7 (22.83)	72.3 (23.61)
Cognitive	82.1 (20.59)	81.5 (22.22)
Social	76.9 (25.58)	72.4 (29.49)
EQ-5D-5L*		
VAS	67 (19.0)	63 (20.8)
EORTC QLQ-LC13 symptom scores†		
Cough	30.7 (27.27)	34.2 (29.61)
Dyspnea	24.9 (20.09)	29.0 (24.08)
Chest pain	20.1 (28.06)	19.0 (26.43)

Note: 'T+' used here denotes 'known TBx positives'

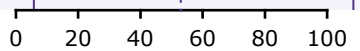
*Higher scores indicate greater function. †Lower scores indicate milder symptoms.
EORTC, European Organisation for Research and Treatment of Cancer; EQ-5D-5L VAS, EuroQol Five-Dimension Five-Level Visual Analogue Scale; GHS, global health status; HRQoL, health-related quality of life; L+, positive for *MET*ex14 skipping in liquid biopsy; QLQ-C30, Quality of Life Questionnaire Core 30; SD, standard deviation; T+, known positive for *MET*ex14 skipping in tissue biopsy (TBx).
Reference: Rolfo C, et al. Presented at ESMO, 2023, Poster 1382P, Supplement.

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

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)



Note: 'T+' used here denotes 'known TBx positives'

*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; MET, mesenchymal-epithelial transition; ORR, objective response rate; T+, known positive detection of *MET*ex14 skipping in tissue biopsy (TBx).
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

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

Cohorts A + C

Feb 2022 cut-off

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

Baseline characteristics		Treatment-naive (n=164)	Previously treated, 2L+		
			All 2L+ (n=149)	2L (n=92)	3L+ (n=57)
Median age, years (range)		74.0 (47–94)	70.8 (41–89)	70.4 (41-89)	71.9 (52-88)
Sex, %	Male	50.6	47.7	50.0	43.9
	Female	49.4	52.3	50.0	56.1
Race*, %	White	68.3	55.7	55.4	56.1
	Asian	30.5	37.6	39.1	35.1
ECOG PS†, %	0	27.4	24.2	25.0	22.8
	1	72.0	75.8	75.0	77.2
Smoking history‡, %	Yes	53.7	40.9	39.2	43.9
	Former smoker	49.4	39.6	37.0	43.9
	Current smoker	4.3	1.3	2.2	0
	No	45.7	53.0	54.3	50.9

*Race was missing/not collected at the study site for eight patients, three patients were Black/African American, and one patient was recorded as 'other'. †One 1L patient was ECOG PS 2. ‡Smoking history was missing in 10 patients.
2L, second line; 2L+, second-or-later line; 3L+, third-or-later line; ECOG PS, Eastern Cooperative Oncology Group performance status; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer.
Reference: Griesinger F, et al. Presented at ELCC, 2023, Poster 34P.

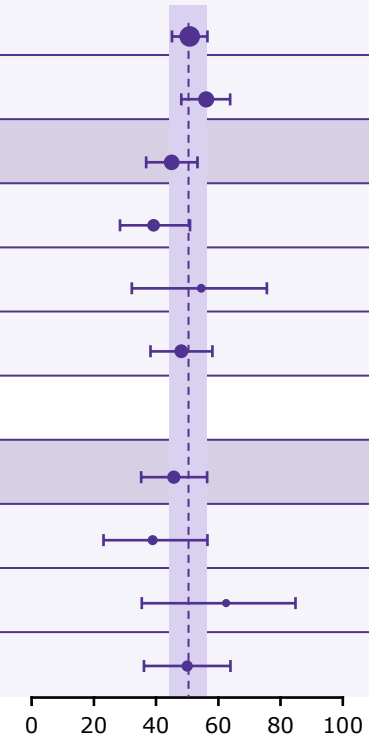
Efficacy by Prior Therapy in Previously Treated Patients (ORR)

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)



