TEPMETKO VISION Trial – Key Thought Leaders' Perspectives on the Largest and Longest *MET*ex14+ mNSCLC Clinical Trial With Long-Term Follow-Up Outcomes

ClinTopics®

TEPMETKO® (tepotinib) 225 mg Tablets

Meet the Experts

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View Detailed Information and Commentary From Experts Inside

Featured Topics

1 ***MET*ex14 Skipping and Its Significance in mNSCLC:** Among your patients with NSCLC, 3-4% may harbor *MET*ex14 skipping alterations and face a significantly worse prognosis than those without *MET*ex14 skipping alterations.[1-4]
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2 **VISION Trial – The Largest and Longest *MET*ex14+ Trial:** The VISION trial is the largest and longest clinical trial to date in *MET*ex14+ mNSCLC which included 313 patients identified by tissue and/or liquid biopsy.[5,6]
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3 **TEPMETKO Data – Efficacy, Safety and Dosing:** TEPMETKO achieved robust and lasting responses in both treatment-naïve (57% ORR; 40% still responding at ≥12 months) and previously treated (45% ORR; 36% still responding at ≥12 months) patients. TEPMETKO has an established safety profile and is also the only approved once-daily oral MET inhibitor.[5,6,7]
pages 4-11

MET=mesenchymal-epithelial transition; *MET*ex14=mesenchymal-epithelial transition exon 14; mNSCLC=metastatic non-small cell lung cancer; NSCLC=non-small cell lung cancer; ORR=objective response rate.

INDICATION

TEPMETKO is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (*MET*) exon 14 skipping alterations.

SELECT SAFETY INFORMATION

TEPMETKO can cause **interstitial lung disease (ILD)/pneumonitis**, which can be fatal. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever). Immediately withhold TEPMETKO 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 TEPMETKO, with one patient experiencing a Grade 3 or higher event; this event resulted in death.

Please see Selected Safety Information throughout the following newsletter and accompanying full Prescribing Information.

Prognosis and Treatment

- Patients with *MET*ex14 skipping NSCLC face a significantly worse prognosis than those without the alterations[1]
- 3% to 4% of your patients with NSCLC may harbor *MET*ex14 skipping alterations[2-4]
- mOS in patients with NSCLC with *MET*ex14 skipping alterations is significantly decreased compared to patients without *MET*ex14 skipping alterations (~1 year vs ~6.25 years, respectively [log-rank *P*=0.0385])[1]
- Targeted treatment may help patients with NSCLC achieve the best possible outcomes[8,9]
  - *MET*ex14 skipping NSCLC responds poorly to standard of care[10,11]
  - In a retrospective analysis of patients with NSCLC harboring *MET*ex14 skipping alterations (n=11/24 with PD-L1 ≥50%), after treatment with single or combination immunotherapy, the ORR was 17% and the mPFS was 1.9 months[12]
  - In real-world studies, patients with *MET*ex14 skipping NSCLC treated with immunotherapy had a mPFS of 2.69 months and a mOS of 12.25 months[13]
- Rapid initiation of targeted treatment is essential for patients with *MET*ex14 skipping NSCLC[10]

"With the availability of targeted therapies for patients with *MET*ex14 skipping alterations, it is important to use comprehensive genomic profiling (including next-generation sequencing, DNA sequencing, and RNA sequencing) to identify the presence of these rarer alterations.[14] I find that liquid biopsies give us another opportunity to obtain results if we cannot get an adequate tissue sample from a patient. Furthermore, the results from liquid biopsies may be available in ~8 days vs 3-4 weeks for tissue-based testing.[15]"
– Robert Hsu, MD

"Alterations like *MET*ex14 skipping may be present in smokers or never smokers, so it's important to use broad-based molecular profiling for all patients with advanced NSCLC, regardless of their age or smoking history, to identify these oncogene-addicted tumors.[14,16] We need to identify these alterations early because, without appropriate targeted therapy, they are more likely to have a poorer prognosis.[14]" ***– Jason Porter, MD***

National Comprehensive Cancer Network® (NCCN®) Recommends

- Clinicians obtain molecular testing results for actionable biomarkers in eligible patients with metastatic NSCLC before administering first-line systemic therapy, if clinically feasible[16]
- Targeted therapies for certain patients with metastatic NSCLC and specific oncogenic drivers independent of PD-L1 levels[16]
- For patients who must immediately start therapy while molecular testing is pending, consider holding immunotherapy for one cycle and use platinum-based chemotherapy regimens[16]
- If a *MET*ex14 skipping mutation is discovered during first-line systemic therapy, interrupt* current therapy and start a *MET* inhibitor[16]

*If there is a good response to current therapy, it is reasonable to continue therapy.[16]

ICI=immune checkpoint inhibitor; *MET*ex14=mesenchymal-epithelial transition exon 14; mOS=median overall survival; mPFS=median progression-free survival; NGS=next-generation sequencing; NCCN=National Comprehensive Cancer Network; NSCLC=non-small cell lung cancer; ORR=objective response rate; PDL-1=programmed death-ligand 1.

