TEPOTINIB SAFETY DATA AND ADVERSE EVENT MANAGEMENT

For additional resources, please visit our US Medical Resources Website Oncology page at https://medical.emdserono.com/en_US/medinfo/therapeutic-areas/oncology.html

US-TEP-00915 06/26

Table of contents

1. Important safety information
2. Mechanism of action
3. VISION (long-term safety)
4. Prescribing information (highlights)
5. Specific AEs

AE, adverse event.

Important notices

- Copyright in this document is owned by Merck KGaA, Darmstadt, Germany and/or its affiliates (except for any third-party content that has been identified as such) unless otherwise specified and all rights are reserved
- All product names referred to in this document are trademarks of Merck KGaA, Darmstadt, Germany and/or its affiliates except for those trademarks that are indicated as owned by other companies and all rights are reserved
- Unless otherwise stated, copyright clearance for the use of images and graphs has been sought throughout this presentation

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

MET, mesenchymal-epithelial transition; NSCLC, non-small cell lung cancer.
TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

FDA-Approved Indication and Usage

- TEPMETKO® (tepotinib) is indicated for the treatment of adult patients with metastatic NSCLC harboring *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.

MET, mesenchymal-epithelial transition; NSCLC, non-small cell lung cancer.

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

Important safety information (1/3)

Interstitial lung disease (ILD)/pneumonitis

- Tepotinib can cause **ILD/pneumonitis**, which can be fatal
- Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (e.g. 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 a 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 to 262)

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

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

Important safety information (2/3)

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%) from 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%)

P-gp, P-glycoprotein.

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

Important safety information (3/3)

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%)

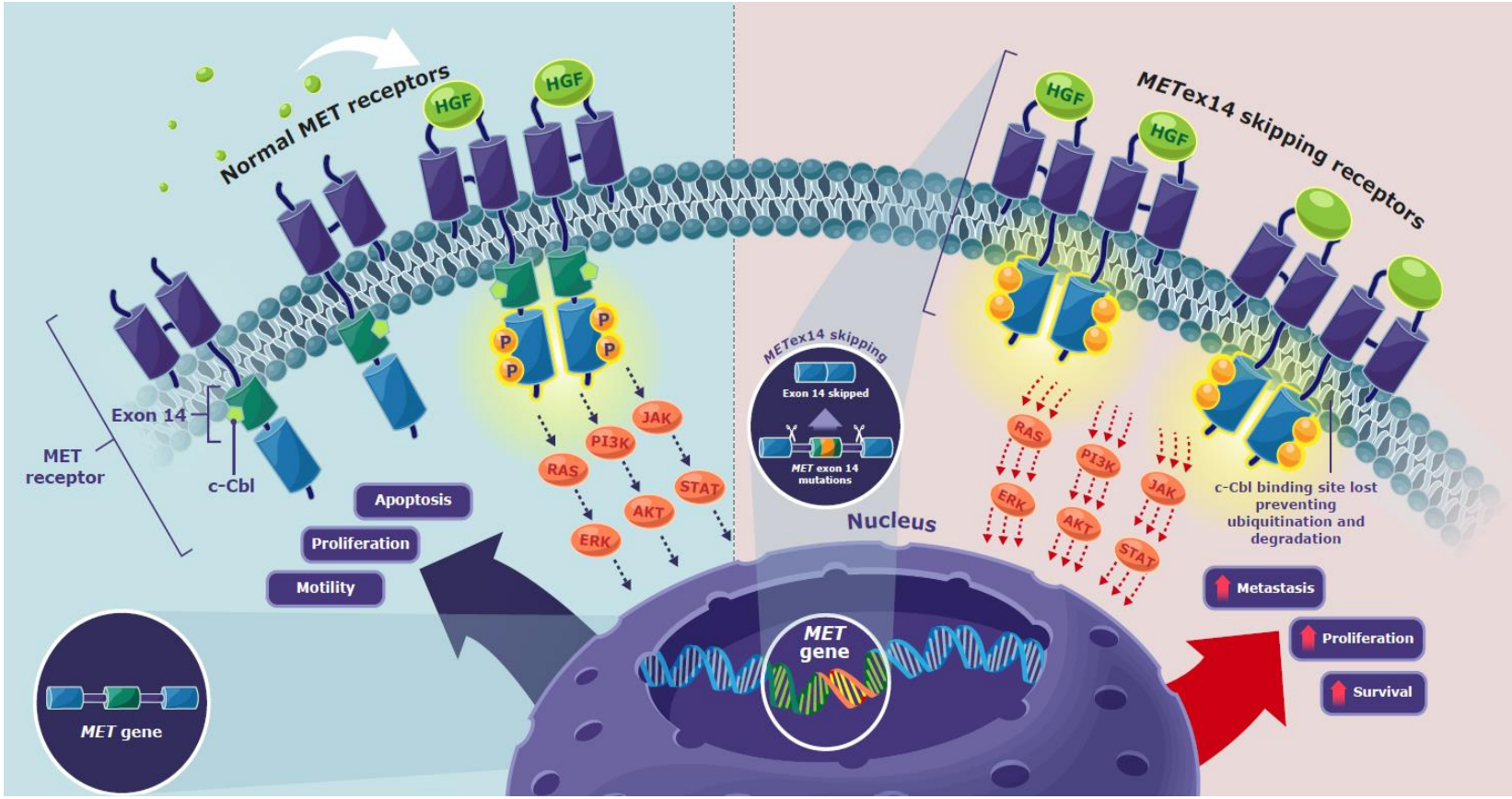
ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; GGT, gamma glutamyl transferase; ILD, interstitial lung disease.

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

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 the c-Cbl binding site, leading to aberrant MET signaling that can drive tumorigenesis[3,4]

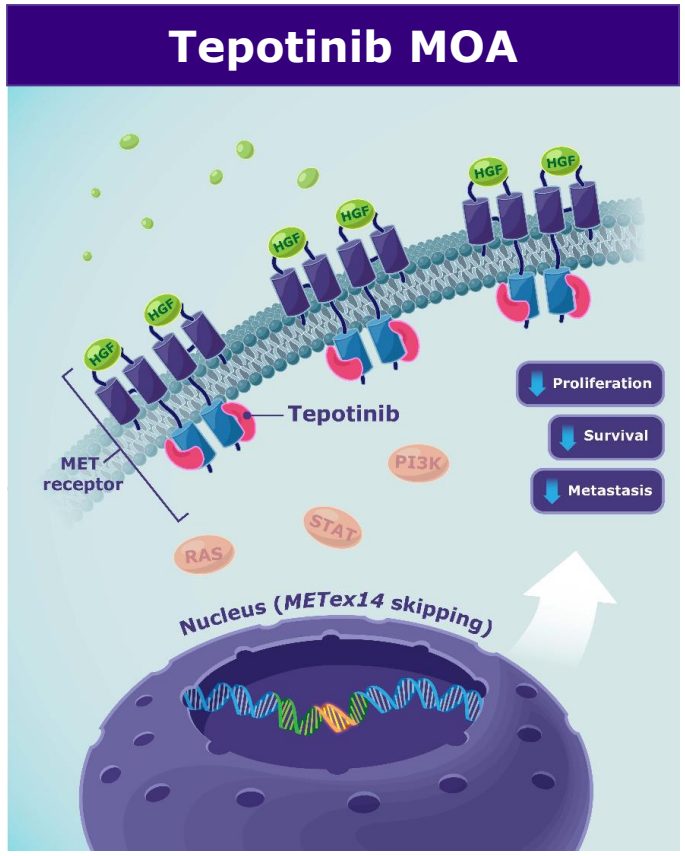
***MET*ex14 skipping and dysregulated MET pathway[4,5]**



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; MOA, mechanism of action; PI3K, phosphoinositide 3-kinase; RAS, RAS GTPase; STAT, signal transducer and activator of transcription.

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.

Tepotinib is thought to bind to the MET receptor to inhibit oncogenic signaling



! Based on preclinical studies, tepotinib is thought to be an ATP-competitive, reversible, type Ib MET inhibitor that binds to the MET receptor with **high selectivity**[1,2]

! By binding to the MET receptor and blocking downstream signaling, tepotinib may prevent cancer cell proliferation, survival, and metastasis[1]

ATP, adenosine triphosphate; HGF, hepatocyte growth factor; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; MOA, mechanism of action; PI3K, phosphoinositide 3-kinase; RAS, RAS GTPase; STAT, signal transducers and activators of transcription.

1. Bladt F, et al. *Clin Cancer Res.* 2013;19:2941–2951; **2.** Reungwetwattana T, et al. *Lung Cancer*. 2017;103:27–37.

VISION clinical trial overview

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

May 2024 data (≥3-year follow-up)

VISION is a single-arm, Phase II trial of the MET inhibitor tepotinib in patients with NSCLC harboring MET alterations (NCT02864992)

Population (N=313)

Eligibility:

- Patients with advanced, metastatic NSCLC harboring *MET*ex14 skipping alterations or *MET* amplification
- No *EGFR mutations* or *ALK* rearrangements
- ≥1 measurable lesion by RECIST v1.1
- ECOG PS 0–1
- Treatment-naïve or patients with up to two lines of prior therapy

Exclusions:

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

Cohort A: *MET*ex14 skipping alterations
Detection of alterations in plasma (DNA-based) or tissue (RNA-based)[1,2]

Cohort B:* *MET* amplification
Detection of alterations in plasma (DNA-based)[3]

Cohort C: *MET*ex14 skipping alterations
Detection of alterations in plasma or tissue[1,2]

Confirmatory Part 2 of study

Tepotinib 500 mg† once daily
21-day cycles until disease progression

Endpoints

Primary endpoint:
Objective response per RECIST v1.1 by independent review committee

Secondary endpoints:

- ORR by investigator assessment
- Duration of response
- Objective disease control
- PFS
- OS
- Safety (per NCI-CTCAE v4.03)
- HRQoL (EORTC QLQ-C30, EQ-5D-5L, EORTC QLQ-LC13 symptom scores)

Data shown here are based on analyses of patients with *MET*ex14 skipping NSCLC

*Enrollment into Cohort B was prematurely discontinued following the pre-planned interim analysis; †500 mg tepotinib hydrochloride hydrate (active ingredient) contains 450 mg tepotinib free-base (active moiety).
ALK, anaplastic lymphoma kinase; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFRwt, epidermal growth factor receptor wild type; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; EORTC QLQ-LC13, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Lung Cancer 13; EQ-5D-5L, European Quality of Life-5 dimension-5 Level HGF, hepatocyte growth factor; HRQoL, health-related quality of life; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

1. Mazieres J, et al. *JAMA Oncology*. 2023;9(9):1260-1266. **2.** Felip E, et al. WCLC 2025. Abstract P3.12.40. **3.** Le X, et al. *Cell Rep Med.* 2023;4(11):1012801.