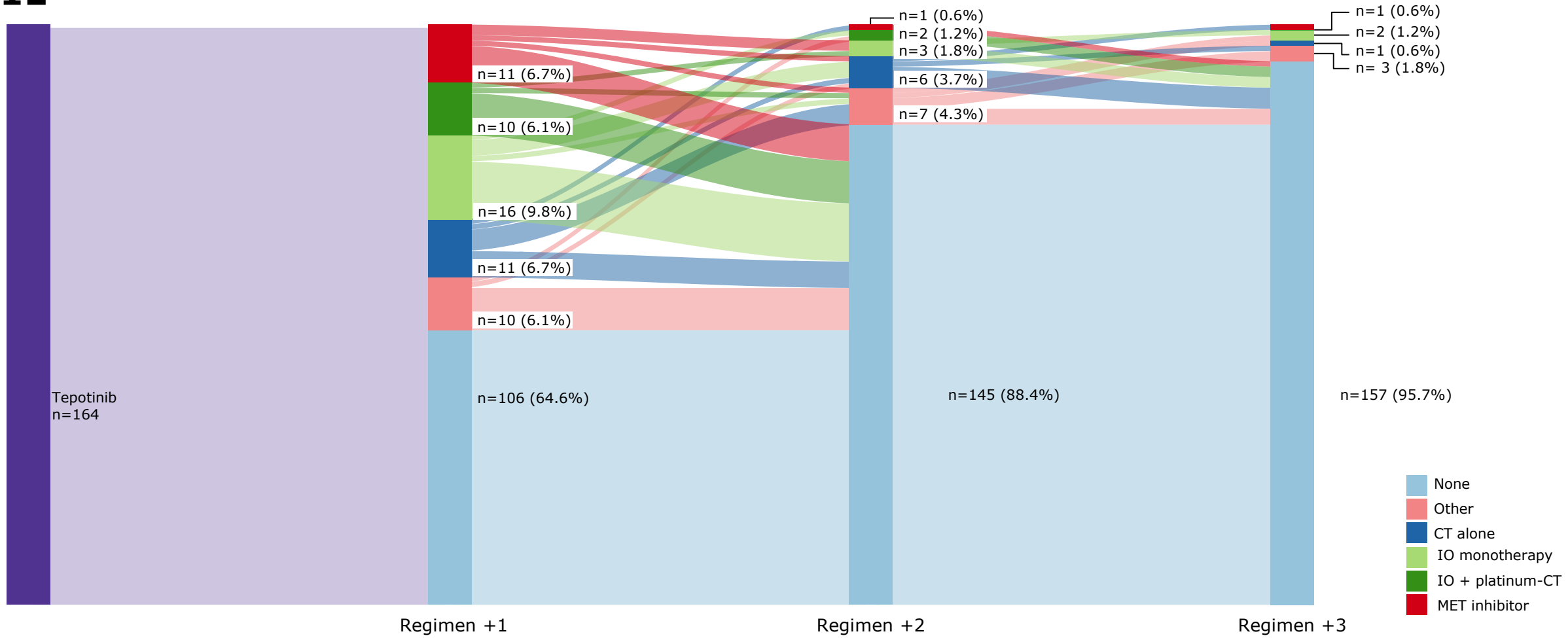
*Patients received IO monotherapy or IO + platinum-based CT.
1L, first line; 2L, second line; 2L+, second-or-later line; CI, confidence interval; CT, chemotherapy; IO, immunotherapy; ORR, objective response rate.
Reference: Smit EF, et al. Presented at ESMO, 2022, Abstract 985P.