IMPORTANT SAFETY INFORMATION

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VISION Trial – The Largest and Longest *MET*ex14+ Trial

The VISION Trial is the largest and longest clinical trial in *MET*ex14+ mNSCLC.[5,6]

"When I consider the patient population included in the VISION trial, I am impressed that there were over 300 eligible patients who had metastatic NSCLC with the rare *MET*ex14 alterations and had EGFR wild-type and ALK- negative status, 1 measurable lesion as defined by RECIST v1.1, and ECOG PS 0-1.[2,5,6] Based on these eligibility criteria, I find the VISION trial to be clinically rigorous." ***– Robert Hsu, MD***

"When I consider gender, age, and smoking history, the patient characteristics from the VISION trial are consistent with what I see in my clinical practice. The patients that I treat with mNSCLC who have *MET*ex14 skipping tend to be either male or female smokers who are ≥70 years.[6]" ***– Jason Porter, MD***

Trial Design & Baseline Characteristics

- The VISION trial was a single-arm, open-label, multicenter, non-randomized, multicohort study in 313 patients with advanced or metastatic NSCLC harboring *MET*ex14 skipping alterations, EGFR wild-type and ALK negative status, 1 measurable lesion as defined by RECIST v1.1, and ECOG PS 0-1[2,5,6]
- Patients with symptomatic CNS metastases, clinically significant uncontrolled cardiac disease, or who received treatment with any MET or HGF inhibitor were not eligible for the study[2,5,6]
- The primary endpoint was objective response by a BIRC according to RECIST v1.1. Secondary endpoints included DOR, DCR, and safety[5,6]
- Of the 313 patients enrolled in VISION Trial, 94% has metastatic disease, 81% had adenocarcinoma histology, and 13% had CNS metastases[5]
    - The efficacy population included 164 treatment naïve patients and 149 previously treated patients
    - Amongst previously treated patients, 84% received prior platinum-based chemotherapy

ALK=anaplastic lymphoma kinase; BIRC=blinded, independent review committee; CNS=central nervous system; DCR=disease control rate; DOR=duration of response; ECOG PS=Eastern Cooperative Oncology Group performance status; EGFR=epidermal growth factor receptor; HGF=hepatocyte growth factor; MET=mesenchymal-epithelial transition; mNCSLC=metastatic non-small cell lung cancer; RECIST=Response Evaluation Criteria in Solid Tumors.

IMPORTANT SAFETY INFORMATION (continued)

TEPMETKO can cause **hepatotoxicity**, which can be fatal. Monitor liver function tests (including alanine aminotransferase [ALT], aspartate aminotransferase [AST], and total bilirubin) prior to the start of TEPMETKO, 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 TEPMETKO. Increased ALT/increased AST occurred in 18% of patients treated with TEPMETKO. 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).

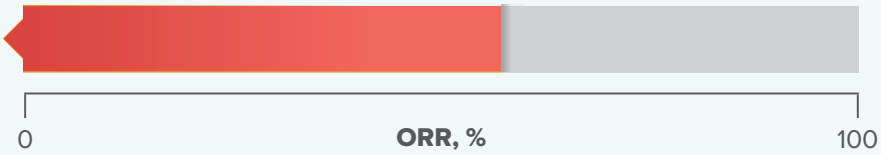
Please see Selected Safety Information throughout the following newsletter and accompanying full Prescribing Information.

Primary and Secondary Efficacy Data

- TEPMETKO provided robust and lasting responses in treatment-naïve patients[2,5,6]

Figure 1: ORR in Treatment-Naïve Patients[6a]

57% ORR
(95% CI: 49, 65)
(n=164)

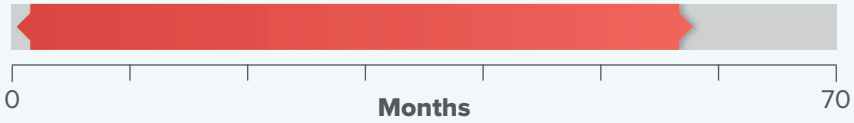


[a]ORR according to RECIST v1.1 as evaluated by a BIRC.