Baseline characteristics of patients in VISION cohorts A+C[1,2]

May 2024 data
(≥3-year follow-up)

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

Patients were generally **elderly,** and more likely to be **white** and had an **ECOG PS of 1**

Nearly **half** of the patients had a history of smoking and about **half** were previously treated

Patients were followed-up for **≥3 years** across cohorts A and C

		Overall (N=313)	Treatment-naive (N=164)	Pretreated (N=149)
Median age, years (range)		72 (41–94)	74 (47–94)	70.8 (41–89)
Female sex, n (%)		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)
Histologic subtype, n (%)§	Adenocarcinoma	252 (80.5)	131 (79.9)	121 (81.2)

*Nine patients had race reported as 'other' or was missing. †One patient receiving tepotinib in 1L was ECOG PS 2. ‡Smoking history was missing in ten patients. ‡In the overall population, 28 patients had squamous cell carcinoma and 10 patients had sarcomatoid carcinoma.

1L, first line; ECOG PS, Eastern Cooperative Oncology Group performance status.

1. Viteri S, et al. ESMO 2025. Abstract 1995P. **2.** Felip E, et al. WCLC 2025. Abstract P3.12.40.

Overall safety profile of tepotinib

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

Summary of ARs per prescribing information (Nov 2022 data)[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 (≥3-year follow-up; May 2024 data)[2]

Patients with at least one, n (%)	Cohort A+C (N=313)	
	All-cause AE	TRAEs
Any AE	310 (99.0)	287 (91.7)
Serious AEs	171 (54.6)	50 (16.0)
Grade ≥3 AE	214 (68.4)	113 (36.1)
Grade ≥4 AE	59 (18.8)	12 (3.8)
AE leading to dose reduction	114 (36.4)	104 (33.2)
AE leading to temporary discontinuation (interruption)	172 (55.0)	137 (43.8)
AE leading to permanent discontinuation	84 (26.8)	49 (15.7)
AE leading to death	43 (13.7)	3 (1.0)

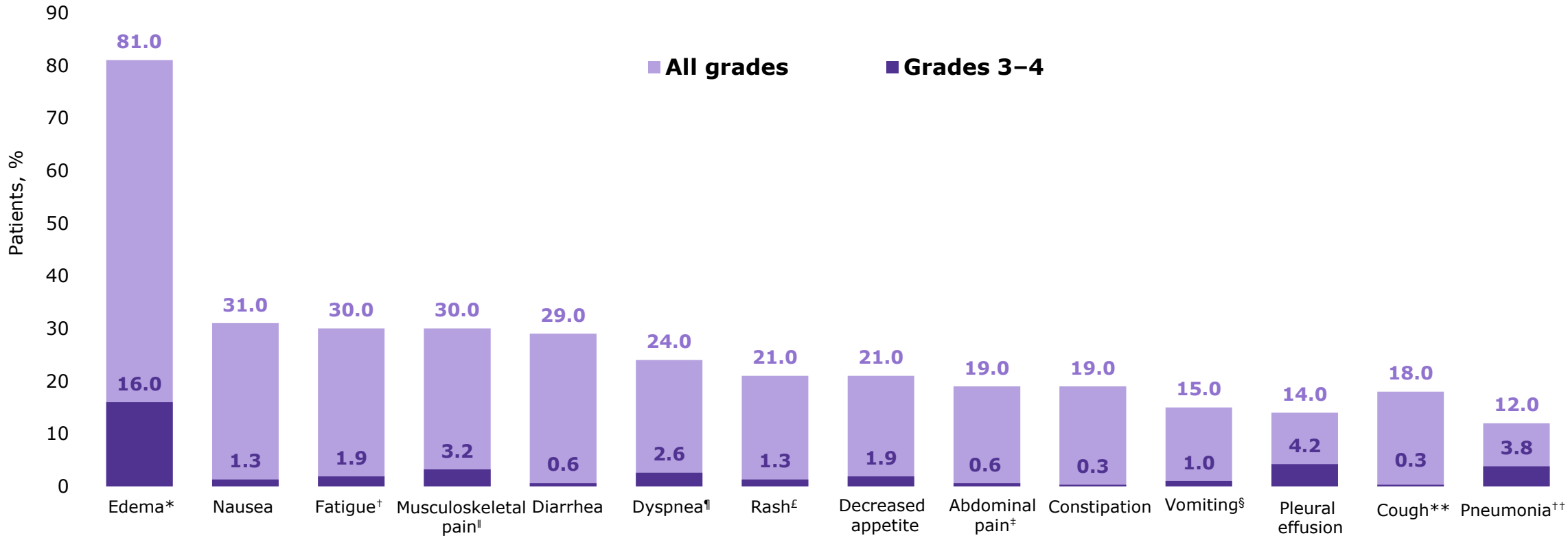
AE, adverse event; ALT, alanine aminotransferase; AR, adverse reaction; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase.

1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf; **2.** Felip E, et al. WCLC 2025. Abstract P3.12.40.

Adverse reactions in ≥10% of patients with *MET*ex14 skipping NSCLC who received tepotinib in VISION (N=313)

Nov 2022 data (US PI)

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



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 arthralgia, arthritis, back pain, bone pain, musculoskeletal chest pain, musculoskeletal pain, myalgia, non-cardiac chest pain, pain in extremity, and spinal pain; ¶Includes dyspnea, dyspnea at rest, and dyspnea exertional; £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 abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper, gastrointestinal pain, and hepatic pain; §Vomiting includes retching and vomiting; **Includes cough and productive cough; ††Includes pneumonia, pneumonia aspiration, and pneumonia bacterial.

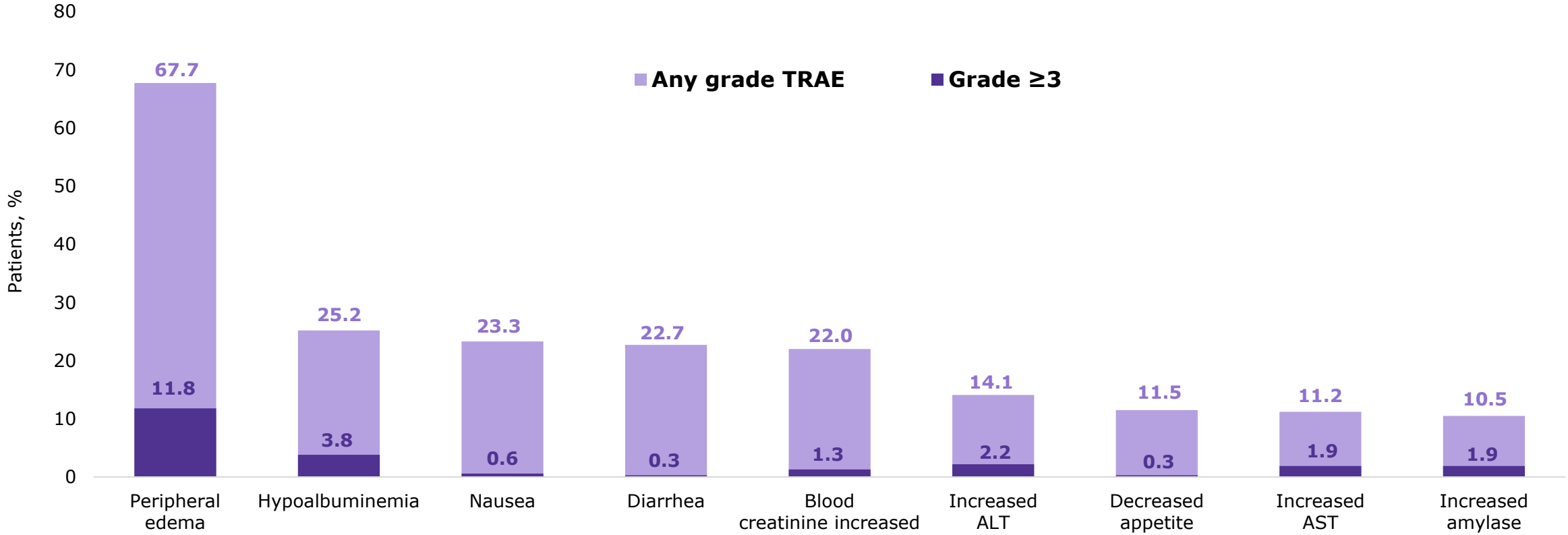
AR, adverse reaction; ILD, interstitial lung disease; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer.

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

TRAEs occurring in >10% of patients with *MET*ex14 skipping NSCLC who received tepotinib in VISION (N=313)

May 2024 data
(≥3-year follow-up)

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



Peripheral edema was the most commonly occurring TRAE

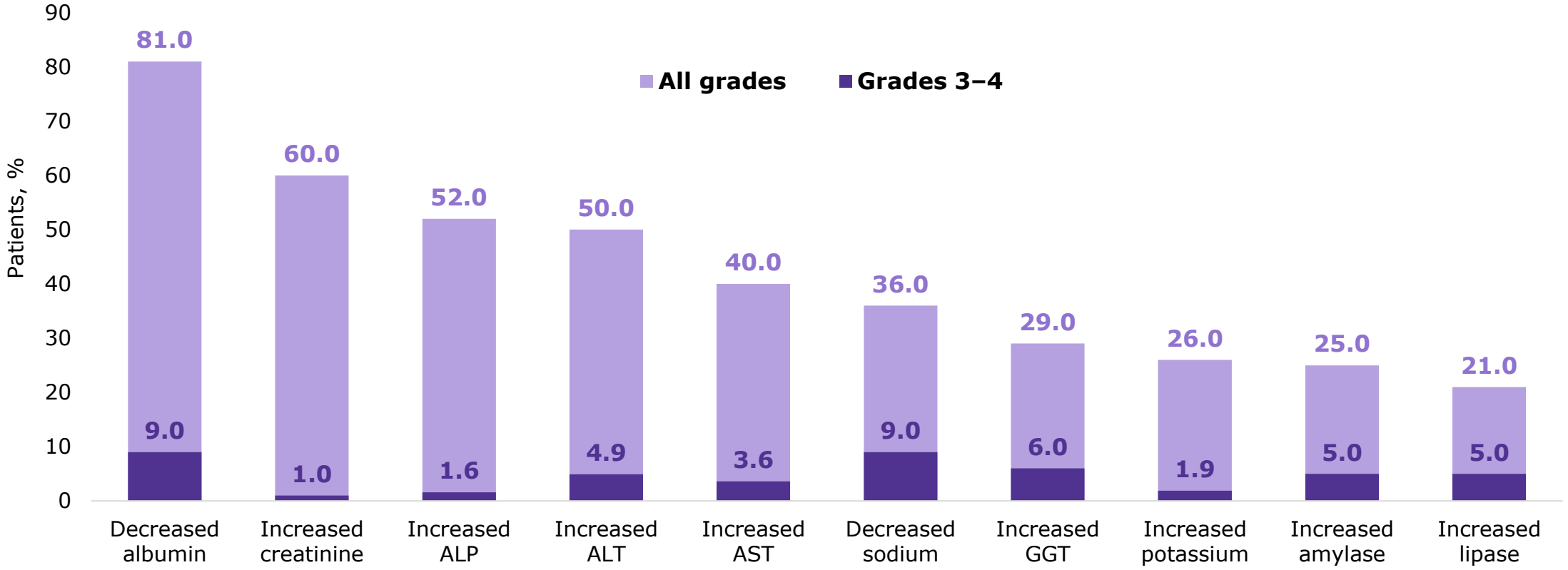
ALT, alanine aminotransferase; AST, aspartate aminotransferase; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer; TRAE, treatment-related adverse event.