Sankey Plots for Treatment Sequencing Post 1L Tepotinib Treatment*

Cohorts A + C

Feb 2022 cut-off

1L

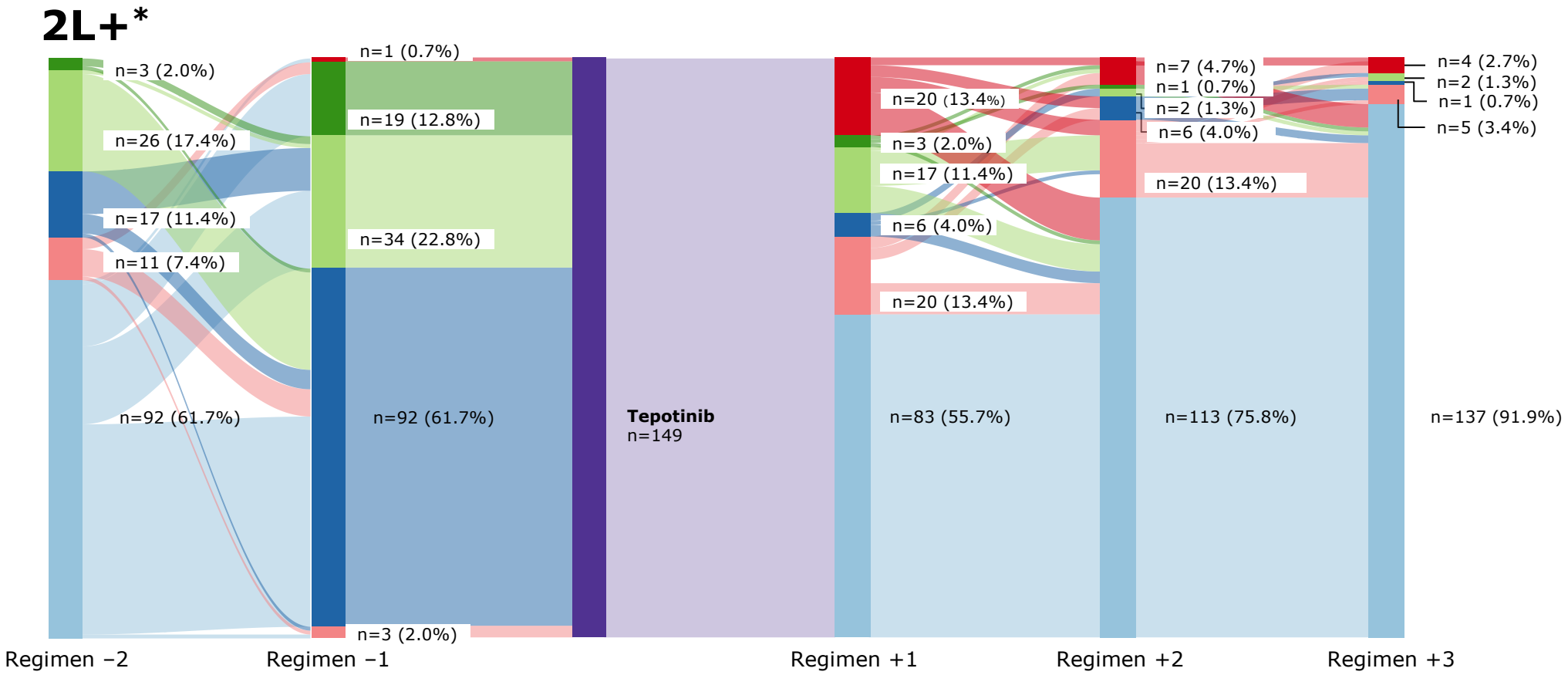


*Overall, 265 patients (84.7%) discontinued tepotinib treatment.
1L, first line; CT, chemotherapy; IO, immunotherapy; MET, mesenchymal-epithelial transition factor.
Reference: Griesinger F, et al. Presented at ELCC, 2023, Poster 34P.

Sankey Plots for Treatment Sequencing Prior to/ Post 2L+ Tepotinib Treatment

Cohorts A + C

Feb 2022 cut-off



- Overall, 265 patients (84.7%) discontinued tepotinib, and of these, 124 patients (46.8%) received subsequent treatment

*Three patients had received three prior lines of therapy.
2L+, second-or-later line; CT, chemotherapy; IO, immunotherapy; MET, mesenchymal-epithelial transition factor.
Reference: Griesinger F, et al. Presented at ELCC, 2023, Poster 34P.