Figure 2: DOR in Treatment-Naïve Patients[5]

1.3 months

56.6 months



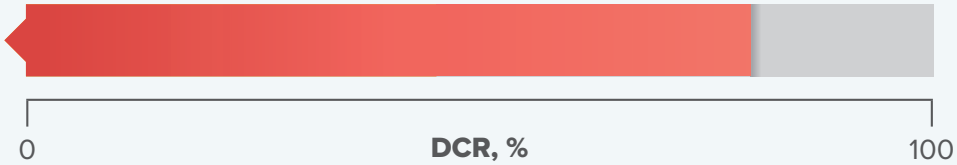
66% of patients were still responding at ≥6 months

40% of patients were still responding at ≥12 months

Long-Term Follow-Up* Data

Figure 3: DCR in Treatment-Naïve Patients[6]

78.7% DCR
(95% CI: 71.6, 84.7)
(n=164)



Limitations: DCR (defined as confirmed CR + PR + SD lasting at least 12 weeks as the best overall response by IRC assessments) from first administration of study treatment to the first observation of PD. In a single-arm trial, it is not possible to determine if SD is a result of natural disease progression or treatment. DCR was analyzed in a descriptive manner.

- Across all treatment-naïve and previously treated patients (n=313), 51% achieved a response with TEPMETKO (n=161)[2,17]:
  - 68% responded within 6 weeks
  - 84% responded within 12 weeks

"As we see in the graphs below, the ORR was 57% in treatment-naïve patients, and the duration of response ranged from 1.3 to 56 months, with 66% of patients responding at ≥6 months and 40% responding at ≥12 months. At long-term follow-up of up to 6 years, the DCR was nearly 80%.[5,6] These data demonstrate the effectiveness of TEPMETKO in treatment-naïve patients with *MET*ex14 skipping alterations. The time to response is also clinically significant to me because a quick response is important for patients with a heavier disease burden." ***– Robert Hsu, MD***

"When considering a first-line treatment option for patients with advanced NSCLC, regardless of alteration status, I look at response rates. The 57% ORR from the VISION trial in treatment-naive patients is an important finding, especially since response rates in advanced NSCLC are generally <60% with monotherapy chemotherapy or immunotherapy.[6,18]" ***– Jason Porter, MD***

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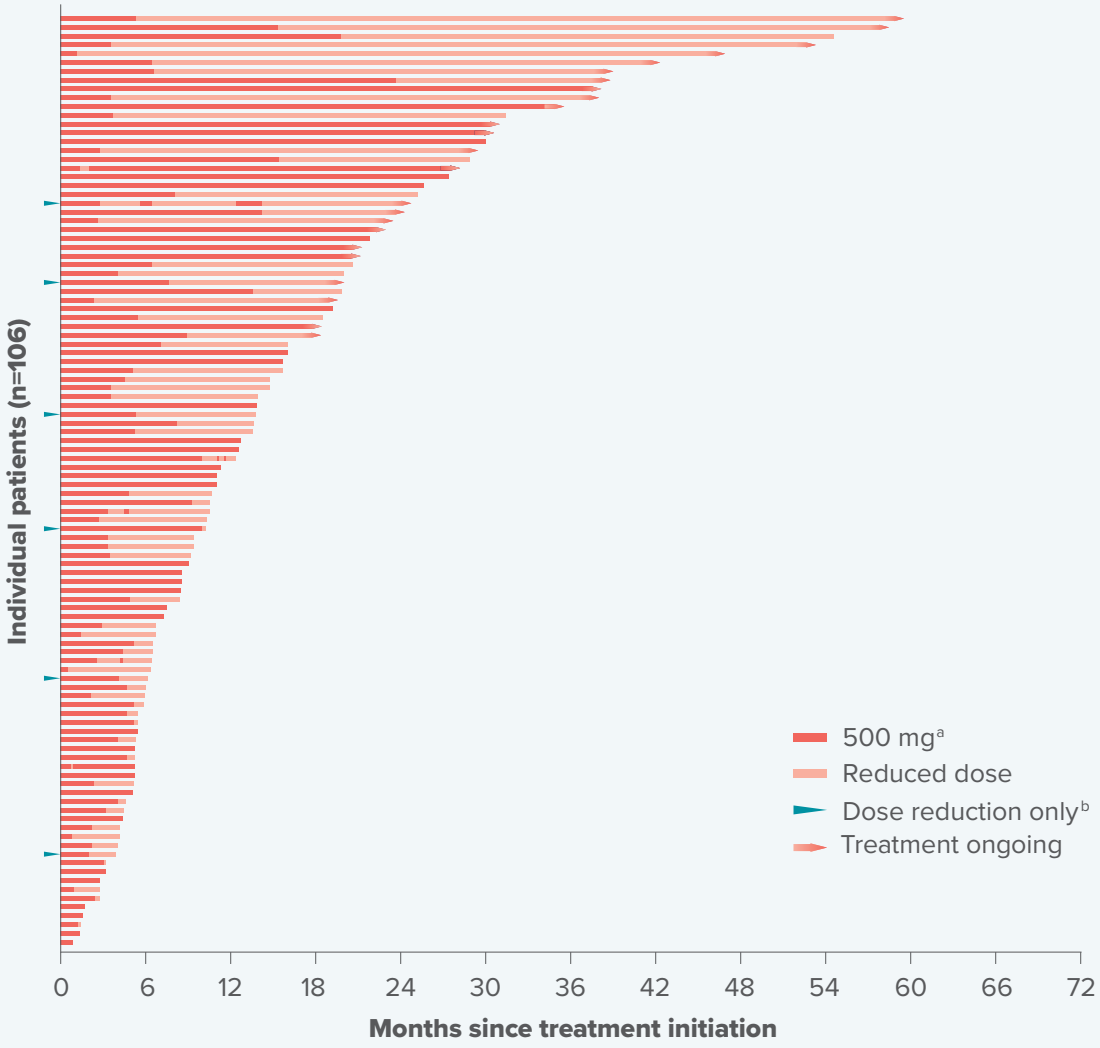
Figure 4: Duration of Treatment with Dose Reductions and/or Interruptions in Treatment-Naïve Paients[17,19]



