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Real-world experience of MET TKI-induced peripheral edema



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CONCLUSIONS

- More than half of the patients with mNSCLC harboring *MET*ex14 skipping may experience PE (mainly mild-moderate in grade) during treatment with MET TKIs
- Physicians considered age, low mobility, and time on treatment as common risk factors, and cardiac disease as the most common comorbidity associated with PE
- Most physicians agreed that PE onset and severity was similar among the four available MET TKIs; crizotinib had less frequent, less durable, and less severe PE
- Over half of the physicians consider preventative measures within their patient management plans; however, these interventions are often started during treatment rather than at the time of initiating MET TKI treatment
- Pain was reported as a significant symptom of PE especially in severe cases and the decision on the intervention for its management lies with the physician. The use of analgesics is one such treatment option

INTRODUCTION

- *MET*ex14 skipping is an oncogenic driver reported in 3-4% of patients with metastatic mNSCLC and is sensitive to MET inhibition¹
- Currently, four oral small molecule MET TKIs (tepotinib, capmatinib, savolitinib, and crizotinib) are available²
- Peripheral edema (PE, usually mild-moderate), a frequently observed class effect of MET TKIs, can impact treatment adherence in patients with mNSCLC harboring *MET*ex14 skipping^{2,3}
- We conducted the Powerhouse Insights from Virtual Oncology Therapeutic Specialists (PIVOTS) survey of physicians' experience with MET TKIs to better understand associated PE and optimize its management

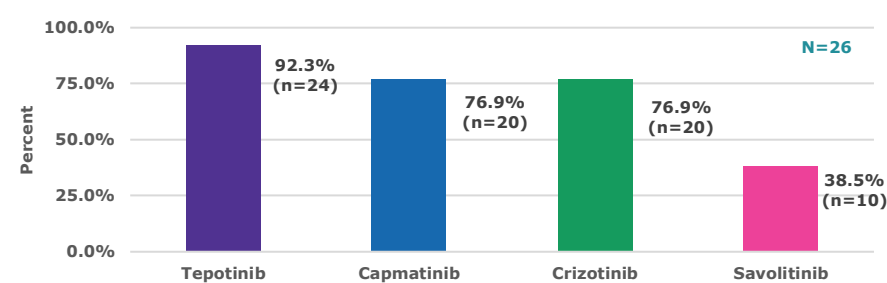
METHODS

- An online survey assessing the onset, time to resolution, symptoms, prevention, and management of PE during treatment with four available MET TKIs (tepotinib, capmatinib, savolitinib and crizotinib) for patients with mNSCLC harboring *MET*ex14 skipping was conducted among physicians globally (Europe, UK, North America and Asia)
- The physicians completing the PIVOTS survey had experience with treating patients with mNSCLC harboring *MET*ex14 skipping with one or more MET TKIs

Physicians' experience with MET TKIs

- In total, 26 physicians participated: Asia (n=14), Europe (n=6), UK (n=2), and North America (n=4)
- A total of 24 physicians had experience with tepotinib, 10 with savolitinib, 20 each with capmatinib and crizotinib, and seven with all four MET TKIs (Figure 1)
- Six physicians had experience with >20 patients, nine with 10-20 patients, six with 5-10 patients and five with <5 patients treated with a MET TKI

Figure 1. Physicians' experience in treating patients with mNSCLC with MET TKIs



PE status and clinical response to MET TKI

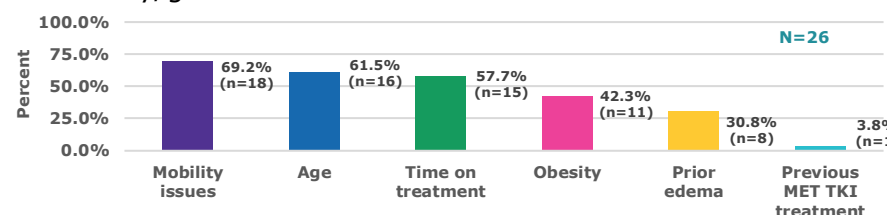
- Overall, 77% of physicians reported that >50% of patients had PE with MET TKIs
- Most of the physicians reported no relationship between clinical response to MET TKI and development of PE

Associated risk factors, onset and severity of PE associated with MET TKIs

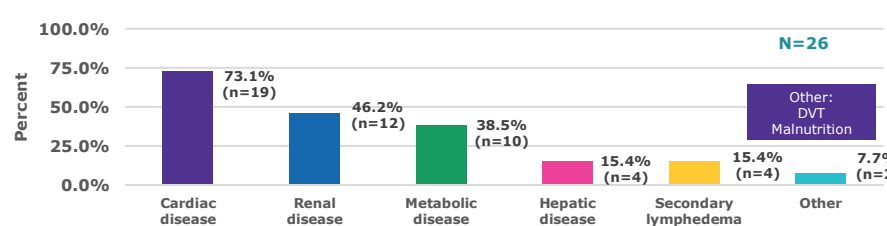
- Low mobility, age, and time on treatment were reported as common risk factors, cardiac disease as the most common comorbidity and antihypertensives as the most common co-medication class in patients experiencing PE while on treatment with MET TKI (Figure 2)

