

Pooled safety of vimseltinib in patients with tenosynovial giant cell tumor who received no prior colony-stimulating factor 1 receptor inhibitor therapy

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Background

- Tenosynovial giant cell tumor (TGCT) is a locally aggressive neoplasm caused by dysregulation of the colony-stimulating factor 1 (CSF1) gene leading to overproduction of CSF1^{1,2}
- Not all patients have disease that is amenable to surgery, and these patients require systemic therapies with manageable toxicity¹
- Vimseltinib is an oral, switch-control tyrosine kinase inhibitor designed to selectively and potently inhibit the CSF1 receptor (CSF1R)^{3,4}
 - Vimseltinib was approved in February 2025 by the US Food and Drug Administration⁵
 - In September 2025, the European Commission approved vimseltinib for the treatment of adult patients with TGCT associated with clinically relevant physical function deterioration and in whom surgical options have been exhausted or would induce unacceptable morbidity or disability⁶
- In the phase 2 expansion of a phase 1/2 study and in the MOTION phase 3 trial, vimseltinib demonstrated robust efficacy and a manageable safety profile⁷⁻⁹
- Here, we report a pooled safety analysis of vimseltinib from the phase 2 expansion and the MOTION phase 3 trial in patients with TGCT who did not receive prior CSF1R inhibitor therapy

Methods

- This safety analysis included patients who received vimseltinib 30 mg twice weekly in cohort A of the phase 1/2 trial (NCT03069469) and in the MOTION phase 3 trial (NCT05059262)
 - Safety data from patients who crossed over from placebo to vimseltinib in MOTION only reflect the time on vimseltinib
 - If dose modifications were required as determined by the investigator, the 30-mg dose of vimseltinib could be reduced to 20 mg and 14 mg in both studies
- Safety was evaluated through frequency of treatment-emergent adverse events (TEAEs), as well as measurements of liver enzymes and creatine phosphokinase (CPK)
- Treatment duration was also measured

Results

- Overall, 164 patients (cohort A: n = 46; MOTION: n = 118) were included in the analysis (**Table 1**)
 - The median age was 44 years
 - The most common disease location was the knee, and most patients had prior surgery

Table 1. Baseline demographics and clinical characteristics

	Cohort A + MOTION N = 164
Age, median (min, max), years	44 (20, 78)
Sex, n (%)	
Female	100 (61)
Male	64 (39)
Race, n (%)	
White	115 (70)
Asian	7 (4)
Black or African American	4 (2)
Not reported/other	38 (23)
Disease location, n (%)	
Knee	106 (65)
Ankle	22 (13)
Hip	15 (9)
Foot	10 (6)
Other ^a	11 (7)
Patients with prior surgery^b, n (%)	118 (72)
1 prior surgery	56 (34)
2-3 prior surgeries	48 (29)
≥4 prior surgeries	14 (9)
Patients with ≥1 prior systemic therapy, n (%)	29 (18)
Imatinib ^c	24 (15)
Nilotinib ^c	5 (3)
Other ^d	1 (1)

Data cutoff: February 22, 2025.

^aIncludes hand, shoulder, wrist, jaw, elbow, and temporomandibular joint.

^bDiagnostic biopsies were not recorded as a prior surgery or procedure.

^cPrior imatinib and nilotinib were permitted in cohort A of the phase 2 expansion and MOTION trials.

^dIncludes an investigational agent (BP 27 672).

max, maximum; min, minimum; TGCT, tenosynovial giant cell tumor.

- The median treatment duration was 20.7 months (0.2-49.9; **Table 2**)
 - 59% (96/164) of patients received treatment for ≥18 months
 - 41% (67/164) of patients received treatment for ≥24 months

Table 2. Treatment duration

	Cohort A + MOTION N = 164
Treatment duration, median (min, max), months	20.7 (0.2, 49.9)
Treatment duration by category, n (%)	
≥1 month	161 (98)
≥3 months	151 (92)
≥6 months	133 (81)
≥12 months	110 (67)
≥18 months	96 (59)
≥24 months	67 (41)

Data cutoff: February 22, 2025.

max, maximum; min, minimum.

Safety

- The majority of TEAEs were grade 1/2 (92%, 2850/3100) and occurred within the first year of treatment (78%, 2418/3100; **Table 3**)
 - The onset of the majority of the most severe events occurred within the first 2 years of treatment (**Figure 1**), and no late-onset AEs or new safety signals emerged
- The most common treatment-related TEAEs, such as edema and rash, were managed by following individual institutional guidelines per protocol