[a]450 mg active moiety.
[b]All other patients had ≥1 treatment interruptions.

- Of total patients, 69 patients (42.07%) had at least one dose reduction, and 100 patients (61%) had at least one dose interruption/delay[17,19]
- Median duration of treatment (n=164) was 8.1 months (range: 0.03-59.37) while median duration of treatment with at least one dose reduction or interruption (n=106) was 11.1 months (range: 0.7-59.4)[17]

*Long-term follow-up of up to 6 years (range: 0.3-71.9 months).

CR=complete response; IRC=independent review committee; PD=progressive disease; PR=partial response; SD=stable disease.

IMPORTANT SAFETY INFORMATION (continued)

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

TEPMETKO can cause **embryo-fetal toxicity**. Based on findings in animal studies and its mechanism of action, TEPMETKO 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 TEPMETKO and for one week after the last dose.

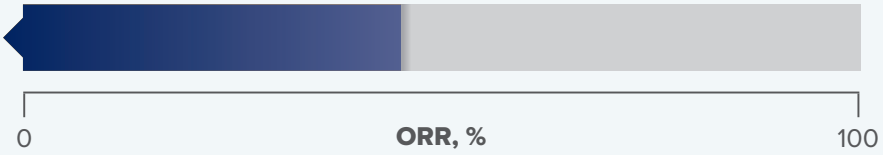
Please see Selected Safety Information throughout the following newsletter and accompanying full Prescribing Information.

Primary and Secondary Efficacy Data

- TEPMETKO provided robust and lasting responses in previously treated patients[2,5,6]

Figure 5: ORR in Previously Treated Patients[6a]

45% ORR
(95% CI: 37, 53)
(n=149)

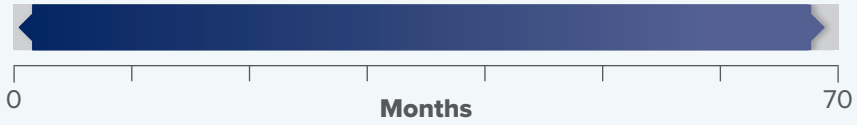


[a]ORR according to RECIST v1.1 as evaluated by a BIRC.