Figure 2. Physician-reported risk factors, co-morbidities, and co-medications in patients experiencing PE associated with MET TKIs

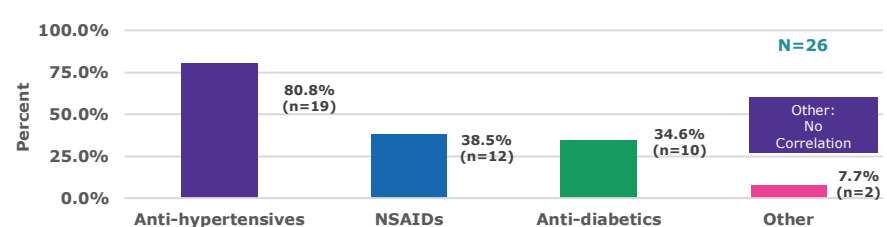
A. The greatest risk factors for MET TKIs-associated PE of any severity/grade



B. The most common co-morbidities

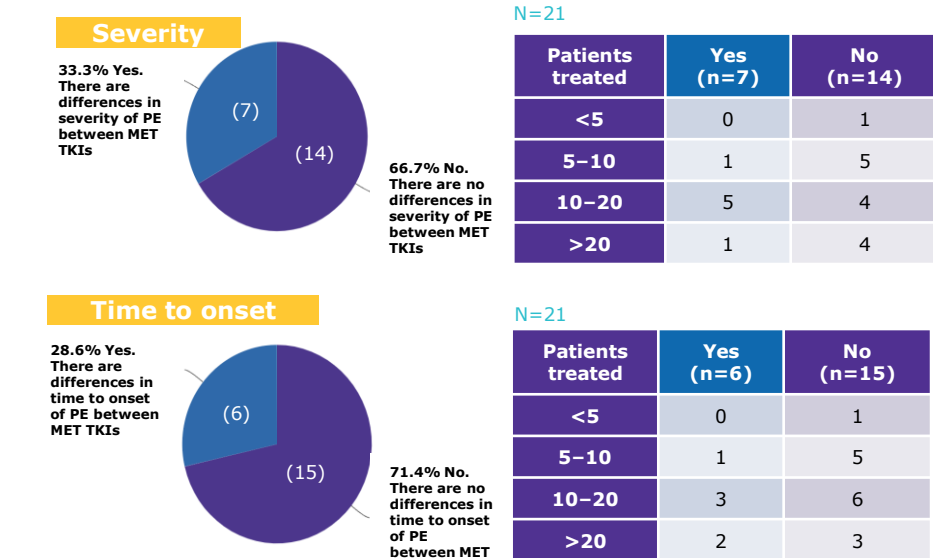


C. The most common concomitant medications



- Of 21 physicians having experience with multiple MET TKIs, most of the physicians reported that time to onset (which may take >6 months), and severity of PE were similar among four MET TKIs (Figure 3)
- A total of nine physicians considered that PE with crizotinib (a multi-kinase TKI) was less frequent, less severe, and less durable

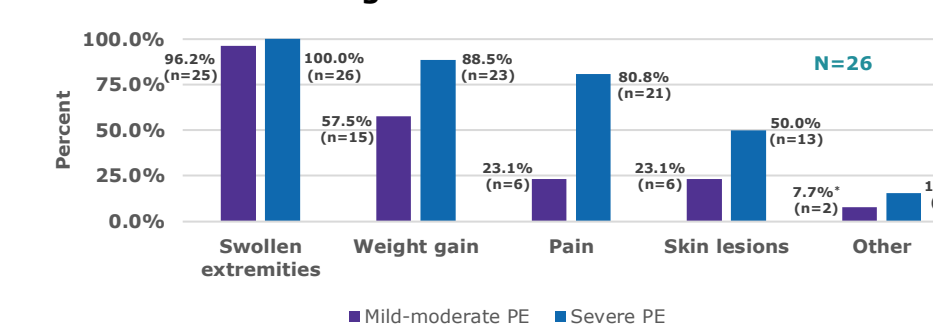
Figure 3. Differences observed by physicians in the severity/time to onset of PE between any of the MET TKIs



Signs and symptoms of PE associated with MET TKIs

- Physicians reported that >40% of the PE associated with MET TKIs in general was mild-moderate in grade; while <10% patients who developed PE were classified as severe
- Swollen extremities were reported by 96% of physicians as the most bothersome symptom followed by pain (46%) and weight gain (31%), with a resolution time of up to 3 months in mild-moderate PE and up to 6 months in severe PE
- Pain (81% vs 23%) and skin lesions (50% vs 23%) were reported as more common in severe versus mild-moderate PE, respectively (Figure 4)

Figure 4. Physician reported signs and symptoms that are most bothersome to patients experiencing mild-moderate or severe PE while taking MET TKIs