Felip E, et al. WCLC 2025. Abstract P3.12.40.

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

Nov 2022 data (US PI)

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



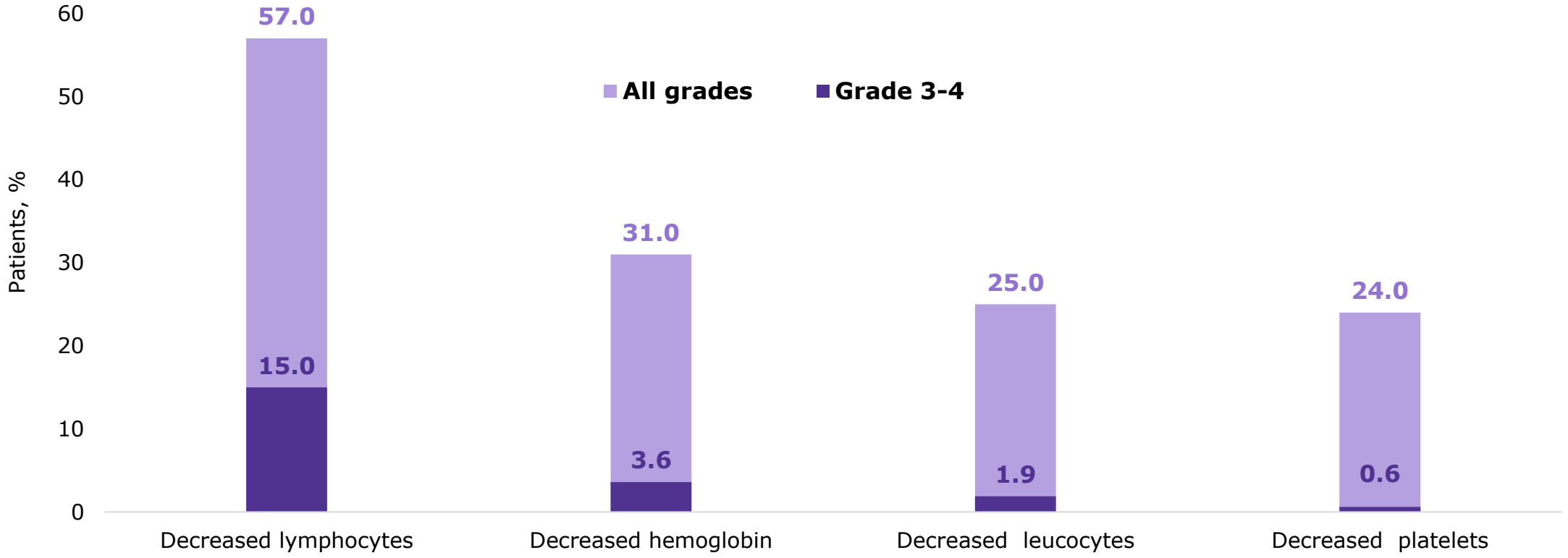
Decreased albumin was the most commonly occurring laboratory abnormality

*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, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase.
TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

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

Nov 2022 data (US PI)

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



Decreased lymphocytes was the most commonly occurring hematology abnormality

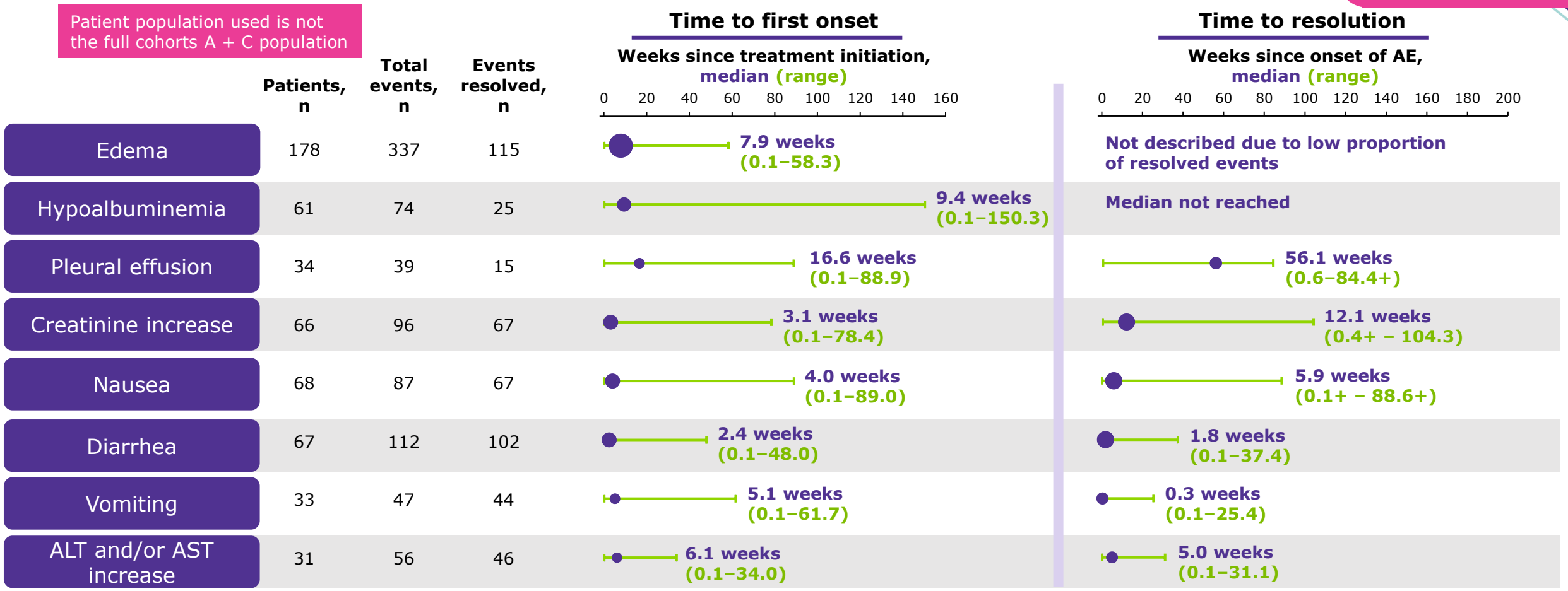
*The denominator used to calculate the rate varied from 268 to 309 based on the number of patients with a baseline value and at least one post-treatment value.
TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

Time to first onset and time to resolution of AECIs

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

July 2020 data

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



	Patients, n	Total events, n	Events resolved, n	Time to first onset	Time to resolution
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.
Veillon R, et al. *Clin Lung Cancer*. 2022;23(4):320-332.

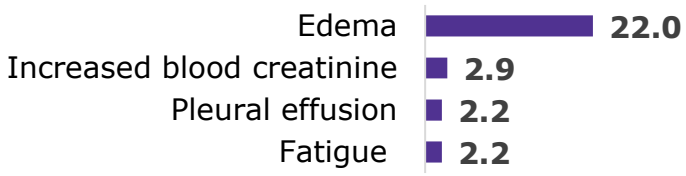
Permanent discontinuations, dosage interruptions and dose reductions for ARs (N=313)

Nov 2022 data (US PI)

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

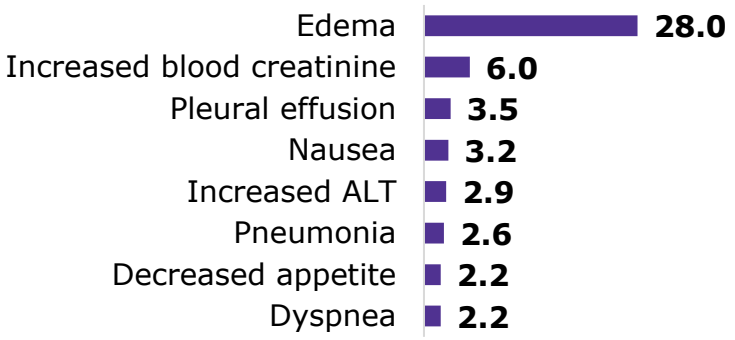
Dose reductions (Overall 36.0%)

ARs leading to dose reductions in >2% of patients who received tepotinib (%)



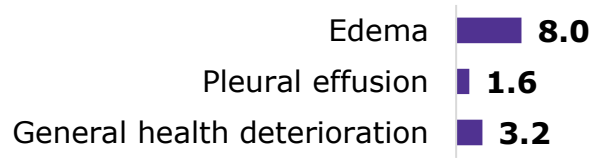
Dosage interruptions (Overall 53.0%)

ARs leading to dosage interruption in >2% of patients who received tepotinib (%)



Permanent discontinuation (Overall 25.0%)

ARs leading to permanent discontinuations in >1% patients who received tepotinib (%)



Dose modifications for ARs

- 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

AR, adverse reaction; ALT, alanine aminotransferase.

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

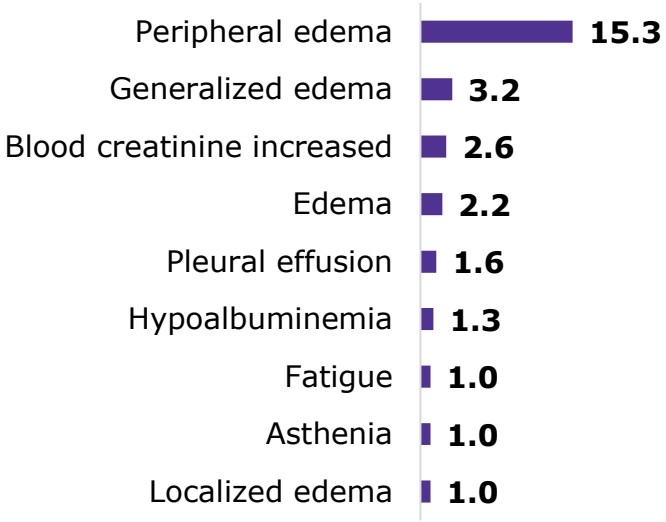
Permanent discontinuations, dosage interruptions, dose reductions for TRAEs* (N=313)

May 2024 data
(≥3-year follow-up)

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

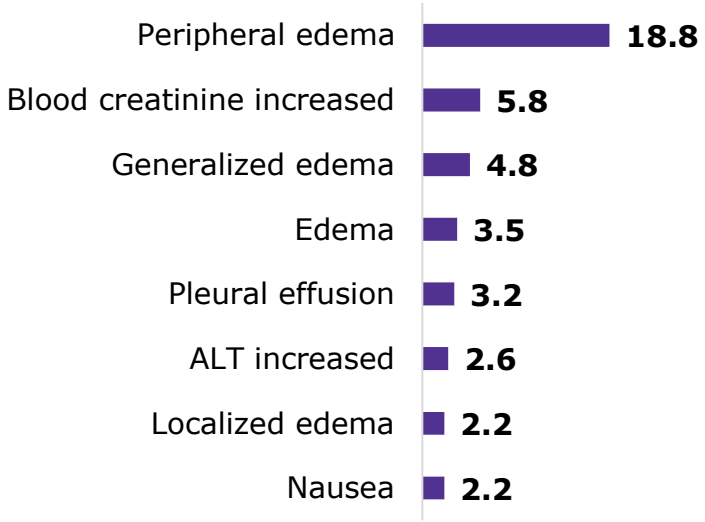
Dose reductions (Overall 33.2%)