Figure 6: DOR in Previously Treated Patients[5]

1.4 months

67.6 months



66% of patients were still responding at ≥6 months

36% of patients were still responding at ≥12 months

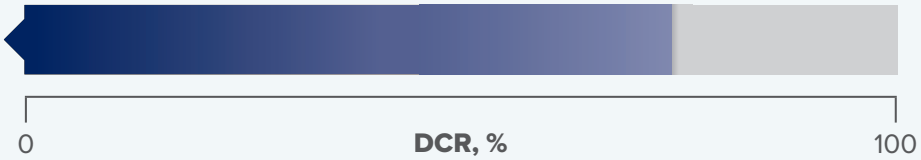
"Among patients who were previously treated, the ORR was 45% and the duration of response ranged from 1.4 to 67.6 months, with 66% of patients responding at ≥6 months and 36% responding ≥12 months. At long-term follow-up of up to 6 years, the DCR was nearly 74%.[5,6] One concern that we have with targeted therapy for other alterations in previously-treated patients with NSCLC is resistance.[20] However, based on the similar ORR between treatment-naive and previously-treated patients, TEPMETKO has demonstrated efficacy in both patient populations.[6] This could be partly because most patients who were previously treated received platinum-based chemotherapy or immunotherapy and not another *MET* inhibitor, so they are less likely to develop resistance.[19]" ***– Robert Hsu, MD***

"While previously-treated patients still responded to TEPMETKO, the response rates were slightly lower at 45%, demonstrating the importance of comprehensive genomic profiling to identify the *MET*ex14 skipping alterations earlier.[6] The duration of response, which ranged from 1.4 to 67.6 months was clinically meaningful to me.5 Finally, disease control rate is an important endpoint for me, especially when we need to stop disease progression or could potentially delay metastasis in previously-treated patients." ***– Jason Porter, MD***

Long-Term Follow-Up* Data

Figure 7: DCR in Previously Treated Patients[6]

73.8% DCR
(95% CI: 66.0, 80.7)
(n=149)



Limitations: DCR (defined as confirmed CR + PR + SD lasting at least 12 weeks as the best overall response by IRC assessments) from first administration of study treatment to the first observation of PD. In a single-arm trial, it is not possible to determine if SD is a result of natural disease progression or treatment. DCR was analyzed in a descriptive manner.

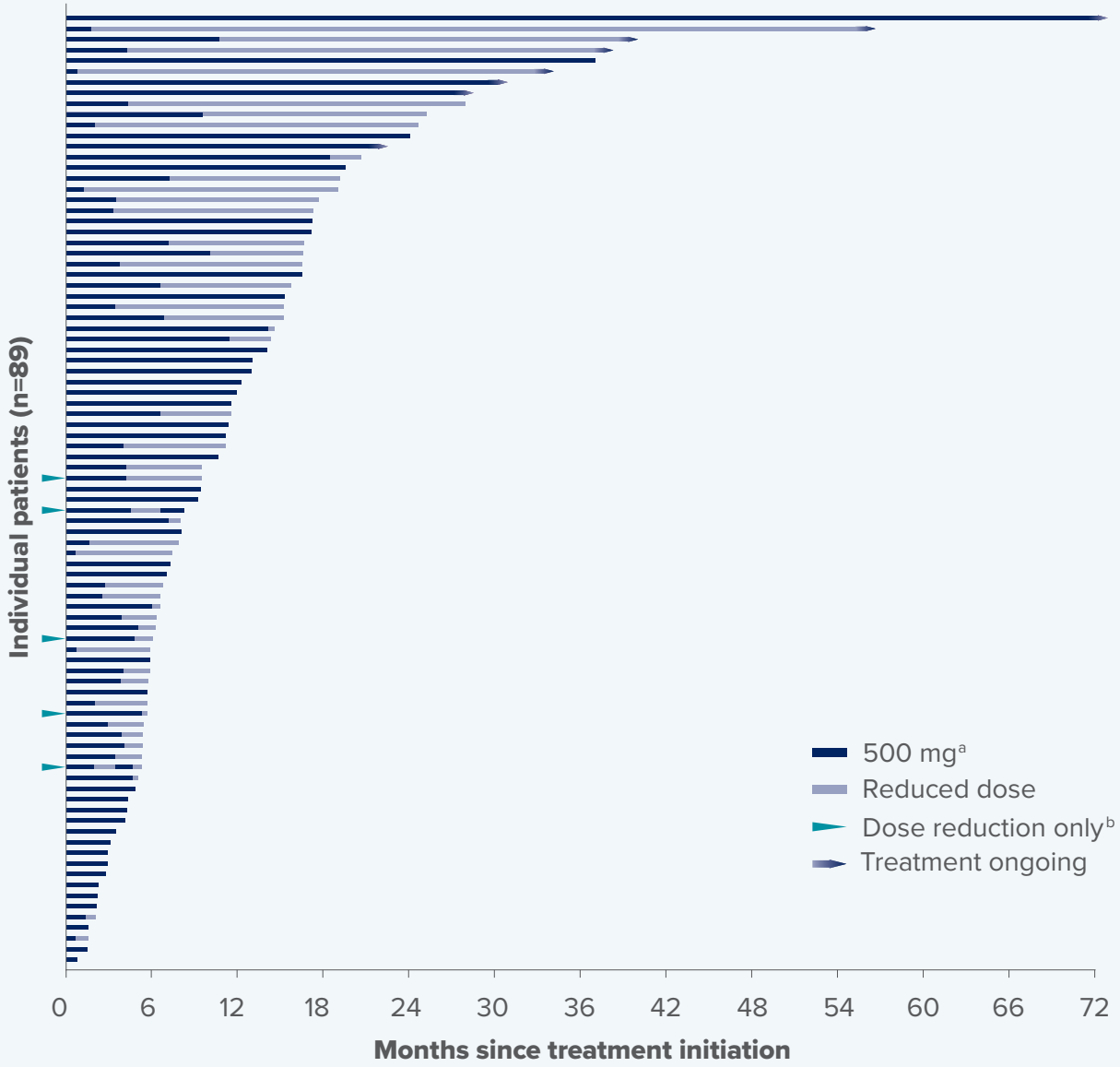
- Across all treatment-naïve and previously treated patients (n=313), 51% achieved a response with TEPMETKO (n=161)[2,17]:
  - 68% responded within 6 weeks
  - 84% responded within 12 weeks

