Abstract: 11558

Long-term clinical outcome assessments in patients with tenosynovial giant cell tumor treated with vimseltinib: 1-year results from the MOTION phase 3 trial

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Introduction

- 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]
- Surgical resection is standard of care, but not all patients have disease that is amenable to surgery[1,2]
  - Recurrence rates after surgery are as high as 72%, and patients who have a recurrence are significantly more likely to have future recurrences[3,4]
- Patients with TGCT experience pain, stiffness, and decreased physical function of affected joints[5]
- Left untreated, TGCT can result in severe functional limitations and substantial morbidity, leading to chronic and disabling impacts on daily activities[1,5]
  - Evaluating functional health is especially important in TGCT due to the symptomatic burden in the young patient population commonly affected by TGCT[5]
- Vimseltinib is an oral, switch-control tyrosine kinase inhibitor designed to selectively and potently inhibit the CSF1 receptor (CSF1R)[6]
  - Vimseltinib was approved in February 2025 by the US Food and Drug Administration for the treatment of adult patients with symptomatic TGCT for which surgical resection will potentially cause worsening functional limitation or severe morbidity[7]
- In part 1 (to week 25) of the MOTION phase 3 trial, patients receiving vimseltinib experienced robust and statistically significant antitumor activity per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) and per Tumor Volume Score (TVS) vs placebo[8]
- Additionally, vimseltinib provided statistically significant and clinically meaningful improvements in clinical outcome assessments (COAs) of active range of motion (ROM), physical function, stiffness, health status, and pain vs placebo[8]
- Here, we report updated (1-year) results for these COAs from patients who were randomized to vimseltinib in MOTION

Methods

- MOTION is a global, randomized, double-blind, placebo-controlled phase 3 trial with double-blind (part 1; to week 25), open-label (part 2; weeks 25–49), and extension periods (NCT05059262; **Figure 1**)
  - This analysis only includes patients randomized to vimseltinib
- Patients received vimseltinib 30 mg twice weekly
- Eligible patients were aged ≥18 years old with a confirmed diagnosis of symptomatic TGCT for which surgical resection would potentially cause worsening functional limitation or severe morbidity
- COAs reported here include change from baseline in active ROM of the affected joint, Patient-Report Outcomes Measurement Information System Physical Function (PROMIS-PF), worst stiffness numeric rating scale (NRS), EuroQol Visual Analogue Scale (EQ-VAS), and Brief Pain Inventory (BPI) worst pain (**Table 1**)
  - BPI worst pain response rate is also reported and defined as a ≥30% decrease in worst pain without a ≥30% increase in narcotic analgesic use

Figure 1. MOTION trial design

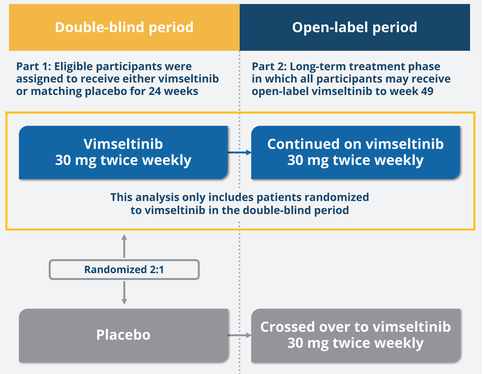


Table 1. Clinical outcome assessments

Assessment	Description
Active ROM	The degree of movement in the affected joint as measured by goniometry and compared to a reference range
PROMIS-PF (TGCT-specific)[9]	A 15-item questionnaire to assess tumor-location–specific physical function
EQ-VAS	Patients were asked "How good or bad is your health today?" on a visual scale of 0 (worst health imaginable) to 100 (best health imaginable)
Worst stiffness NRS	Patients were asked to rate their worst stiffness in the last 24 hours on a scale from 0 (no stiffness) to 10 (worst imaginable)
BPI worst pain	Patients were asked to rate their worst pain in the last 24 hours on a scale from 0 (no pain) to 10 (pain as bad as you can imagine)

BPI, Brief Pain Inventory; EQ-VAS, EuroQol Visual Analogue Scale; NRS, numeric rating scale; PROMIS-PF, Patient-Reported Outcomes Measurement Information System Physical Function; ROM, range of motion; TGCT, tenosynovial giant cell tumor.