Tepotinib post VISION

Cohorts A + C

Feb 2022 cut-off

- Three patients received subsequent tepotinib treatment

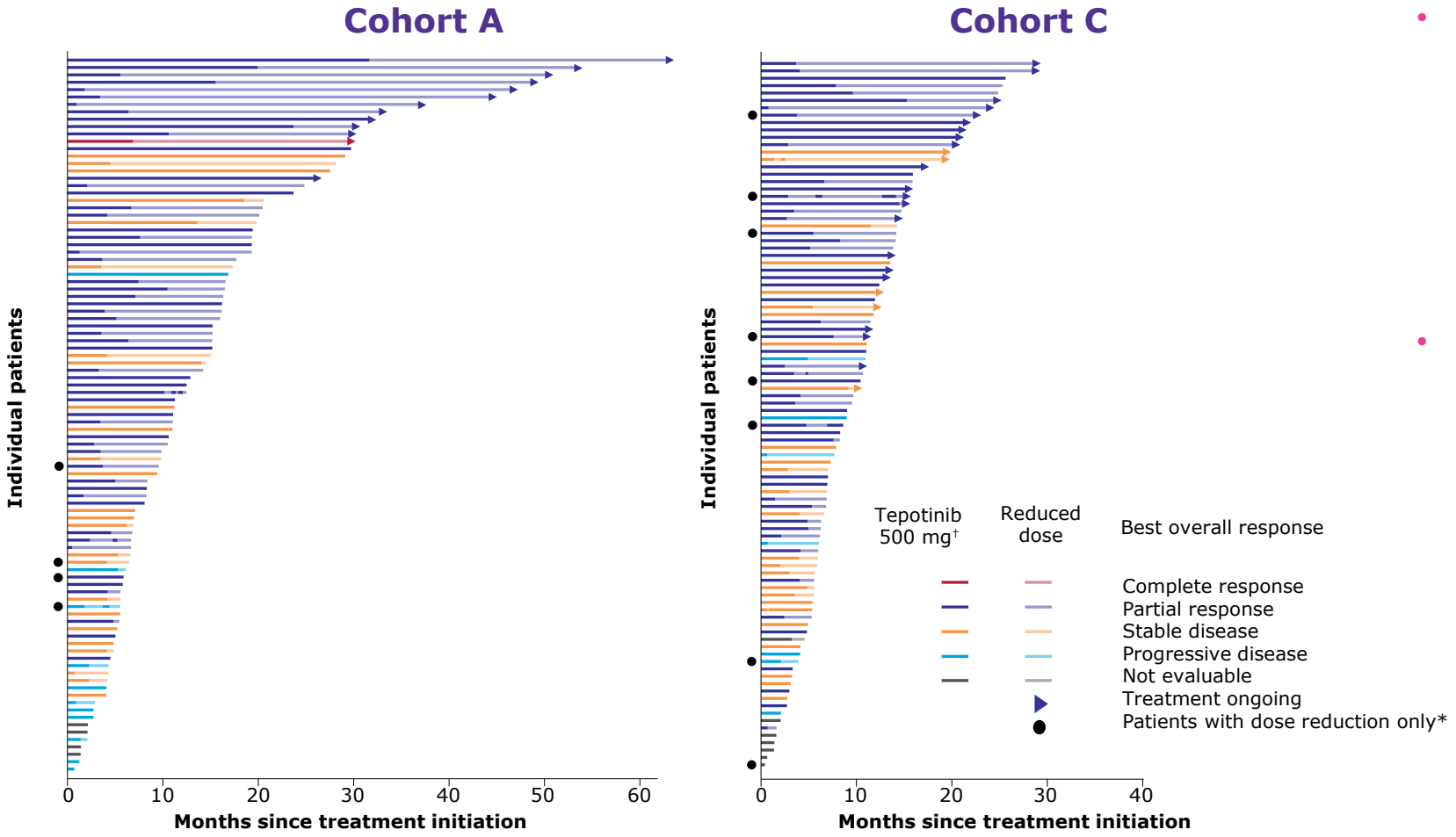
	VISION	Post VISION	
Patient	**Tepotinib DOT (BOR)**	**Subsequent treatment**	**Subsequent tepotinib DOT**
1	6.1 months (PR)	Atezolizumab → docetaxel → tepotinib	10.1 months
2	8.5 months (PR)	Docetaxel/ramucirumab → tepotinib	2.7 months
3	9.7 months (PR)	Nephrectomy for a single new lesion in kidney → tepotinib	5.6 months

BOR, best overall response; DOT, duration of treatment; PR, partial response.
Reference: Griesinger F, et al. Presented at ELCC, 2023, Poster 34P.

Time on Treatment in Patients With Dose Reductions or Interruptions

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

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.