TRAEs leading to dose reductions in ≥1% of patients who received tepotinib (%)



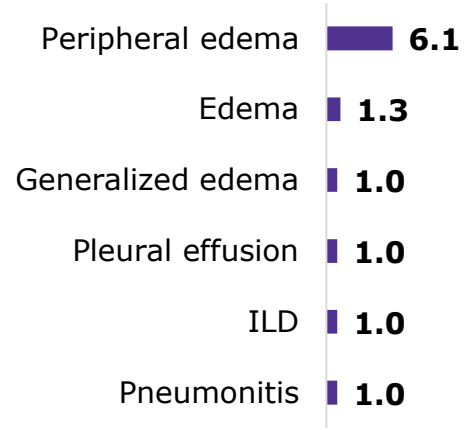
Dosage interruptions (Overall 43.8%)

TRAEs leading to dosage interruption in >2% of patients who received tepotinib (%)



Permanent discontinuation (Overall 15.7%)

TRAEs leading to treatment discontinuation in ≥1% of patients who received tepotinib (%)

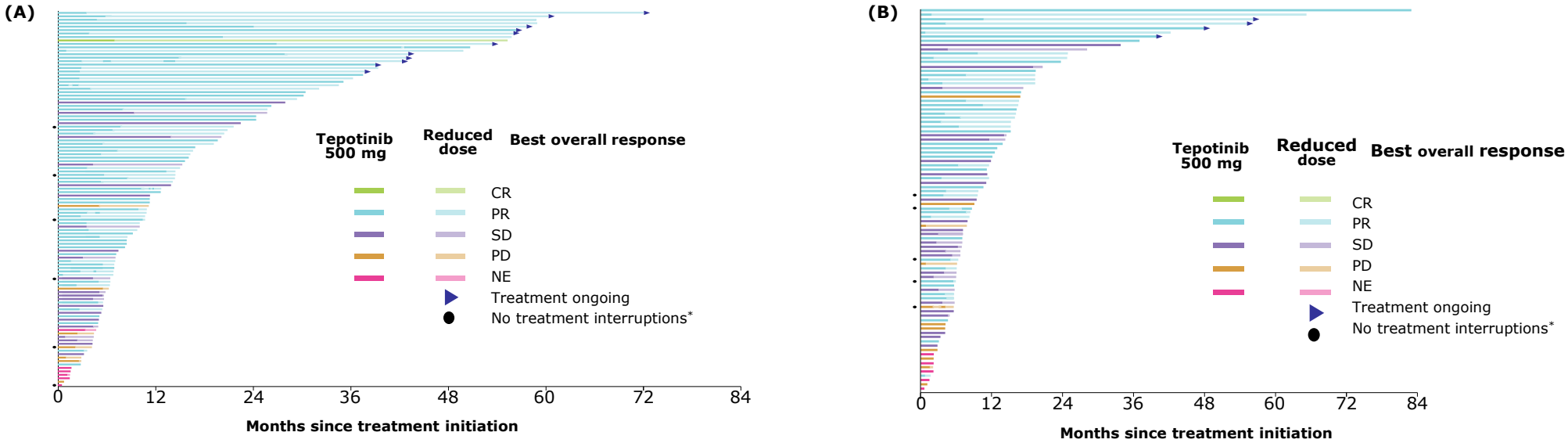


*MedDRA terms reported here.
ALT, alanine aminotransferase; ILD, interstitial lung disease; MedDRA, Medical Dictionary for Regulatory Activities; TRAE, treatment related adverse event.
Felip E, et al. WCLC 2025. Abstract P3.12.40.

Patients requiring treatment interruptions and dose reductions were able to continue treatment with tepotinib

May 2024 data (≥3-year follow-up)

The duration of treatment in patients with dose reductions and/or treatment interruptions receiving tepotinib in (A) 1L (n=108) and (B) 2L+ (n=89)[1]



To view the enlarged graphs, please click ***here***

Median duration of treatment, months (range)[1]

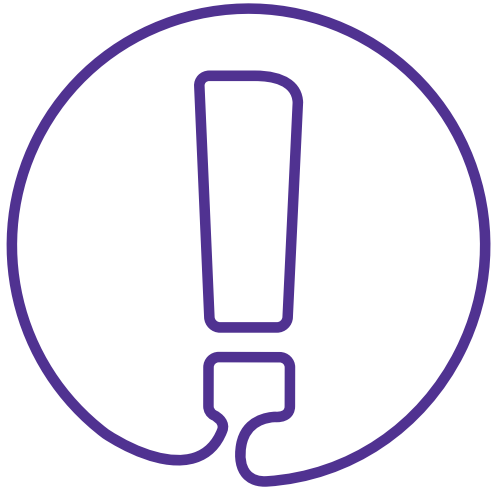
Overall population (N=313)[2]	Dose reductions and/or interruptions (n=197)	Dose reductions only	Treatment interruptions only
7.5 (0.03-83.12)	10.7 (0.7-83.1)	11.0 (1.4-71.5)	11.0 (0.7-83.1)

*All patients had treatment interruptions except those indicated with a circle.
1L, first line; 2L+, second-or-later line; CR, complete response; NE, not evaluable; PD, progressive disease; PR, progressive response; SD, stable disease.

1. Viteri S, et al. ESMO 2025. Abstract 1995P. **2.** Felip E, et al. WCLC 2025. Abstract P3.12.40.

Tepotinib: Prescribing information[1]

Nov 2022 data (US PI)



- The pooled safety population described in the 'warnings and precautions' reflect **exposure to tepotinib in 506 patients with solid tumors** enrolled in five open-label, single-arm studies receiving single-agent tepotinib at a dosage of 450 mg once daily
- **This included 313 patients with NSCLC positive for *MET*ex14 skipping alterations who received tepotinib in VISION**
- Among 506 patients who received tepotinib, 44% were exposed for 6 months or longer and 22% were exposed for greater than 1 year

Warnings and precautions: ILD/pneumonitis, hepatotoxicity, pancreatic toxicity, and embryo-fetal toxicity

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

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

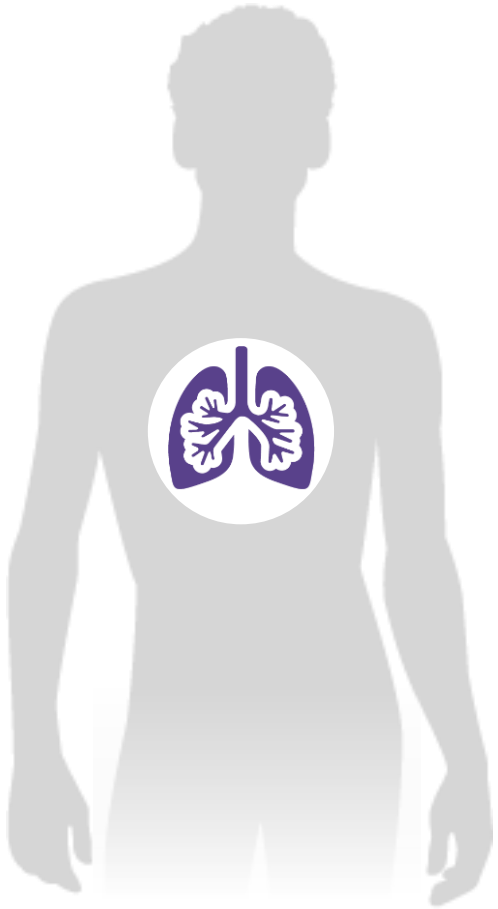
Interstitial lung disease/pneumonitis[1]

Nov 2022 data (US PI)

ILD/pneumonitis, which can be fatal, occurred in patients treated with tepotinib	
ILD/pneumonitis	
All grades	2%
Grade ≥3	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 (e.g. dyspnea, cough, fever)

Recommended dose modifications for ILD/pneumonitis (any grade)
Immediately withhold tepotinib in patients with suspected ILD/pneumonitis and permanently discontinue if no other potential causes of ILD/pneumonitis are identified



Severity as defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.
ILD, interstitial lung disease.
1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

Hepatotoxicity[1] (1/2)

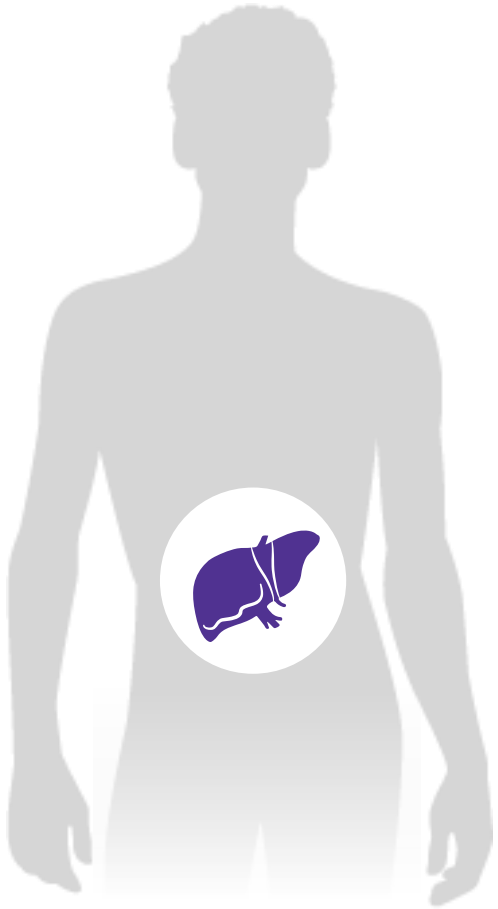
Nov 2022 data (US PI)

Hepatotoxicity occurred in patients treated with tepotinib	
Increased ALT/AST	
All grades	18%
Grade 3 or 4	4.7%
Fatal adverse reaction 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) before 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

Recommended dose modifications for hepatotoxicity

Based on the severity of the adverse reaction, withhold, reduce, or permanently discontinue tepotinib (details on the next slide)



Severity as defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.
ALT, alanine aminotransferase; AST, aspartate aminotransferase.

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

Dose modifications for hepatotoxicity[1] (2/2)

Nov 2022 data (US PI)

Increased ALT and/or AST without increased total bilirubin

Grade 3

Increased total bilirubin without concurrent increased ALT and/or AST

Grade 3

Withhold tepotinib until recovery to baseline ALT/AST/bilirubin

If recovered to baseline within 7 days, then resume tepotinib at the same dose; otherwise resume tepotinib at a reduced dose

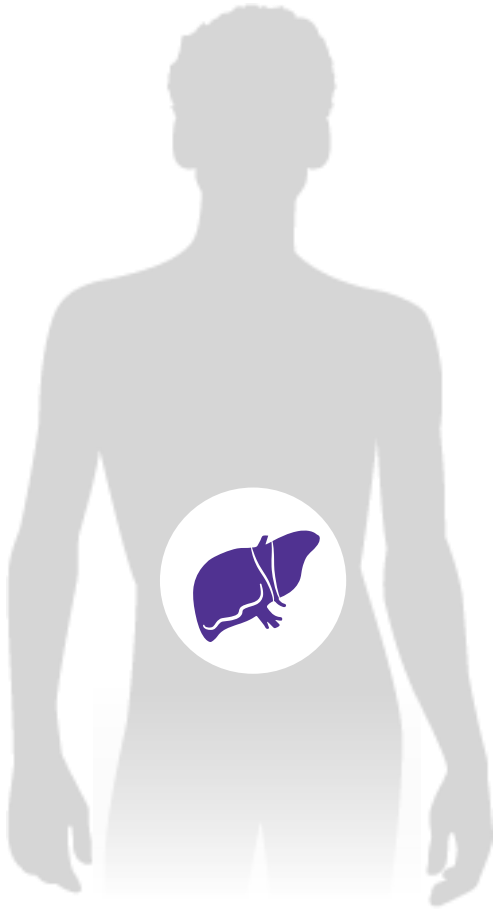
Grade 4

Grade 4

Permanently discontinue tepotinib

Increased ALT and/or AST with increased total bilirubin in the absence of cholestasis or hemolysis

ALT and/or AST >3× ULN with total bilirubin >2× ULN



Severity as defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal.