Results

- Overall, 83 patients were randomized to vimseltinib in the double-blind period; the most common disease location was the knee, and most patients had a prior surgery or procedure for TGCT (**Table 2**)
  - Of these patients, 73 continued treatment in the open-label period and 54/73 (74%) remained on treatment at data cutoff

Table 2. Patient demographics and baseline characteristics

	Vimseltinib n = 83
Age, years, median (IQR)	45 (33–53)
Sex, n (%)	
Female	46 (55)
Male	37 (45)
Race, n (%)	
White	59 (71)
Asian	1 (1)
Black or African American	4 (5)
Other[a]	19 (23)
Affected joint, n (%)	
Knee	56 (67)
Ankle	9 (11)
Hip	11 (13)
Other[b]	7 (8)
Prior TGCT surgery or procedure[c], n (%)	64 (77)
Prior TGCT systemic therapy, n (%)	19 (23)
Imatinib	16 (19)
Nilotinib	2 (2)
Other[d]	1 (1)

Data obtained from Gelderblom H, et al. *Lancet*. 2024;403(10445):2709-19.
[a]Includes not reported and unknown. [b]Includes foot, wrist, hand, shoulder, elbow, and temporomandibular joint. [c]All patients had histologically confirmed TGCT per diagnostic biopsy or existing pathology report; diagnostic biopsies were not recorded as a prior surgery or procedure. [d]Includes an investigational agent (BP 27 672). IQR, interquartile range; TGCT, tenosynovial giant cell tumor.

Clinical outcome assessments

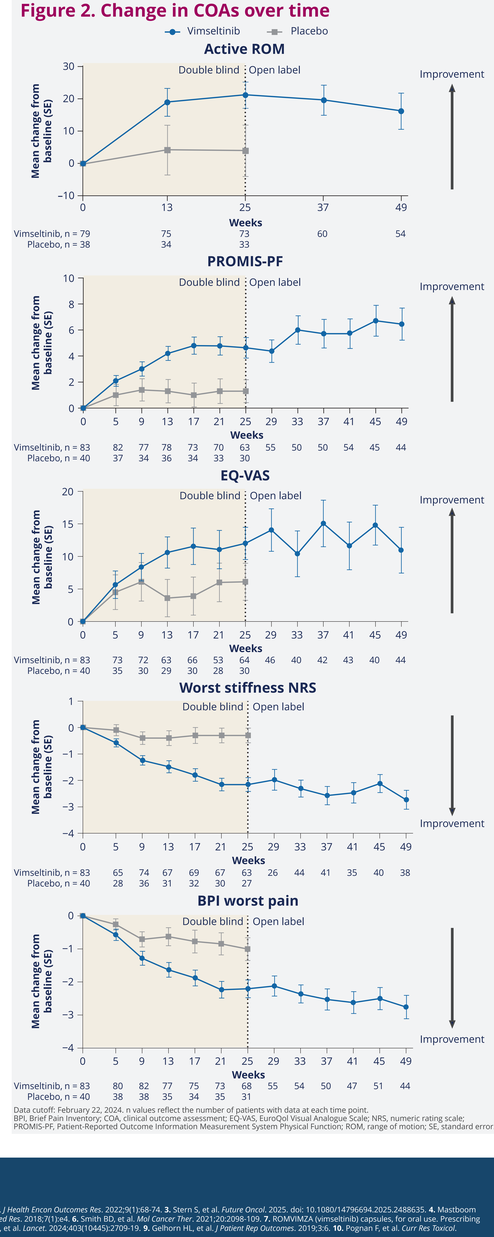
- Consistent with results from part 1, COAs at 1 year continued to show improvement from baseline (**Table 3, Figure 2**)
- Vimseltinib provided clinically meaningful improvements from baseline in active ROM, PROMIS-PF, worst stiffness NRS, EQ-VAS, and BPI worst pain
  - The BPI worst pain response rate was also maintained through 1 year (40%, 33/83)

Table 3. COAs in part 1 (week 25) and part 2 (week 49)

