2024 ASCO ANNUAL MEETING

Efficacy, safety, and patient-reported outcomes of vimseltinib in patients with tenosynovial giant cell tumor: Results from the phase 3 MOTION trial

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June 3, 2024

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Chief of Sarcoma Medical Oncology Service at Memorial Sloan Kettering Cancer Center

MOTION was a positive phase 3 study and met its primary and all key secondary endpoints

- MOTION is a phase 3 study designed to evaluate antitumor activity and safety as well as how participants with TGCT feel and function while treated with vimseltinib
- Vimseltinib demonstrated significant antitumor activity vs placebo, with a favorable safety profile
- Participants receiving vimseltinib experienced statistically significant and clinically meaningful improvements in active range of motion (ROM) and self-reported physical function, stiffness, health status, and pain
- If approved, vimseltinib may offer an effective systemic treatment for people with TGCT

TGCT, tenosynovial giant cell tumor.

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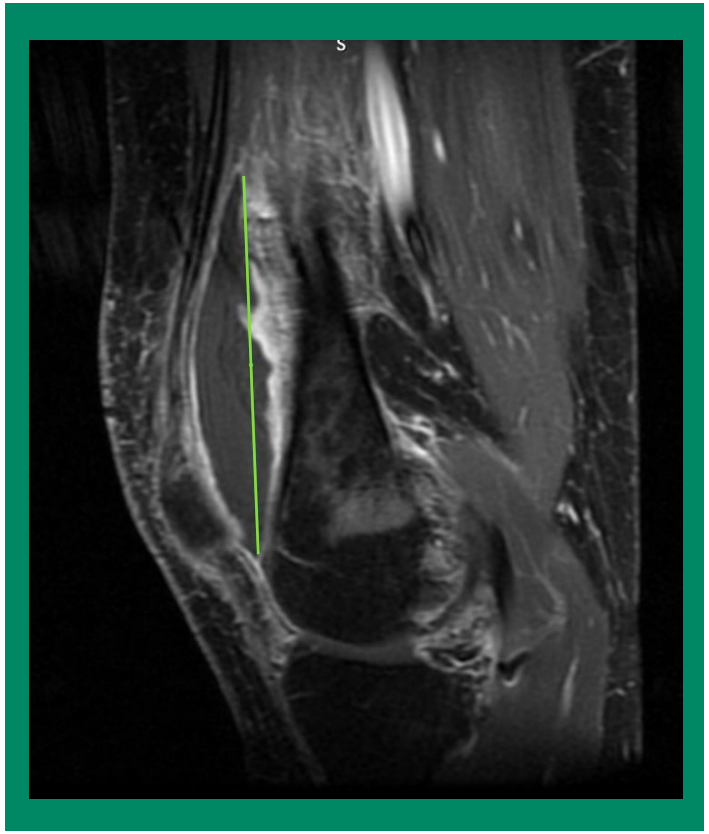
Tenosynovial giant cell tumor (TGCT) – locally aggressive neoplasm with an unmet treatment need

- TGCT is a locally aggressive neoplasm caused by dysregulation of the *CSF1* gene leading to overproduction of CSF1[1]
- People with TGCT experience pain, stiffness, and decreased physical function of affected joints[2]
  - Evaluating functional health is especially important in TGCT due to the symptomatic burden in this younger population[2]
- Surgical resection is standard of care, but not all people have disease that is amenable to surgery[1,3]
- Systemic treatment options are limited, and people require therapies with manageable toxicity due to the need for long-term treatment[1]
  - An unmet need remains for an effective CSF1R-targeted therapy with a favorable safety profile



TGCT in the right knee

1) Stacchiotti S, et al. *Cancer Treat Rev*. 2023;112:102491. 2) Mastboom MJ, et al. *J Med Res*. 2018;7(1):e4. 3) Lin F, et al. *J Health Econ Outcomes Res*. 2022;9(1):68-74.
CSF1, colony-stimulating factor 1; CSF1R, CSF1 receptor; TGCT, tenosynovial giant cell tumor.