Table 3. Summary of adverse events

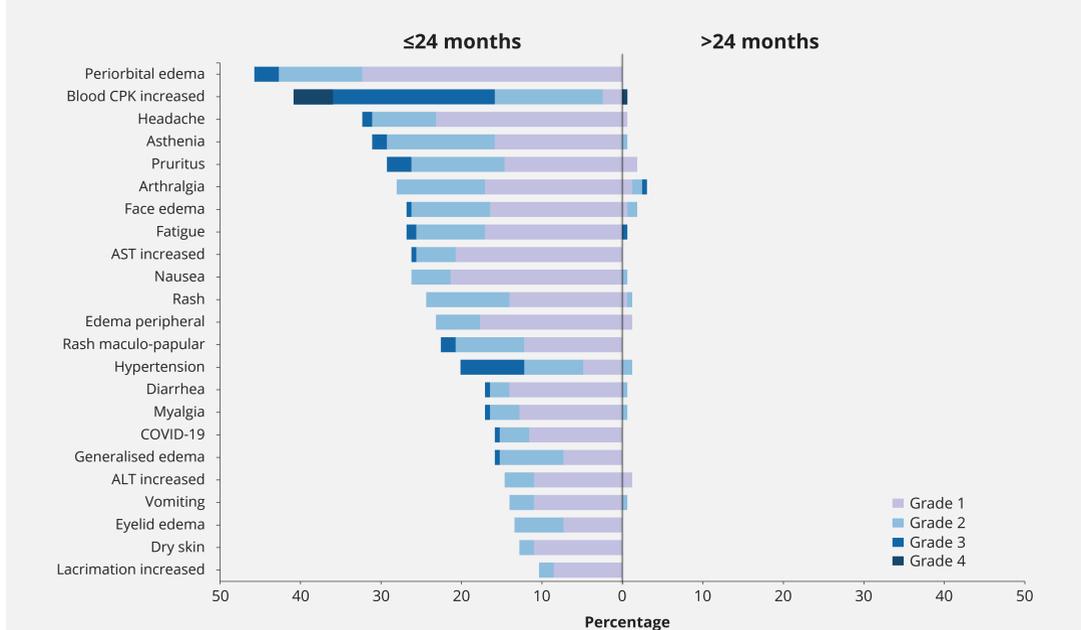
Preferred term, n (%)	Cohort A + MOTION N = 164
Any TEAE	163 (99)
Any treatment-related TEAE	159 (97)
Any serious TEAE	32 (20)
Serious treatment-related TEAE	3 (2)
Any TEAE leading to dose modification	125 (76)
TEAE leading to dose interruption	106 (65)
TEAE leading to dose reduction	96 (59)
Any treatment-related TEAE leading to dose modification	117 (71)
Treatment-related TEAE leading to dose interruption	91 (55)
Treatment-related TEAE leading to dose reduction	96 (59)
Any TEAE leading to treatment discontinuation	20 (12)
Treatment-related TEAE leading to treatment discontinuation	14 (9)
Any TEAE leading to death	1 (1) ^a
Treatment-related TEAE leading to death	0

Data cutoff: February 22, 2025.

^aReported reason due to "fall."

TEAE, treatment-emergent adverse event.

Figure 1. Percentage of TEAEs by maximum grade in ≥10% of patients occurring before and after 24 months on treatment



Data cutoff: February 22, 2025.

Severity was assessed by the investigator according to the toxicity grade described in the NCI CTCAE version 4.03 for the phase 1/2 study and NCI CTCAE version 5.0 for the MOTION study. Time denotes the earliest start date of the worst grade for each TEAE; if the highest grade TEAE occurred within the first 24 months of treatment, lower grade events that occurred after 24 months were not captured in this figure.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, Corona Virus Disease of 2019; CPK, creatine phosphokinase; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; TEAE, treatment-emergent adverse event.

- There was no evidence of cholestatic hepatotoxicity or drug-induced liver injury (**Table 4**)
 - Serum enzyme elevations were consistent with the known effect of Kupffer cell inhibition on enzyme clearance^{10,11}
 - Grade ≥2 aspartate aminotransferase (AST) or alanine aminotransferase (ALT) elevations occurred in 9% (15/164) of patients, and grade ≥2 CPK elevation occurred in 52% (86/164) of patients
 - The median time to normalization (defined as grade 1 or baseline grade) was 4.0 weeks and 15.1 weeks for AST/ALT and CPK elevation, respectively
 - At data cutoff, 2 patients had AST/ALT elevations that did not return to grade 1 or baseline grade while on study, and 25 patients had CPK elevation that did not return to grade 1 or baseline grade while on study

Table 4. Change from baseline in AST, ALT, and CPK per CTCAE grade

Patients, n (%)	Cohort A + MOTION N = 164
AST	
No change in grade from baseline	12 (7)
AST increased	
Any increase in grade from baseline	152 (93)
Increase to grade ≤2	151 (92)
Increase to grade 3/4	1 (1)
Increase to grade 3	1 (1)
Increase to grade 4	0
ALT	
No change in grade from baseline	117 (71)
ALT increased	
Any increase in grade from baseline	47 (29)
Increase to grade ≤2	47 (29)
Increase to grade 3/4	0
Increase to grade 3	0
Increase to grade 4	0
CPK^a	
No change in grade from baseline	0
No baseline grade	118 (72)
CPK increased	
Any increase in grade from baseline	46 (28)
Increase to grade ≤2	17 (10)
Increase to grade 3/4	29 (18)
Increase to grade 3	21 (13)
Increase to grade 4	8 (5)

Data cutoff: February 22, 2025.

^aThe 118 patients from MOTION were not included due to no baseline CPK assessment.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; CTCAE, Common Terminology Criteria for Adverse Events.

CONCLUSIONS

- In this pooled safety analysis, vimseltinib demonstrated a manageable safety profile in patients who did not receive prior CSF1R inhibitor therapy, consistent with prior reports
- There were no new cumulative or late-onset AEs, no new safety signals, and no evidence of cholestatic hepatotoxicity or drug-induced liver injury
- Nearly two-thirds (59%) of patients remained on treatment for at least 18 months
- These results support the continued use of vimseltinib in patients with TGCT not amenable to surgery

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