TRAE by Line of Therapy

Cohorts A + C

Feb 2022 cut-off

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.

EFFICACY AND SAFETY DATA (JULY 2020)

Baseline Characteristics

Cohorts A

Jul 2020 cut-off

	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
Brain metastases at baseline§, %	14.5	15.7	15.1

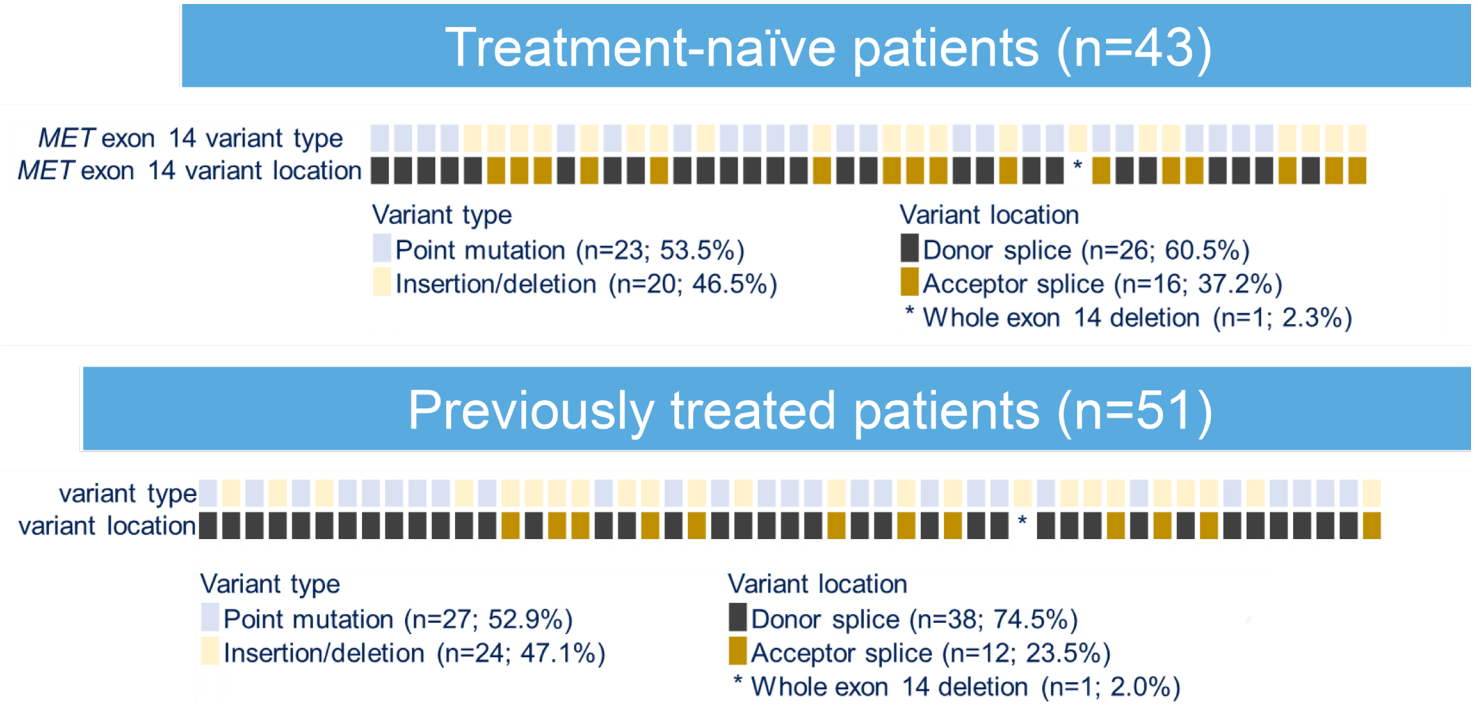
*Race was unknown or missing in 4 patients; 1 patient was Black/African American, and 1 patient was 'other'. †Smoking history was missing in 8 patients. ‡Two patients had adenosquamous histology (1 treatment naive and 1 previously treated), 3 patients had sarcomatoid (all treatment naive), and 1 patient 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.

Mutational Profile at Baseline

Cohorts A

Jul 2020 cut-off

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; *MET*ex14, *MET* exon 14.