IMPORTANT SAFETY INFORMATION (continued)

Avoid concomitant use of TEPMETKO 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.

Please see Selected Safety Information throughout the following newsletter and accompanying full Prescribing Information.

Figure 8: Duration of Treatment With Dose Reductions and/or Interruptions in Previously Treated Patients[17,19]



[a]450 mg active moiety.
[b]All other patients had ≥1 treatment interruptions.

- Of total patients, 47 patients (31.5%) had at least one dose reduction, and 84 patients (56%) had at least one dose interruption/delay[17,19]
- Median duration of treatment (n=149) was 7.0 months (range: 0.03-71.85) while median duration of treatment with at least one dose reduction or interruption (n=86) was 9.4 months (range: 0.7-71.9)[17]

*Long-term follow-up of up to 6 years (range: 0.3-71.9 months).

IMPORTANT SAFETY INFORMATION (continued)

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 occurred in 51% of patients who received TEPMETKO. 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%).

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Safety Profile

- The safety and tolerability of TEPMETKO were established in 313 patients[5,6]
- Most ARs observed in the VISION Trial were mild to moderate (Grade 1 or 2)[5]

Table 1: ARs in ≥10% of Patients With mNSCLC Harboring *MET*ex14+[5a]

	All grades (%)	Grades 3-4 (%)
Edema[b]	81	16
Fatigue[c]	30	1.9
Nausea	31	1.3
Diarrhea	29	0.6
Abdominal pain[d]	19	0.6
Constipation	19	0.3
Vomiting[e]	15	1
Musculoskeletal pain[f]	30	3.2
Dyspnea[g]	24	2.6
Cough[h]	18	0.3
Pleural effusion	14	4.2
Decreased appetite	21	1.9
Rash[i]	21	1.3
Pneumonia[j]	12	3.8

[a]Severity as defined by NCI CTCAE version 4.03.[5]
[b]Edema includes eye edema, face edema, generalized edema, localized edema, edema, genital edema, peripheral edema, peripheral swelling, periorbital edema, and scrotal edema.[5]
[c]Fatigue includes asthenia and fatigue.[5]
[d]Abdominal pain includes abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper, gastrointestinal pain, and hepatic pain.[5]
[e]Vomiting includes retching and vomiting.[5]
[f]Musculoskeletal pain includes arthralgia, arthritis, back pain, bone pain, musculoskeletal chest pain, musculoskeletal pain, myalgia, non-cardiac chest pain, pain in extremity, and spinal pain.[5]
[g]Dyspnea includes dyspnea, dyspnea at rest, and dyspnea exertional.[5]
[h]Cough includes cough, and productive cough.[5]
[i]Rash includes rash, palmar-plantar erythrodysesthesia 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.[5]
[j]Pneumonia includes pneumonia, pneumonia aspiration, and pneumonia bacterial.[5]

IMPORTANT SAFETY INFORMATION (continued)

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

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

Please see Selected Safety Information throughout the following newsletter and accompanying full Prescribing Information.