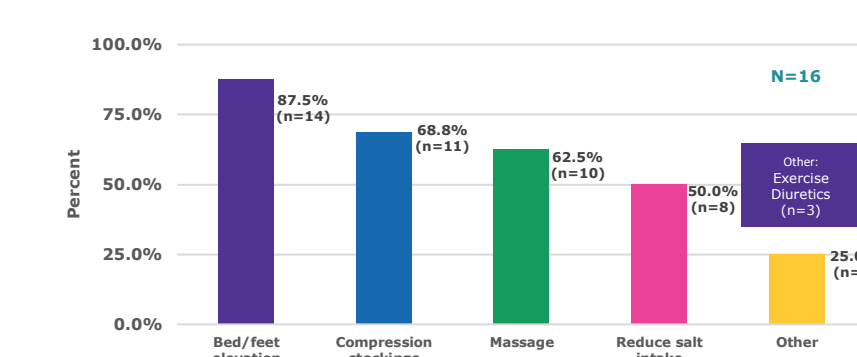
Prevention and management of PE associated with MET TKIs

- A total of 62% of physicians incorporated multiple preventative measures simultaneously (bed/feet elevation [88%], compression stockings [69%], massage [63%], salt intake reduction [50%], exercise/diuretics [25%]); only 13% incorporated at treatment initiation (Figure 5A)
- The most common interventions to manage PE were diuretics (89%), non-pharmacologic measures (i.e. compression stockings, bed elevation, reduced salt intake, massage; 85%), MET TKI interruption (73%), and dose reduction (65%)

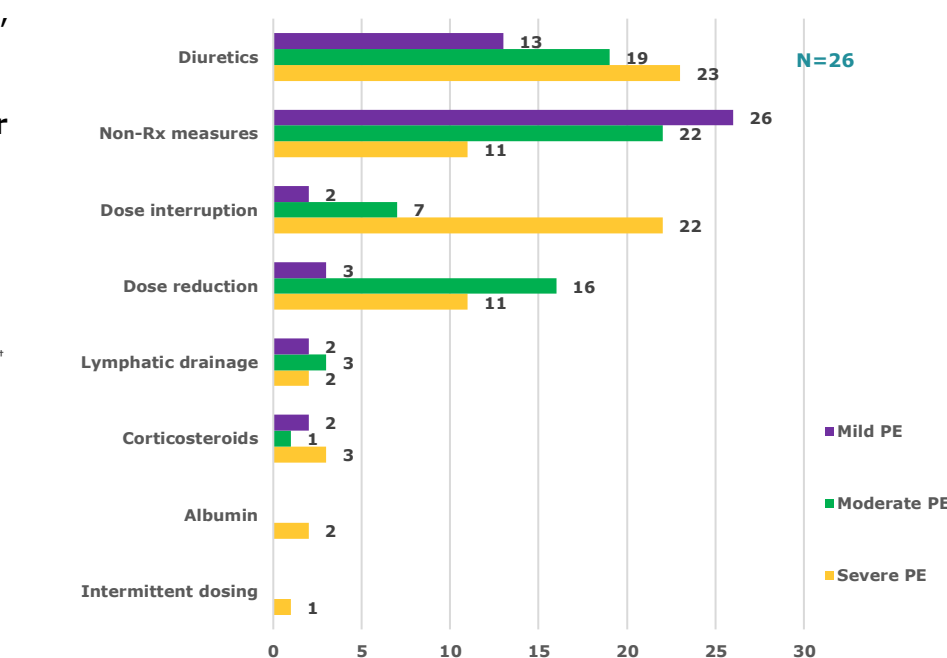
- Overall, 80.8% of physicians reported use of multiple interventions simultaneously based on the severity and grade of PE
- Physicians from China, Japan, and South Korea tend not to use multiple interventions simultaneously
 - A total of 4/5 Chinese physicians reported consulting vascular specialists for PE management
- The physician's preference to recommend diuretic for the management of PE increased as the grade level of PE increased, although some physicians may prefer to use diuretics early for mild PE (Figure 5B)
- Physicians preferred to recommend non-pharmacologic measures for mild-moderate PE
- MET TKI dosing modifications were mostly considered in moderate-severe edema
 - Dose reduction is more common in moderate edema, while dose interruption is preferred in severe cases

Figure 5. Preventive measures and treatments prescribed by physicians for PE associated with MET TKIs

A. Preventive measures prescribed by physicians for PE associated with MET TKIs



B. Preferred treatment(s) for the management of three grades of PE associated with MET TKIs



Patients' expectations in management of PE associated with MET TKIs

- Most physicians (73%) reported that patients stay on therapy even when experiencing moderate grade PE
- Over 50% of the patients expect an intervention to reduce PE symptoms to a mild grade

Abbreviations: DVT, deep vein thrombosis; MET, mesenchymal-epithelial transition factor; *MET*ex14, MET exon 14; mNSCLC, metastatic non-small cell lung cancer; NSAID, non-steroidal anti-inflammatory drugs; PE, peripheral edema; Rx, medical prescription; TKI, tyrosine kinase inhibitor; UK, United Kingdom.

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