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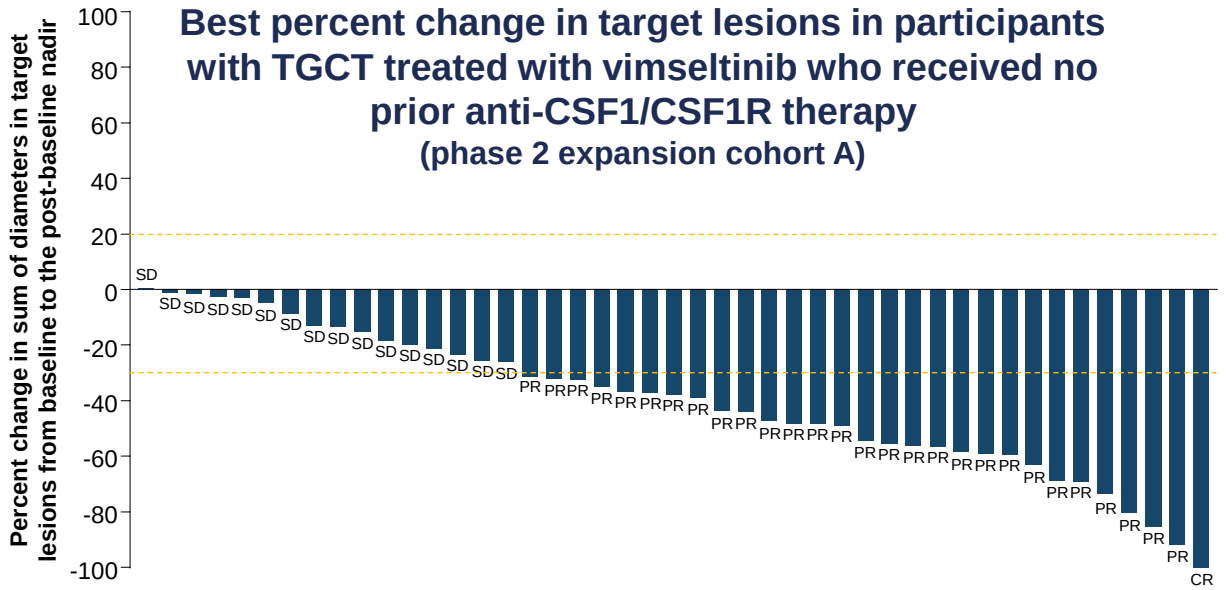
Vimseltinib demonstrated efficacy and was generally well tolerated in phase 1/2 study

- Vimseltinib is an investigational, oral, switch-control tyrosine kinase inhibitor specifically designed to selectively and potently inhibit CSF1R[1,2]
- In a phase 1/2 study, vimseltinib was well tolerated and demonstrated promising antitumor activity and clinically meaningful changes in PROs[3–5]
  - In participants who received no prior anti-CSF1/CSF1R therapy (phase 2 expansion, cohort A), the overall ORR was 64%
  - In cohort A, the median (range) treatment duration was 21.0 months (0.2 to 30.3)
  - Vimseltinib also demonstrated promising antitumor activity in a pretreated population (phase 2 expansion, cohort B)



Adapted from Blay J-Y, et al. Poster presented at: Connective Tissue Oncology Society Annual Meeting; 2023. Using RECIST v1.1 by IRR, includes all available follow-up visits. Dotted line at 20% represents threshold for PD; dotted line at −30% represents threshold for PR. Graph shows individual participant values.

1) Smith BD, et al. *Mol Cancer Ther*. 2021;20(11):2098-109. 2) Caldwell TM, et al. *Bioorg Med Chem Lett*. 2022;74:128928. 3) Gelderblom H, et al. Presented at: Connective Tissue Oncology Society Annual Meeting; 2023. 4) Blay J-Y, et al. Poster presented at: Connective Tissue Oncology Society Annual Meeting; 2023. 5) Wagner AJ, et al. Poster presented at: Connective Tissue Oncology Society Annual Meeting; 2023.