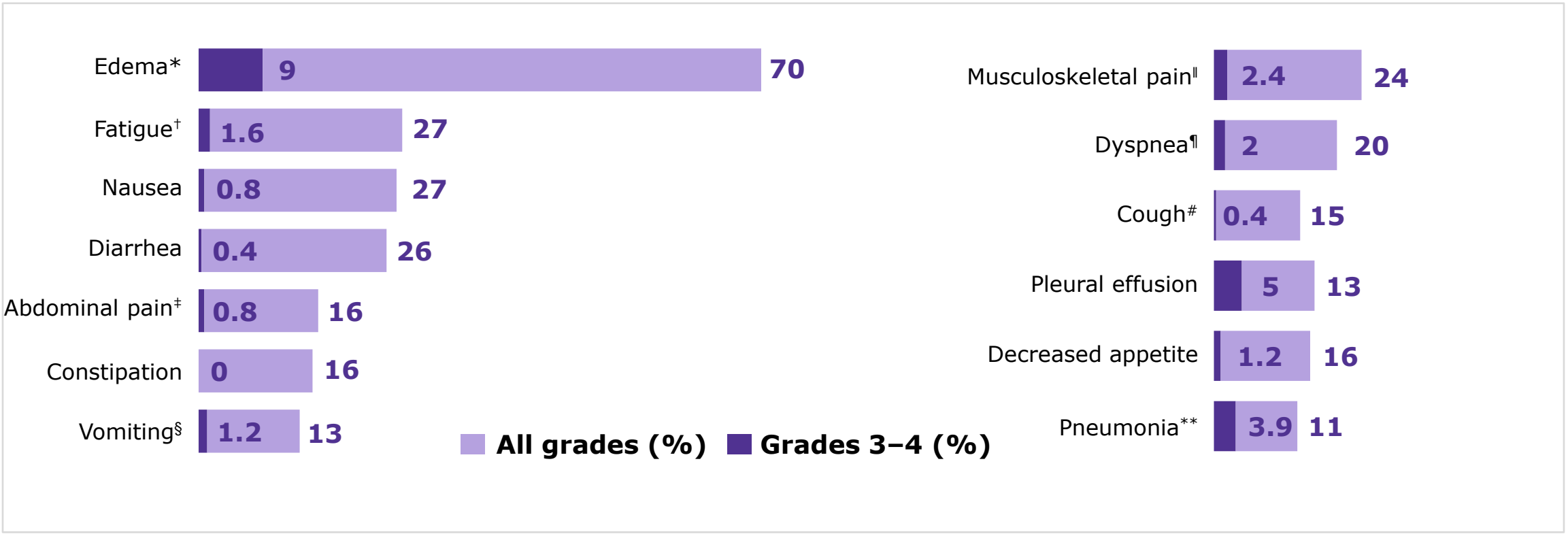
Reference: Paik PK, et al. Presented at ASCO Annual Meeting, 2021, Abstract 9012.

Safety and Tolerability Profile of Tepotinib as Studied in 255 Patients

Cohorts A + C

Jul 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, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14.