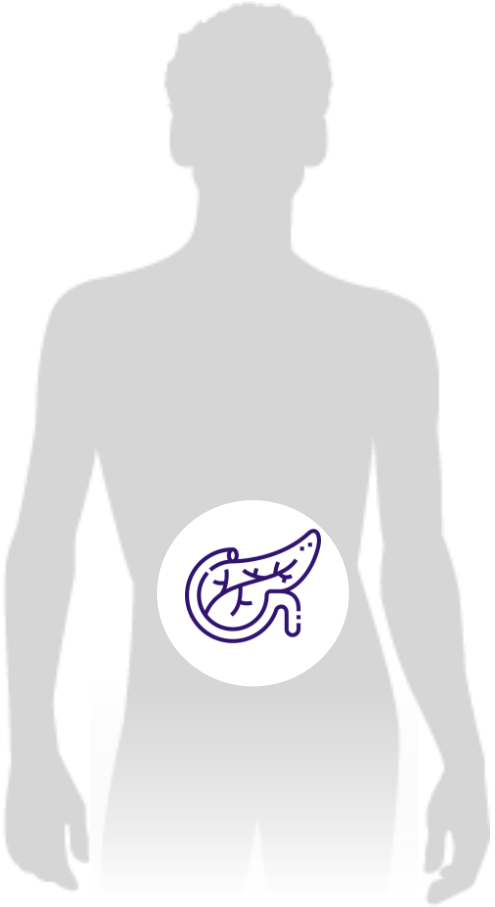
1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

Pancreatic toxicity[1] (1/2)

Nov 2022 data (US PI)

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

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



Recommended dose modifications for pancreatic toxicity
Temporarily withhold, dose reduce, or permanently discontinue tepotinib (details on the next slide)

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

Dose modifications for pancreatic toxicity[1] (2/2)

Nov 2022 data (US PI)

Increased lipase or amylase

Grade 3

Withhold tepotinib until ≤ Grade 2 or baseline

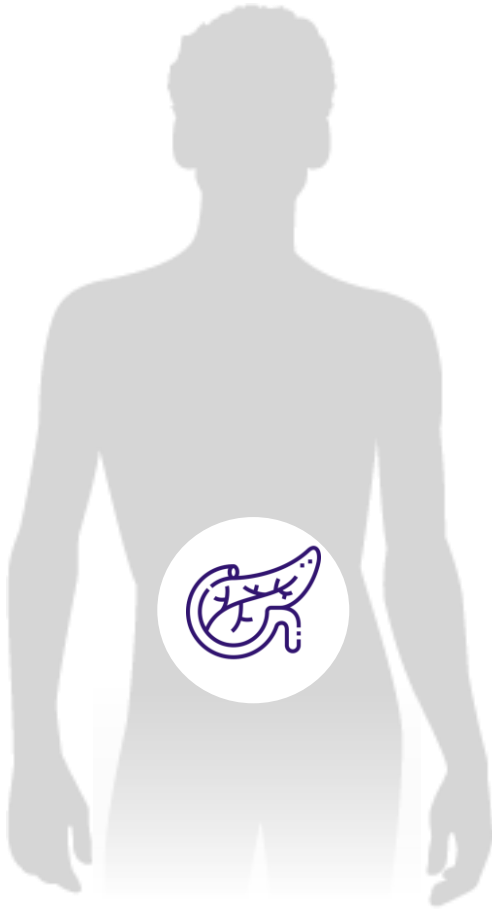
If recovered to baseline or ≤ Grade 2 within 14 days, then resume tepotinib at a reduced dose; otherwise permanently discontinue tepotinib

Grade 4

Pancreatitis

Grade 3 or 4

Permanently discontinue tepotinib



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

Embryo-fetal toxicity[1]

Nov 2022 data (US PI)

- Based on findings from animal studies and its mechanism of action, tepotinib can cause fetal harm when administered to pregnant women
- Oral administration of tepotinib to pregnant rabbits during the period of organogenesis resulted in malformations (teratogenicity) and anomalies at exposures less than the human exposure based on AUC at the 450 mg daily clinical dose
- Advise pregnant women of the potential risk to a fetus
- Advise females of reproductive potential or males with female partners of reproductive potential to use effective contraception during treatment with tepotinib and for 1 week after the last dose

AUC, area under the curve.

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

Dose modifications for other adverse reactions[1]

Nov 2022 data (US PI)

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

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

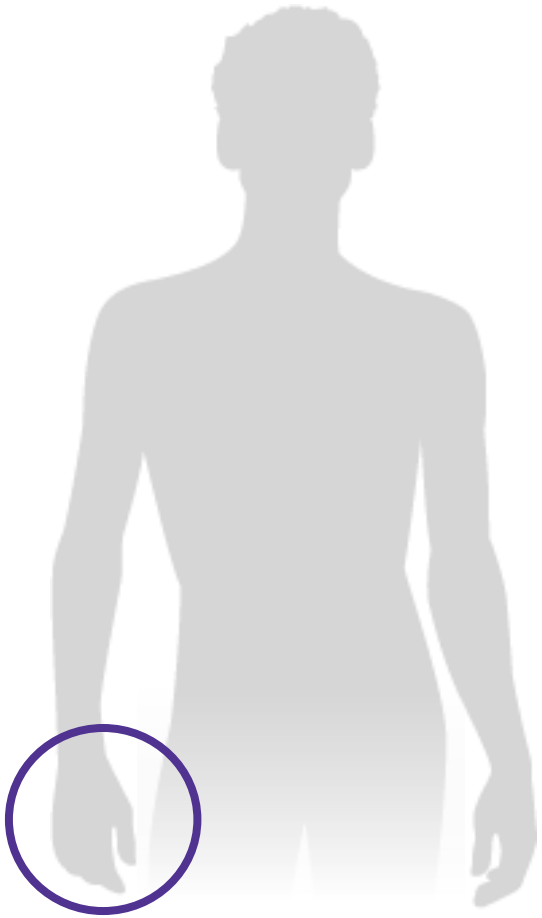
Edema[1]

Nov 2022 data (US PI)

Edema (composite term)* was one of the most common ARs that occurred in patients treated with tepotinib

Edema	
Grades 1–4	81%
Grades 3–4	16%
Serious ARs in >2% of patients included edema	5%
Permanent discontinuation due to edema	8%
Dose interruption due to edema	28%
Dose reduction due to edema	22%

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



*Edema includes eye edema, face edema, generalized edema, localized edema, edema, genital edema, peripheral edema, peripheral swelling, periorbital edema, and scrotal edema. AR, adverse reaction.

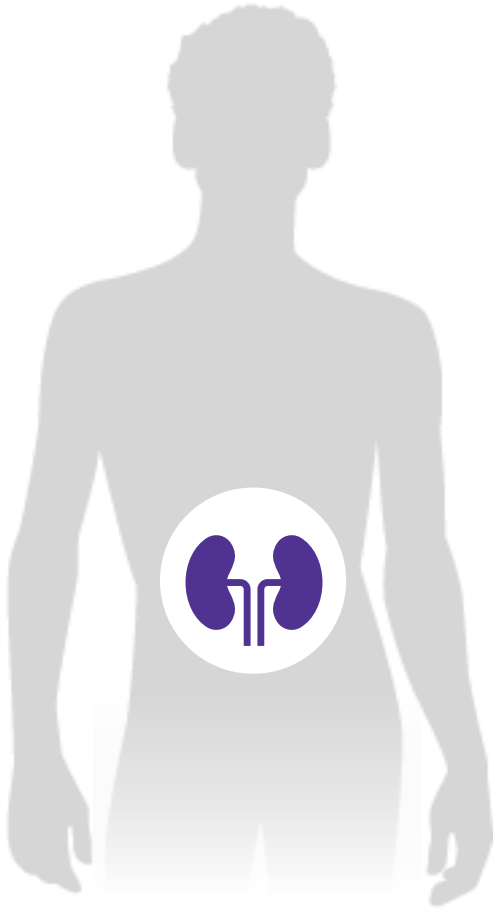
1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf.

Increased creatinine[1]

Nov 2022 data (US PI)

A median increase in serum creatinine was reversible upon treatment completion*

Increased creatinine	
Grades 1–4	60%
Grades 3–4	1%
Dose interruption of tepotinib due to increased blood creatinine	6%
Dose reduction of tepotinib due to increased blood creatinine	2.9%



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

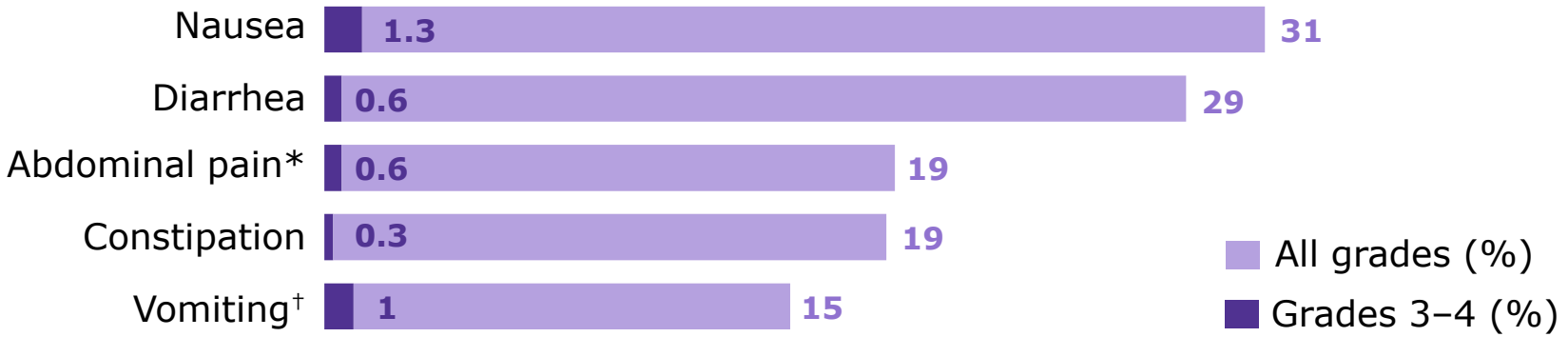
*A median increase in serum creatinine of 30% was observed 21 days after tepotinib initiation. The serum creatinine increases persisted throughout treatment and were reversible upon treatment completion.