Laboratory Abnormalities*†

- **Selected laboratory abnormalities (≥20%)** from baseline in patients receiving TEPMETKO® (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%)[5]
- **The most common Grades 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%)[5]

Discontinuation, Dose Interruptions, and Dose Reductions

- Due to an AR in Patients Who Received TEPMETKO[5]
  - **Permanent discontinuation (25%)** The most frequent adverse reactions (>1%) leading to permanent discontinuations of TEPMETKO were edema (8%), pleural effusion (1.6%), and general health deterioration (1.6%)
  - **Dosage interruptions (53%)** ARs which required dosage interruption in >2% of patients who received TEPMETKO included edema (28%), increased blood creatinine (6%), pleural effusion (3.5%), nausea (3.2%), increased ALT (2.9%), pneumonia (2.6%), decreased appetite (2.2%), and dyspnea (2.2%)
  - **Dose reductions (36%)** ARs which required dose reductions in >2% of patients who received TEPMETKO included edema (22%), increased blood creatinine (2.9%), fatigue (2.2%), and pleural effusion (2.2%)

Fatal and Serious Adverse Reactions

- Fatal adverse reactions occurred in 1.9% of patients who received TEPMETKO, including pneumonitis (0.3%), hepatic failure (0.3%), dyspnea from fluid overload (0.3%), pneumonia (0.3%), sepsis (0.3%), and death of unknown cause (0.3%)[5]
- Serious adverse reactions occurred in 51% of patients who received TEPMETKO. 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%)[5]

Peripheral Edema

- Peripheral edema was observed in the VISION Trial and can be managed[6,7]
- Edema was managed with dose reduction, temporary interruption, or discontinuation[2,5]
  - TRAEs due to peripheral edema occurred in 67.1% of patients, with 11.2% experiencing Grade 3 or higher instances[6,7]
  - Proactive monitoring for peripheral edema is recommended[2]
  - TEPMETKO can be dose reduced in one step from two 225 mg tablets (450 mg total) to one 225 mg tablet
  - Compensatory management of peripheral edema included[2]:
    - Limb elevation
    - Compression stockings
    - Dietary salt reduction
    - Diuretics

"The most common adverse events with TEPMETKO include peripheral edema, fatigue, and nausea.[5] While Grade 1 or 2 edema may impact a patient's quality of life, I find that it can be managed with supportive care. I counsel my patients to wear compression stockings and will consider dose interruptions or reductions if needed.[2] Many of my patients report an improvement in edema with dose reductions. Even though they may still experience some degree of edema, my patients report that it does not significantly impact their quality of life."
– Robert Hsu, MD

"The incidence rates of edema, diarrhea, constipation, and abdominal pain are similar to what I see in my clinical practice and consistent with what I would expect from a *MET* inhibitor. It is important to educate patients upfront about the potential for these common adverse events so they can be prepared. Sometimes, compression stockings and orthopedic shoes can help with swollen feet, as well as, wardrobe changes to help with cosmetic concerns associated with swelling in legs and ankles. With these modifications, patients may remain on TEPMETKO treatment without compromising their daily activities."
– Jason Porter, MD

*Severity as defined by NCI CTCAE version 4.03.[5]

†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.[5]

ALT=alternative lengthening of telomeres; ALP=alkaline phosphatase; AST=aspartate aminotransferase; AR=adverse reaction; CTCAE=Common Terminology Criteria for Adverse Events; GGT=gamma-glutamyl transferase; NCI=National Cancer Institute; TRAE=treatment-related adverse event.

Please see Selected Safety Information throughout the following newsletter and accompanying full Prescribing Information.

"The standard TEPMETKO dose is 450 mg, administered as two 225-mg tablets. For patients with difficulty swallowing, I find it useful that TEPMETKO can be dissolved and administered through an NG tube or PEG tube. For patients who require a dose reduction due to an adverse event, I find it convenient, and my patients find it simple to go from the 450-mg dose with 2 tablets to the 225-mg reduced dose with 1 tablet.[1]" **– Jason Porter, MD**

"Based on data from the VISION trial, I find it reassuring that patients who require dose reductions or interruptions can continue treatment with TEPMETKO without being concerned about the impact on efficacy.[17,19]" ***– Robert Hsu, MD***