Reference: TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

AECIs

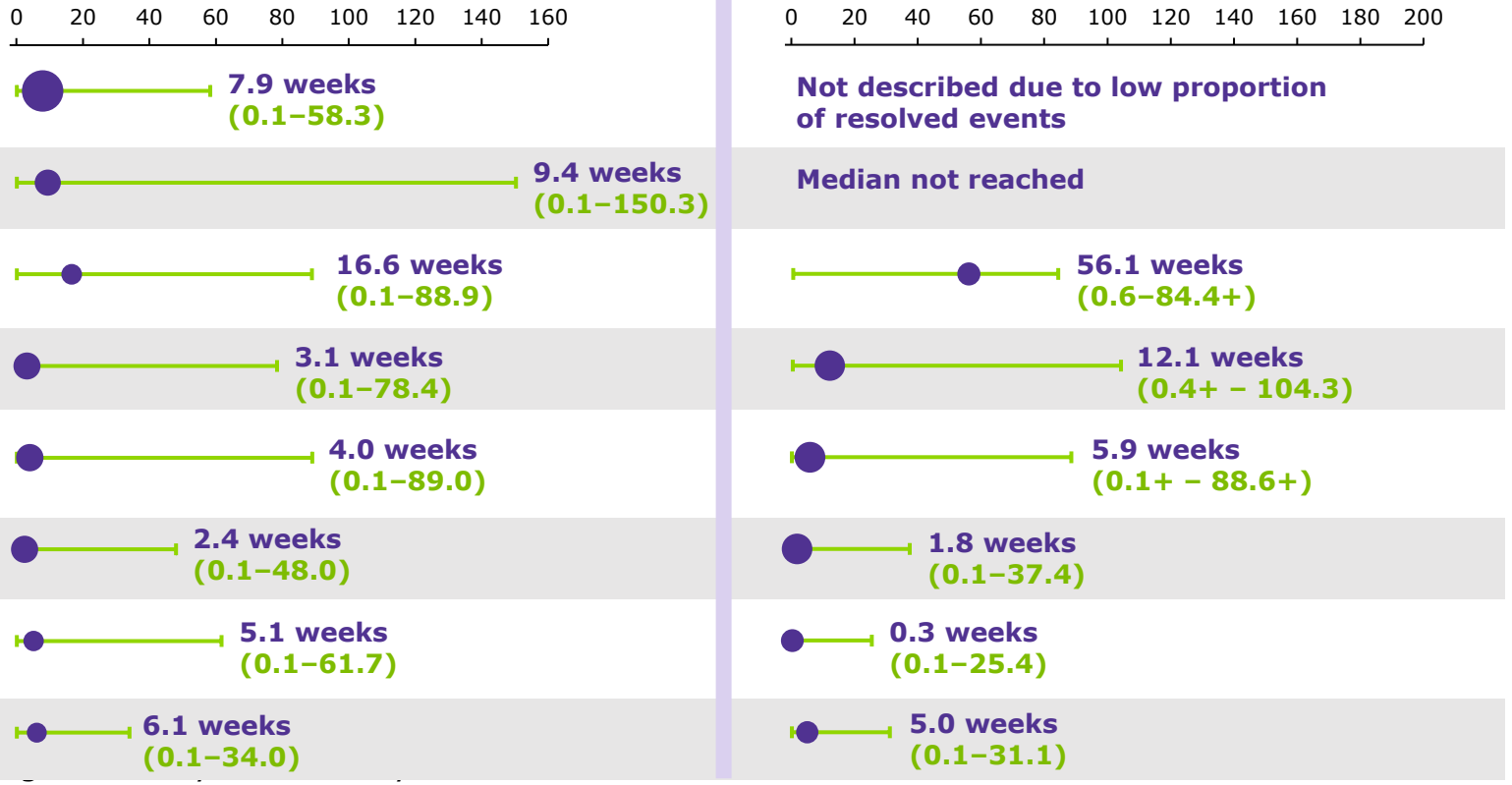
Patient population used is not the full Cohorts A + C population

Cohorts A + C

Jul 2020 cut-off

Time to first onset and time to resolution of AECIs[1]

	Patients, n	Total events, n	Events resolved, n	Time to first onset: Weeks since treatment initiation, median (range)	Time to resolution: Weeks since onset of AE, median (range)
Edema	178	337	115	7.9 weeks (0.1–58.3)	Not described due to low proportion of resolved events
Hypoalbuminemia	61	74	25	9.4 weeks (0.1–150.3)	Median not reached
Pleural effusion	34	39	15	16.6 weeks (0.1–88.9)	56.1 weeks (0.6–84.4+)
Creatinine increase	66	96	67	3.1 weeks (0.1–78.4)	12.1 weeks (0.4+ – 104.3)
Nausea	68	87	67	4.0 weeks (0.1–89.0)	5.9 weeks (0.1+ – 88.6+)
Diarrhea	67	112	102	2.4 weeks (0.1–48.0)	1.8 weeks (0.1–37.4)
Vomiting	33	47	44	5.1 weeks (0.1–61.7)	0.3 weeks (0.1–25.4)
ALT and/or AST increase	31	56	46	6.1 weeks (0.1–34.0)	5.0 weeks (0.1–31.1)