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

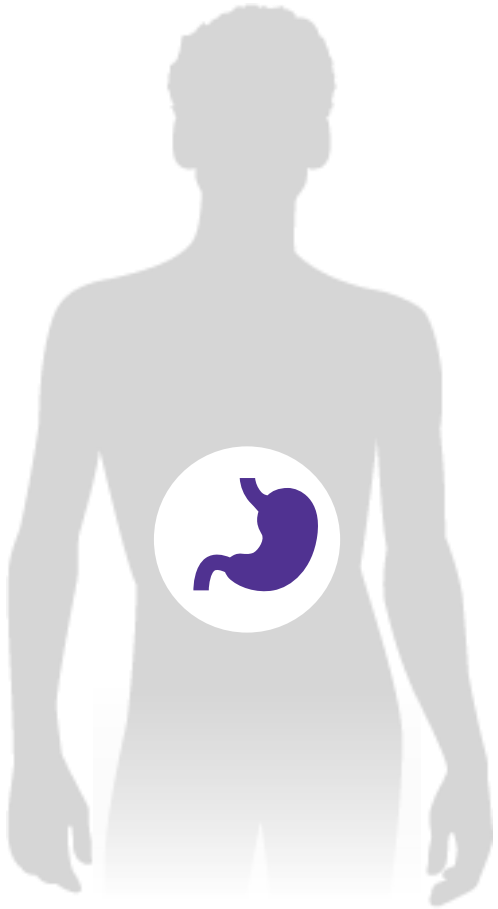
Gastrointestinal disorders[1]

Nov 2022 data (US PI)

All-cause incidence of gastrointestinal adverse events



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



*Abdominal Pain includes abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper, gastrointestinal pain, and hepatic pain; †Vomiting includes retching and vomiting.

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

Use in specific populations[1] (1/1)

Nov 2022 data (US PI)

Population	Safety recommendation
 **Pregnant women**	Based on findings from animal studies and the mechanism of action, tepotinib can cause fetal harm when administered to pregnant women There are no available data on the use of tepotinib in pregnant women Advise pregnant women of the potential risk to a fetus In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively
 **Lactation**	There are no data regarding the secretion of tepotinib or its metabolites in human milk or its effects on the breastfed infant or milk production Advise women not to breastfeed during treatment with tepotinib and for one week after the last dose
 **Females and males of reproductive potential**	Based on animal data, tepotinib can cause malformations at doses less than the human exposure based on AUC at the 450 mg clinical dose Advise females of reproductive potential to use effective contraception during tepotinib treatment and for one week after the last dose Advise male patients with female partners of reproductive potential to use effective contraception during tepotinib treatment and for one week after the last dose

*AUC, area under curve.

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

Use in specific populations[1] (2/2)

Nov 2022 data (US PI)

Population	Safety recommendation
Pediatric patients	The safety and efficacy of tepotinib in pediatric patients have not been established
Geriatric patients	Of 313 patients with *MET*ex14 skipping alterations in VISION who received 450 mg tepotinib once daily: • 79% were 65 years or older • 41% were 75 years or older No clinically important differences in safety or efficacy were observed between patients aged 65 years or older and younger patients
Patients with renal impairment	No dosage modification is recommended in patients with mild or moderate renal impairment (CLcr 30–89 mL/min, estimated by Cockcroft–Gault) The recommended dosage has not been established for patients with severe renal impairment (CLcr <30 mL/min)
Patients with hepatic impairment	No dosage modification is recommended in patients with mild (Child–Pugh Class A) or moderate (Child–Pugh Class B) hepatic impairment The pharmacokinetics and safety of tepotinib in patients with severe hepatic impairment (Child–Pugh Class C) have not been studied

CLcr, creatinine clearance; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14.

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

Tepotinib drug-drug interactions[1]

Nov 2022 data (US PI)

- Tepotinib is a P-gp inhibitor
- Concomitant use of tepotinib increases the concentration of P-gp substrates, which may increase the incidence and severity of ARs of these substrates

Effects of tepotinib on other drugs:

- 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

AR, adverse reactions; P-gp, P-glycoprotein.

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

Summary

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

In VISION, comprising the largest population of patients with *MET*ex14 skipping NSCLC (N=313):

Most common AEs (≥20%) were **edema, fatigue, nausea, diarrhea, musculoskeletal pain, dyspnea, decreased appetite, and rash**[1]

- After ≥3-years follow-up, most common TRAEs in >10% of patients were **peripheral edema, hypoalbuminemia, nausea and diarrhea, blood creatinine increased, ALT increased, decreased appetite, AST increased and amylase increased**[2]

Consistent with previously reported results, tepotinib continues to demonstrate a manageable safety profile with no new safety signals; **peripheral edema** was the most common TRAE[2]

Clinically relevant adverse reactions in <10% of patients who received tepotinib included **ILD/pneumonitis, fever, dizziness, pruritus, and headache**[1]

Notable warnings and precautions for toxicities, and AR management guidance, from the prescribing information include:

The warnings and precautions for tepotinib include **ILD/pneumonitis, hepatotoxicity, pancreatic toxicity, and embryo-fetal toxicity**[1]

The recommended dose reduction of tepotinib for the management of ARs is **225 mg orally** once daily

- Management of some ARs may require temporary withhold, dose reduction, or permanent discontinuation[1]

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AR, adverse reaction; ILD, interstitial lung disease; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer; TRAE, treatment related adverse event.

1. TEPMETKO® (tepotinib) [Prescribing Information], https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf. **2.** Felip E, et al. WCLC 2025. Abstract P3.12.40.

SPECIFIC ADVERSE EVENTS

Peripheral edema/edema (1/2)

Incidence and potential mechanism

Median time to first onset:[1]
7.9 weeks (0.1–58.3)

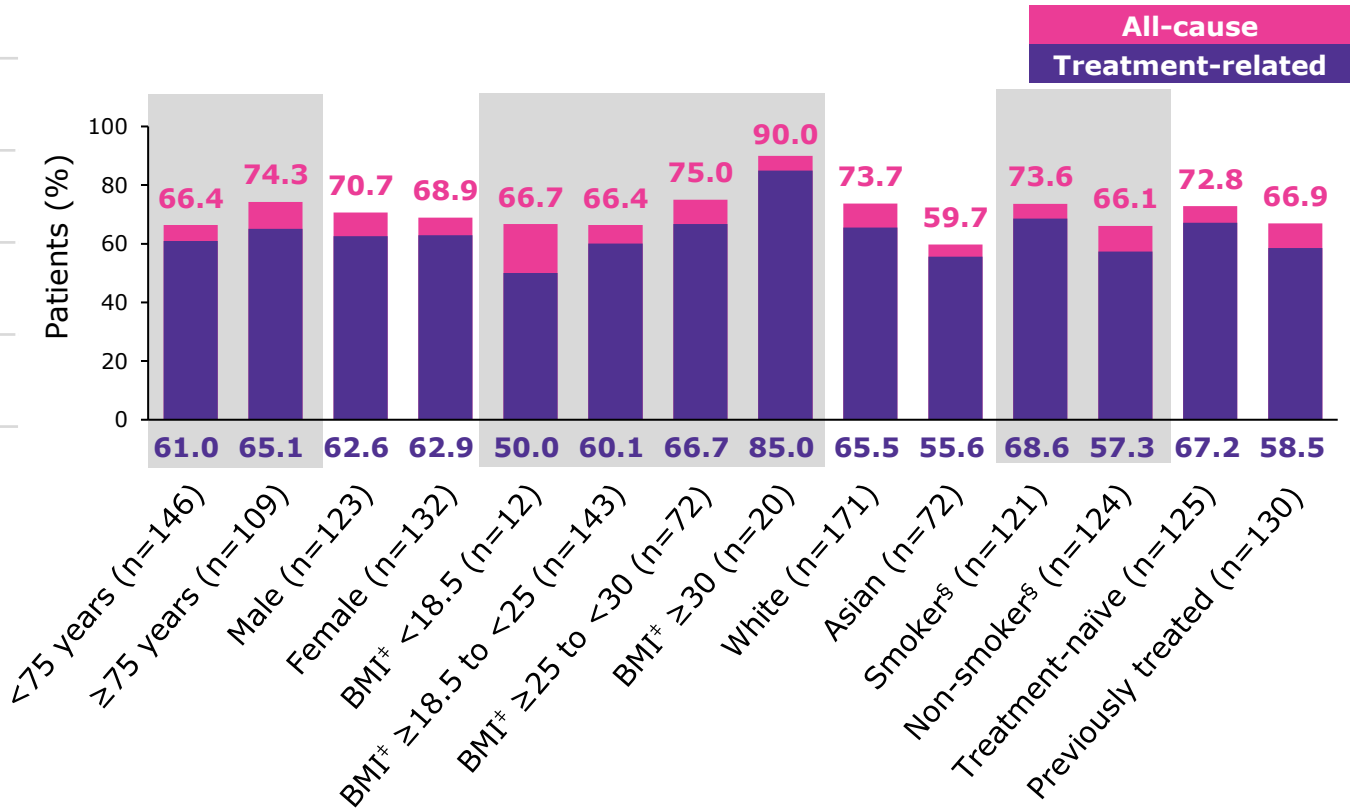
Incidence of all-cause AEs*/TRAEs** with tepotinib treatment in VISION[1,7]

Peripheral edema, %	N=255 (all-cause AEs)	N=313 (TRAEs)
Data cut	July 2020	May 2024 (≥3-year follow-up)
All grades	60.0	67.7
Grade 3–4	7.8†	11.8 (Grade ≥3)

Background and potential mechanism

- Peripheral edema is a class effect[1–4]
- Peripheral edema is very common, mostly mild or moderate, and can be slow to resolve[1]
- It is not life-threatening but can adversely affect QoL if advanced[6]
- The mechanism is not clear[7]

Edema (composite term) **incidence by subgroup**[1]



*Denotes the percentage of patients with all-cause AEs that occurred with tepotinib treatment in the *MET*ex14 skipping population of VISION (N=255); **Denotes the percentage of patients with TRAEs that occurred with tepotinib treatment in the *MET*ex14 skipping population of VISION (N=313); †No Grade 4 events were observed; ‡BMI was missing for eight patients; §Smoking history was missing for ten patients.

AE, adverse event; BMI, body mass index; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; QoL, quality of life; TRAE, treatment-related adverse event.

1. Veillon R, et al. *Clin Lung Cancer*. 2022;23(4):320-332; **2.** Wolf J, et al. *N Engl J Med*. 2020;383:944–957; **3.** Lu S, et al. *Lancet Respir Med*. 2021;9(10):1154–1164; **4.** Drilon A, et al. *Nat Med*. 2020;26:47–51; **5.** Hirose C, et al. *Support Care Cancer*. 2020;28(12):5943–5952; **6.** Cortot A, et al. *Clin Lung Cancer*. 2022;23(3):195-207; **7.** Felip E, et al. WCLC 2025. Abstract P3.12.40.