	Week 25	Week 49
Active ROM		
Patients, n	73	54
% Mean change from baseline (SE)	19.3 (3.7)	14.9 (5.0)
PROMIS-PF		
Patients, n	63	44
Mean change from baseline (SE)	4.6 (0.8)	6.5 (1.2)
EQ-VAS		
Patients, n	64	44
Mean change from baseline (SE)	12 (2.5)	11.0 (3.5)
Worst stiffness NRS		
Patients, n	63	38
Mean change from baseline (SE)	−2.2 (0.3)	−2.7 (0.4)
BPI worst pain		
Patients, n	68	44
Mean change from baseline (SE)	−2.2 (0.3)	−2.8 (0.4)
Response rate,[a] n (%)	40 (48)	33 (40)

Data cutoff: February 22, 2024. n values reflect the number of patients with data at each time point.
[a]Responder: Experienced at least a 30% decrease in mean BPI worst pain and did not experience a 30% or greater increase in narcotic analgesic use. Value for the denominator was N = 83 for both weeks.
BPI, Brief Pain Inventory; COA, clinical outcome assessment; EQ-VAS, EuroQol Visual Analogue Scale; NRS, numeric rating scale; PROMIS-PF, Patient-Reported Outcome Information Measurement System Physical Function; ROM, range of motion; SE, standard error.

Figure 2. Change in COAs over time



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BPI, Brief Pain Inventory; COA, clinical outcome assessment; EQ-VAS, EuroQol Visual Analogue Scale; NRS, numeric rating scale; PROMIS-PF, Patient-Reported Outcome Information Measurement System Physical Function; ROM, range of motion; SE, standard error.

Safety

- With continued follow-up, most treatment-emergent adverse events (TEAEs) were grade 1/2 with no evidence of cholestatic hepatotoxicity or drug-induced liver injury (**Table 4**)
- Hair hypopigmentation has not been observed with longer exposure to vimseltinib
- Serum enzyme elevations were consistent with the known mechanism of action of CSF1R inhibitors[10,11]
- At data cutoff, TEAEs led to treatment discontinuation in 10% (8/83) of patients randomized to vimseltinib
- Median (range) treatment duration was 14.4 (1.5–25.0) months

Table 4. TEAEs in ≥15% of patients randomized to vimseltinib

	Vimseltinib → vimseltinib (combined parts 1 + 2) n = 83	
Preferred term, n (%)	**All grades**	**Grade 3/4**
Periorbital edema	39 (47)	3 (4)
Fatigue	30 (36)	1 (1)
Pruritus	29 (35)	3 (4)
Face edema	28 (34)	1 (1)
Asthenia	27 (33)	1 (1)
Blood CPK increased[a]	26 (31)	10 (12)
Headache	24 (29)	1 (1)
Arthralgia	23 (28)	0
AST increased	22 (27)	1 (1)
Nausea	22 (27)	0
Rash	22 (27)	0
Rash maculopapular	20 (24)	2 (2)
Hypertension	18 (22)	6 (7)
Edema peripheral	17 (20)	0
COVID-19	16 (19)	1 (1)
Diarrhea	15 (18)	1 (1)
Generalized edema	14 (17)	1 (1)

Data cutoff: February 22, 2024. Previously presented at ESMO 2024, September 13–17; Barcelona, Spain. Presentation LBA78.
[a]Central monitoring of CPK was added in protocol amendment 3.
AST, aspartate aminotransferase; COVID-19, coronavirus disease-2019; CPK, creatine phosphokinase; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- These updated results demonstrate clinically meaningful, durable, and sustained improvements in active ROM, physical function, stiffness, health status, and pain with ongoing vimseltinib treatment
- Continued treatment with vimseltinib provides clinically meaningful benefit in functional health and symptomatic improvement beyond week 25
- Patients receiving vimseltinib experienced mostly grade 1/2 TEAEs consistent with previous analyses, with no evidence of cholestatic hepatotoxicity or drug-induced liver injury
- Vimseltinib offers an effective treatment option that improves quality of life for patients with symptomatic TGCT whose disease is not amenable to surgery

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Please scan to read the primary results from MOTION