There was no clear association between edema, hypoalbuminemia, pleural effusion, and creatinine increase when analyzed irrespective of event timing

Plots indicate the median value (blue circles, size proportional to the number of patients) and range (green bars). The '+' signs denote censored values.
AE, adverse event; AECI, adverse event of clinical interest; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

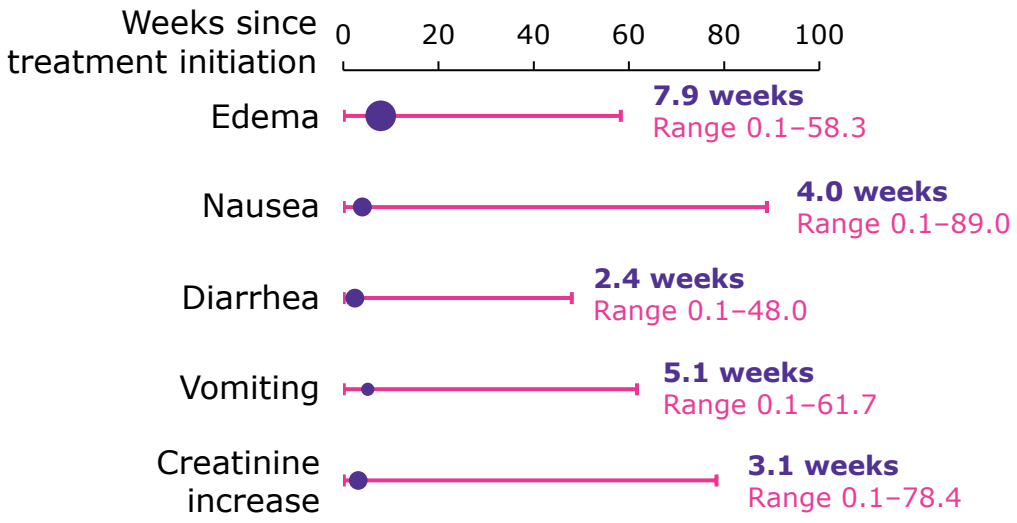
Reference: 1. Veillon R, et al. Clin Lung Cancer. 2022;23(4):320-332.

AEs of Clinical Interest: Time to First Onset and Resolution

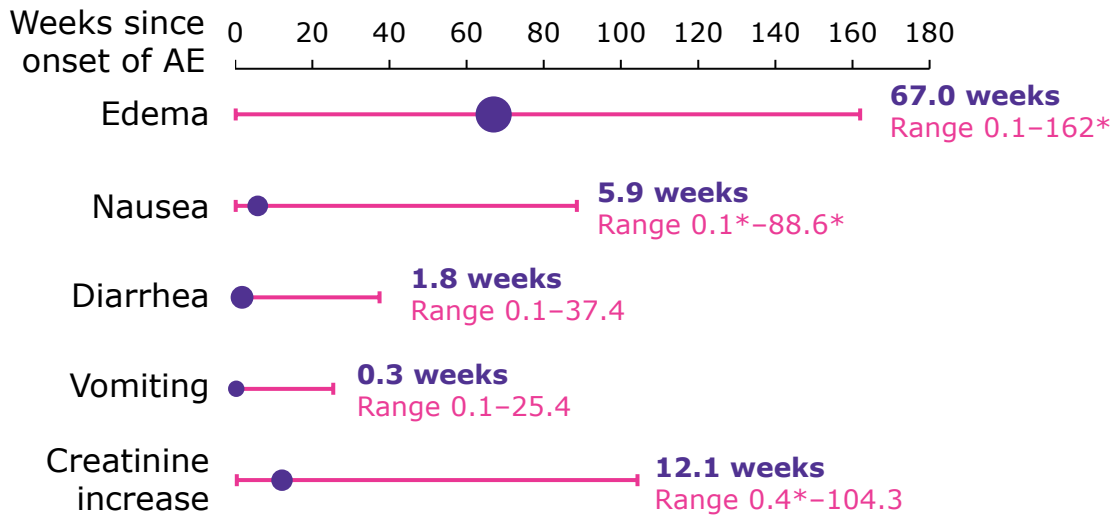
Cohorts A + C

Jul 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.

Thank you!