Peripheral edema/edema (2/2)

Dose modification and management

Hand edema in patients receiving tepotinib

Image credit: Linda Ahn

Monitoring[1,2]

- Early recognition is key to mitigating severity
- Regularly monitor body weight, inspect limbs for swelling or skin erosion, and measure limb circumference

Management[3,4]

- Edema was managed with dose reduction, temporary interruption, or discontinuation in the VISION study
- Compensatory management of peripheral edema included limb elevation, compression stockings, dietary salt reduction, and diuretics

1. Veillon R, et al. *Clin Lung Cancer*. 2022;23(4):320-332. **2.** Alexander T, et al. ONS 2021. Abstract 8970. **3.** Veillon R, et al. WCLC 2020. Abstract 821. **4.** Viteri S, et al. ESMO 2025. Abstract 1995P.

GI AEs (1/2)

Incidence

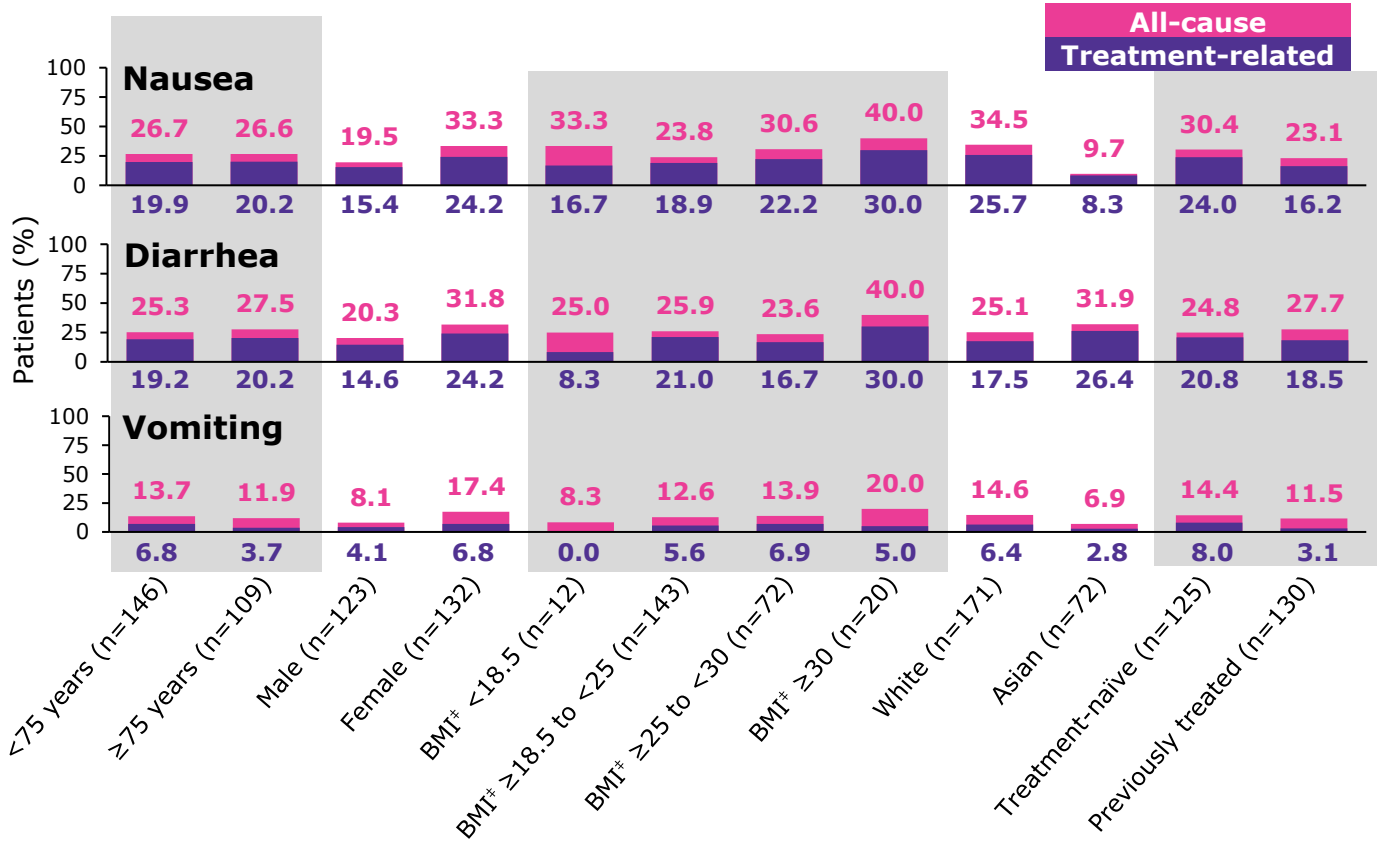
Median time to first onset:[1]
Nausea: 4.0 weeks (0.1–89.0)
Diarrhea: 2.4 weeks (0.1–48.0)
Vomiting: 5.1 weeks (0.1–61.7)

Median time to resolution:[1]
Nausea: 5.9 weeks (0.1+ to 88.6+)
Diarrhea: 1.8 weeks (0.1–37.4)
Vomiting: 0.3 weeks (0.1–25.4)

Incidence of all-cause AEs*/TRAEs** with tepotinib in VISION*[1,5]

GI AE, %		N=255 (all-cause AEs)	N=313 (TRAEs)
Data cut		July 2020	May 2024 (≥3-year follow-up)
Nausea	All grades	26.7	23.3
	Grade 3–4	0.8†	0.6 (Grade ≥3)
Diarrhea	All grades	26.3	22.7
	Grade 3–4	0.4†	0.3 (Grade ≥3)
Vomiting	All grades	12.9	
	Grade 3–4	1.2†	

Incidence by subgroup[1]



Background

- GI AEs are very common in the first weeks, but generally mild or moderate, and typically resolve in days to weeks[1]
- GI events have been reported with other TKIs[1–4]
- A low proportion of patients in the VISION study had a treatment modification due to GI AEs[1]

*Denotes the percentages of patients with all-cause GI AEs that occurred with tepotinib treatment in the *MET*ex14 skipping population of VISION (N=255); **Denotes the percentage of patients with TRAEs that occurred with tepotinib treatment in the *MET*ex14 skipping population of VISION (N=313); †No Grade 4 events were observed; ‡BMI was missing for eight patients.

AE, adverse event; BMI, body mass index; GI, gastrointestinal; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; TKI, tyrosine kinase inhibitor; TRAE, treatment-related adverse event.

1. Veillon R, et al. *Clin Lung Cancer*. 2022;23(4):320-332. **2.** Wolf J, et al. *N Engl J Med*. 2020;383:944–957; **3.** Lu S, et al. *Lancet Respir Med*. 2021;9(10):1154–1164; **4.** Drilon A, et al. *Nat Med*. 2020;26:47–51; **5.** Felip E, et al. WCLC 2025. Abstract P3.12.40.

GI AEs (2/2)

Dose modification and management

July 2020 data

Patients* with at least one event leading to:[1]	All-cause nausea	All-cause diarrhea	All-cause vomiting
Dose reduction, n (%)	2 (0.8)	0	0
Temporary interruption, n (%)	5 (2.0)	5 (2.0)	1 (0.4)
Permanent discontinuation, n (%)	1 (0.4)	1 (0.4)	0

Monitoring[2]

If GI AEs occur, ensure adequate hydration and monitor for dehydration and electrolyte imbalances

Proactive management[2]

GI AEs may be reduced by taking tepotinib with/soon after a meal and adjusting eating patterns to more frequent small meals

Reactive management[2]

Diarrhea can be managed with standard anti-diarrheal treatments, such as loperamide, and treatment can be temporarily interrupted to manage GI AEs

*Updated safety results from *MET*ex14 skipping advanced NSCLC population of VISION (N=255).

AE, adverse event; GI, gastrointestinal; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer.

1. Veillon R, et al. *Clin Lung Cancer*. 2022;23(4):320-332. **2.** Alexander T, et al. ONS 2021. Abstract 8970.

Increased creatinine (1/1)

Incidence and potential mechanism

Median time to first onset:[1]
3.1 weeks (0.1–78.4)

Median time to resolution:[1]
12.1 weeks (0.4+ to 104.3)

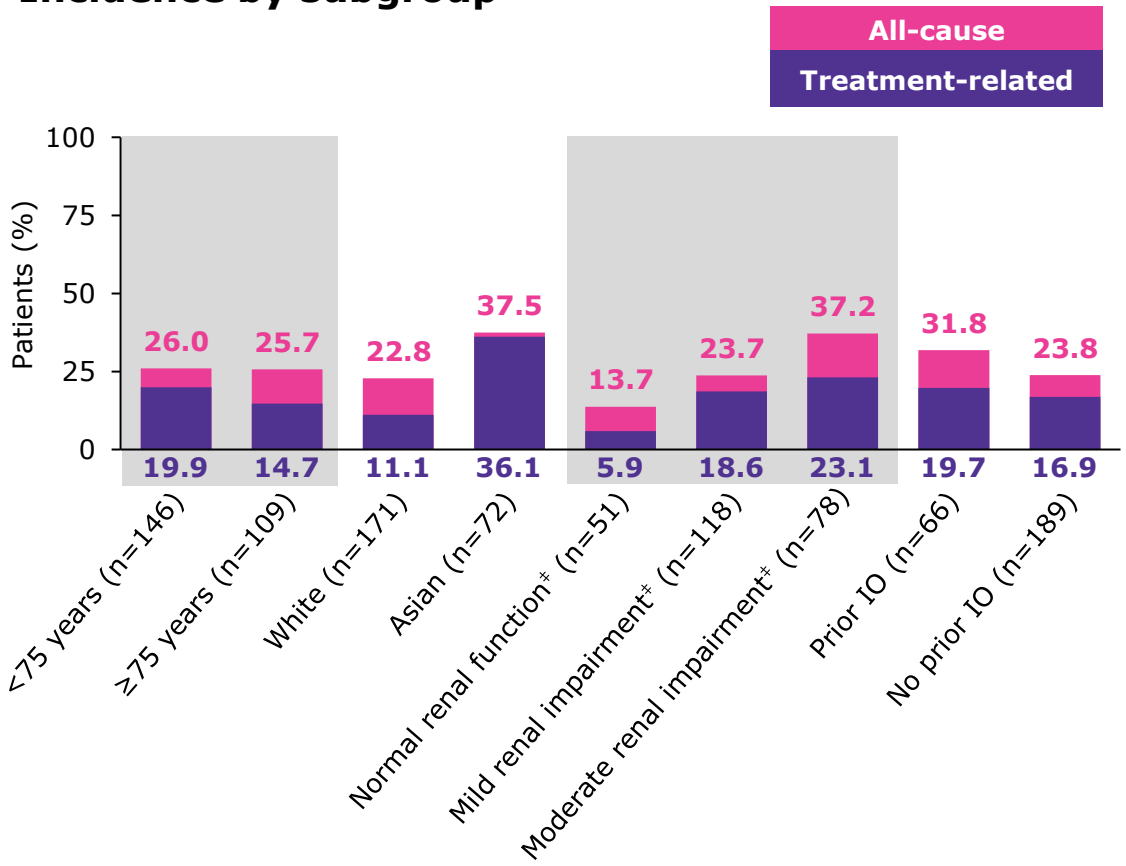
Incidence of all-cause AEs*/TRAEs** with tepotinib treatment in VISION[1,4]

Increased creatinine, %	N=255 (all-cause AEs)	N=313 (TRAEs)
Data cut	**July 2020**	**May 2024 (≥3-year follow-up)**
All grades	25.9	22.0
Grade 3–4	0.4†	1.3 (Grade ≥3)

Background and potential mechanism

- Creatinine increase is very common, especially in the first weeks of treatment, but is mostly mild or moderate[1]
- Creatinine increase with tepotinib does not generally indicate renal dysfunction[1]
- Based on non-clinical studies, increases in creatinine may reflect direct inhibitory effects on renal tubular transporters[1]
- In vitro studies suggest other TKIs have the potential to increase serum creatinine levels by inhibiting OCT2 and MATE1 transporters at clinically relevant concentrations[2,3]

Incidence by subgroup[1]



*Denotes the percentages of patients with all-cause AEs that occurred following treatment with tepotinib in the *MET*ex14 skipping population of VISION (N=255); **Denotes the percentage of patients with TRAEs that occurred with tepotinib treatment in the *MET*ex14 skipping population of VISION (N=313); †No Grade 4 events were observed; ‡Renal impairment status was missing for eight patients.