- TEPMETKO is the ONLY approved once-daily oral MET inhibitor[5]
- Provide your patients with mNSCLC with a convenient dosing regimen[5]
  - **One dose. Once a day**
  - **Recommended starting dosage: 450 mg (two 225 mg tablets)**
- Advise patients to:
  - Take their dose at approximately the same time every day until disease progression or unacceptable toxicity
  - Swallow tablets whole. Do not chew, crush, or split tablets
  - Never make up a missed dose within 8 hours of the next scheduled dose. If vomiting occurs after taking a dose, take the next dose at the scheduled time
- Can be dissolved for patients who have difficulty swallowing and/or have a naso-gastric tube[5]
- One-step dose reduction[5]
  - Remove one tablet to reduce dose to 225 mg once daily
- Permanently discontinue in patients who are unable to tolerate the 225 mg once-daily dose
- Management of some ARs may require temporary interruption or permanent discontinuation. See the full Prescribing Information for recommended dose modifications of TEPMETKO
- Patient selection[5]
  - Select patients for treatment with TEPMETKO based on the presence of *MET*ex14+ in plasma or tumor specimens. Testing for the presence of *MET*ex14+ 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, reevaluate the feasibility of biopsy for tumor tissue testing. An FDA-approved test for detection of *MET*ex14+ in mNSCLC for selecting patients for treatment with TEPMETKO is not available

The only MET inhibitor that offers a convenient one-step dose reduction.

FDA=United States Food and Drug Administration.

IMPORTANT SAFETY INFORMATION (continued)

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

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Robert Hsu, MD, is an Assistant Professor of Medicine in the Division of Medical Oncology at University of Southern California focusing on thoracic cancers. He completed his medical school training at Tulane University School of Medicine followed by Internal Medicine residency training at University of Miami/Jackson Memorial and then hematology and oncology training at Los Angeles County, University of Southern California where he served as chief fellow for medical oncology.

His research interests are focused on lung cancer research along with cancer disparities across multiple solid tumor types. His research includes projects involving comprehensive genomic profiling looking at biomarkers in lung cancer, retrospective database work looking at lung cancer patients treated at USC looking at mutation differences among different ethnicities particularly Hispanics, epidemiological research looking at lung and thyroid cancer incorporating the California Cancer Registry, and translational research looking at tumor microenvironment and ethnicities in lung and breast cancer.

Jason Porter, MD
Medical Oncologist and Hematologist
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Jason Porter, MD, is a medical oncologist and hematologist at the West Cancer Center and Research Institute. He completed his undergraduate degree at Christian Brothers University and medical training at the University of Tennessee Health Science Center. His clinical and research interests include early detection and screening for all cancers, local and advanced lung cancers, and benign hematology. He has published research on hypertension, advanced lung cancer therapy, and side effects as well as acute leukemia. He derives a great sense of fulfillment from helping patients and their families navigate the therapies and complications of these illnesses.

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Please see Selected Safety Information throughout the following newsletter and accompanying full Prescribing Information.

VISION Trial – Key Takeaways

"Based on the efficacy data for TEPMETKO in treatment-naïve and previously treated patients with *MET*ex14 skipping alterations, it is essential that we identify this alteration early with comprehensive genomic profiling in our patients with advanced NSCLC. Once we identify *MET*ex14 skipping alterations, we can start treatment with TEPMEKO, a *MET* inhibitor, because these patients do not respond well to chemotherapy and immunotherapy.[6]" ***– Robert Hsu, MD***

"I recommend next-generation sequencing for every patient diagnosed with advanced NSCLC. By identifying the *MET*ex14 skipping alterations before starting therapy, we can avoid administering chemotherapy or immunotherapy and initiate targeted therapy with TEPMETKO in the first-line setting. TEPMETKO also has demonstrated efficacy in previously treated patients, as evidenced by ORR, duration of response, and disease control rate. Based on these data, I would consider TEPMETKO an effective, once-daily treatment option for treatment-naïve and previously treated patients with *MET*ex14 skipping alterations." ***– Jason Porter, MD***

- TEPMETKO achieved robust and lasting responses in both treatment-naïve and previously treated patients[2,5-7]
  - Largest and longest clinical trial in *MET*ex14+ mNSCLC to date
  - Evaluated in patients diagnosed by tissue and/or liquid biopsy
  - Established safety profile
  - The **ONLY** approved once-daily oral *MET* inhibitor

Learn More About TEPMETKO

NCCN Preferred

Tepotinib is an NCCN Category 2A preferred regimen for first-line/subsequent line* setting for patients with *MET*ex14+ mNSCLC[16†‡§]

For all eligible patients with *MET*ex14+, start with TEPMETKO

*If MET inhibitors have not previously been given.
†Based upon lower-level evidence, there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.
‡See the NCCN Guidelines for detailed recommendations, including other preferred options.
§The NCCN Guidelines for NSCLC provide recommendations for individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.[16]

IMPORTANT SAFETY INFORMATION (continued)

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%).

Please see Important Safety Information throughout and accompanying full Prescribing Information.

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Dr Hsu and Dr Porter each received an honorarium for participation in this program.

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