AE, adverse event; IO, immunotherapy; MATE, multidrug and toxin extrusion; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; OCT, organic cation transporter; TKI, tyrosine kinase inhibitor; TRAE, treatment-related adverse event.

1. Veillon R, et al. *Clin Lung Cancer*. 2022;23(4):320–332; **2.** Arakawa H, et al. *J Pharm Sci.* 2017;106(9):2899–2903; **3.** Omote S, et al. *Sci Rep.* 2018;8(1):9237; **4.** Felip E, et al. WCLC 2025. Abstract P3.12.40.

July 2020 data

Increased creatinine (2/2)

Dose modifications and management

Patients* with at least one all-cause creatinine increase event leading to:[1]	Tepotinib (N=255)
Dose reduction, n (%)	7 (2.7)
Temporary interruption, n (%)	16 (6.3)
Permanent discontinuation, n (%)	2 (0.8)

Monitoring[1-3]

- Monitor creatinine levels closely during the first 2 months of treatment
- Alternative markers for measuring GFR (such as urea, uric acid, electrolytes, cystatin C, and β-trace protein) can determine if creatinine elevation reflects renal impairment

Management[3,4]

- Patients typically experience a rapid creatinine increase that plateaus without renal impairment
- If creatinine increase is Grade 3, withhold tepotinib until resolved, then resume tepotinib at a reduced dose; if Grade 4, permanently discontinue tepotinib

*Updated safety results from *MET*ex14 skipping advanced NSCLC population of VISION (N=255).
AE, adverse event; GFR, glomerular filtration rate; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; NSCLC, non-small cell lung cancer.
1. Veillon R, et al. *Clin Lung Cancer*. 2022;23(4):320-332; **2.** Gowda S, et al. *N Am J Med Sci*. 2010;2(4):170–173; **3.** Alexander T, et al. ONS 2021. Abstract 8970. **4.** Cortot A, et al. *Clin Lung Cancer*. 2022;23(3):195-207.

Liver enzyme elevations

Incidence, potential mechanism, and monitoring

Incidence of all-cause AEs*/TRAEs** with tepotinib treatment in VISION[1,3]

Common but generally mild or moderate, reversible

		N=255 (all-cause AEs)	N=313 (TRAEs)
Data cut		**July 2020**	**May 2024 (≥3-year follow-up)**
Increased ALT, %	All grades	11.4	14.1
	Grade 3–4	3.1	2.2 (Grade ≥3)
Increased AST, %	All grades	7.5	11.2
	Grade 3–4	1.2	1.9 (Grade ≥3)

Monitoring[2]

Monitor ALT/AST regularly to enable early recognition

Management[2]

Dose reduction or interruption is not generally required unless accompanied by symptoms (e.g. jaundice, abdominal pain)†

*Denotes the percentages of patients with all-cause AEs that occurred following treatment with tepotinib in the *MET*ex14 skipping population of VISION (N=255); **Denotes the percentage of patients with TRAEs that occurred with tepotinib treatment in the *MET*ex14 skipping population of VISION (N=313); †In patients with Grade 3 ALT/AST increase without total bilirubin increase, tepotinib should be interrupted until recovery to baseline. Tepotinib should then be resumed at the reduced dose (225 mg) or, if recovery was within 7 days, at the standard dose. Tepotinib should be permanently discontinued in patients with Grade 4 ALT/AST increase without total bilirubin increase, or for ALT and/or AST >3 times the ULN with total bilirubin >2 times the ULN.

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; MET, mesenchymal-epithelial transition; *MET*ex14, *MET* exon 14; TRAE, treatment-related adverse event; ULN, upper limit of normal.

1. Veillon R, et al. *Clin Lung Cancer*. 2022;23(4):320-332; **2.** Alexander T, et al. ONS 2021. Abstract 8970; **3.** Felip E, et al. WCLC 2025. Abstract P3.12.40.

July 2020 data

Pleural effusion

Incidence, potential mechanism, and monitoring

Incidence of all-cause events with tepotinib treatment in VISION[1]*

Pleural effusion, %	Tepotinib (N=255)
All grades	13.3
Grade 3–4	5.1

Background and potential mechanism

- Pleural effusion is common in patients receiving tepotinib[1]
- Pleural effusion is a known comorbidity in NSCLC[2]
- Causes include tumor infiltration of the pleura (malignant pleural effusion with a prevalence of 15.9%[3]), indirect effects of the tumor, or treatments including chemo- or radiotherapy and MET inhibitors[4,5]

Monitoring[2]

If pleural effusion occurs, thoracentesis is recommended to rule out a malignant cause

Management[2,5]

If attributed to tepotinib after consideration of potential other causes (for e.g. prior chemo- or radiotherapy), tepotinib dose reduction of interruption may be considered†

*Table depicts the percentages of patients with all-cause AEs that occurred following tepotinib treatment in the *MET*ex14 skipping population of VISION (N=255); †Tepotinib should be interrupted in patients with Grade 3 events and resumed at the reduced dose of 225 mg once daily once resolved. Tepotinib should be permanently discontinued if Grade 4 events occur.

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

1. Veillon R, et al. *Clin Lung Cancer*. 2022;23(4):320–332; **2.** Cortot A, et al. *Clin Lung Cancer*. 2022;23(3):195–207; **3.** Morgensztern D, et al. *J Thorac Oncol*. 2012;7(10):1485–1489; **4.** Zhao J, et al. *Oncotarget*. 2017;8:97623–97632; **5.** Alexander T, et al. ONS 2021. Abstract 8970.

Common TRAEs with MET-targeting TKIs in NSCLC

TRAEs reported for ≥2 MET-targeting TKIs include:[1–5]*

- Edema/peripheral edema
- Elevated transaminases
- Nausea
- Vomiting
- Decreased appetite
- Diarrhea
- Fatigue
- Constipation
- Asthenia
- Increased creatinine
- Hypoalbuminemia

> Edema/peripheral edema is the most common TRAE among select MET TKIs and is considered a class effect[1].

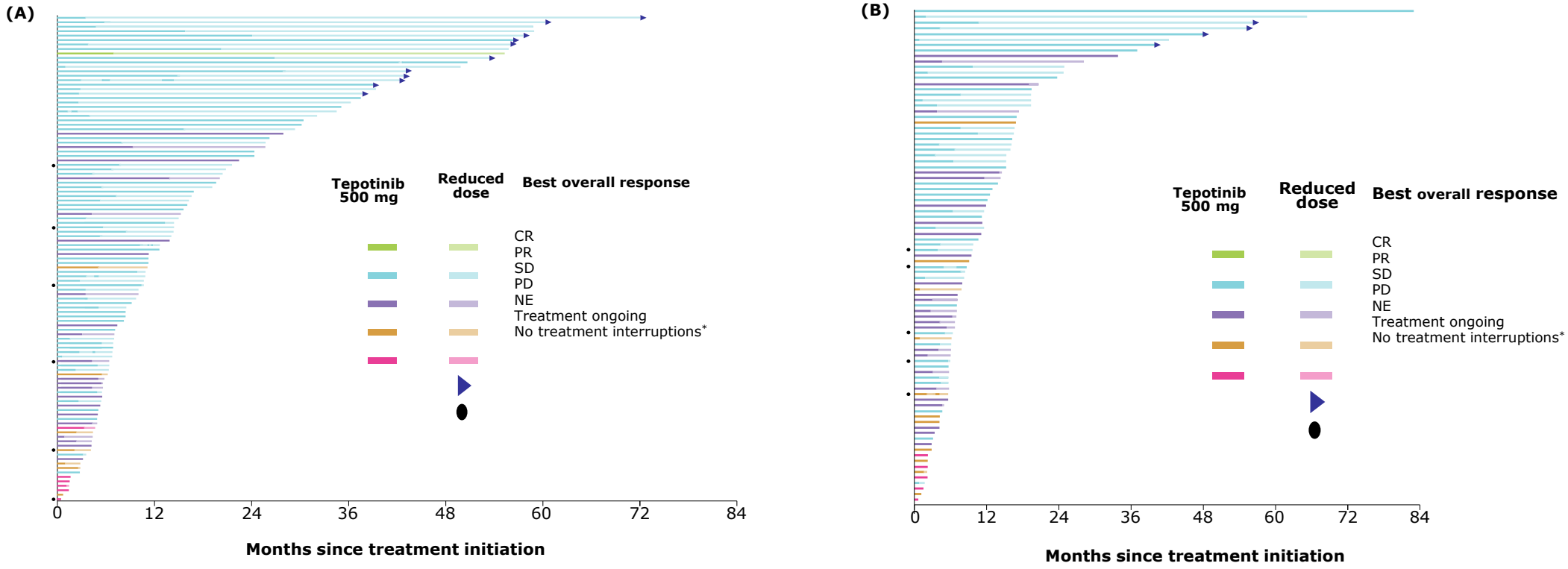
*Minimum cut-off for reporting TRAEs varies across publications.
MET, mesenchymal-epithelial transition; NSCLC, non-small-cell lung cancer; TKI, tyrosine kinase inhibitor; TRAE, treatment-related adverse event.

1. Veillon R, et al. *Clin Lung Cancer*. 2022;23(4):320–332; **2.** Wolf J, et al. *N Engl J Med*. 2020;383:944–957; **3.** Lu S, et al. *Lancet Respir Med*. 2021;9(10):1154–1164; **4.** Drilon A, et al. *Nat Med*. 2020;26:47–51; **5.** Scagliotti G, et al. *J Thorac Oncol.* 2020;15(1):80–90.

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

May 2024 data
(≥3-year follow-up)

The duration of treatment in patients with dose reductions and/or treatment interruptions receiving tepotinib in (A) 1L (n=108) and (B) 2L+ (n=89)



To return to the main slide, please click *here*

*All patients had treatment interruptions except those indicated with a circle.
1L, first line; 2L+, second-or-later line; CR, complete response; NE, not evaluable; PD, progressive disease; PR, progressive response; SD, stable disease.

1. Viteri S, et al. ESMO 2025. Abstract 1995P. **2.** Felip E, et al. WCLC 2025. Abstract P3.12.40.