CR, complete response; CSF1, colony-stimulating factor 1; CSF1R, CSF1 receptor; IRR, independent radiological review; ORR, objective response rate; PR, partial response; PRO, patient-reported outcome; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease; TGCT, tenosynovial giant cell tumor.

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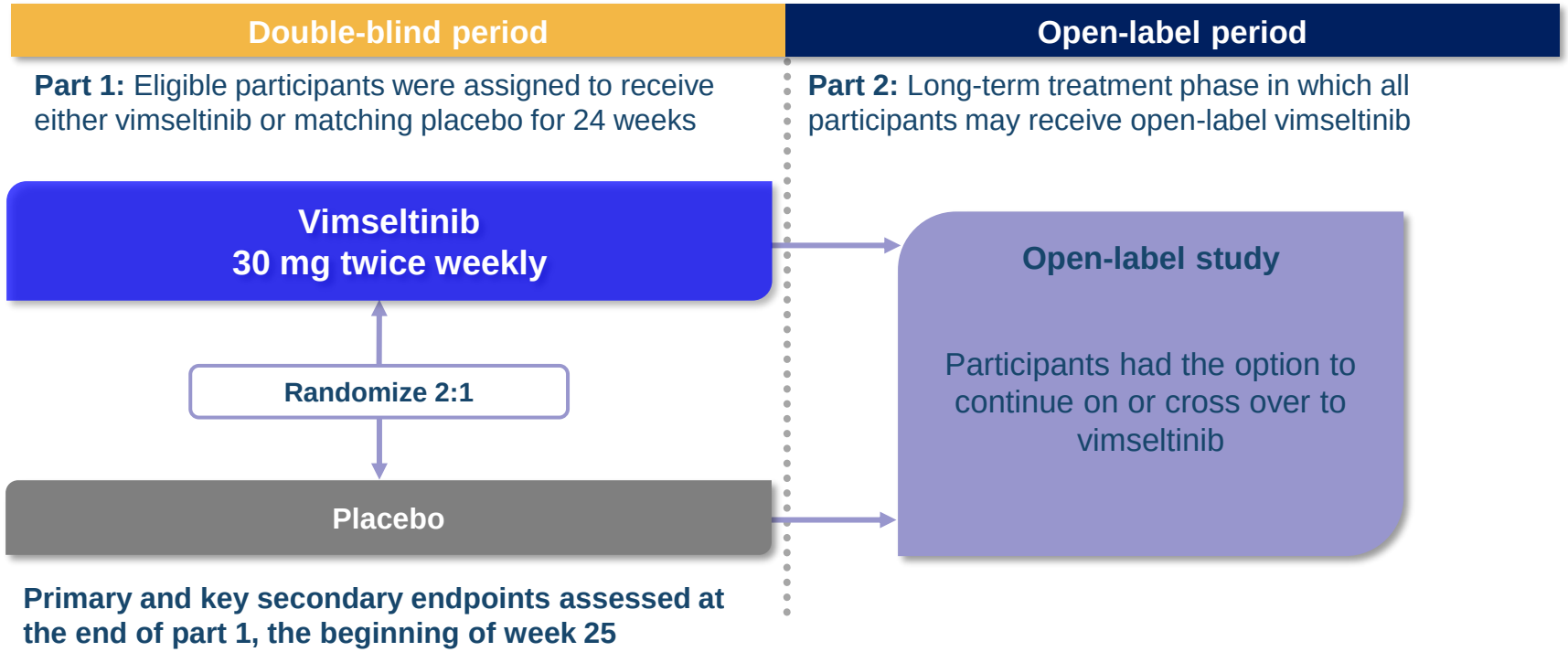
MOTION trial design: an international, randomized, double-blind, placebo-controlled phase 3 study

Key eligibility criteria

Participants ≥18 years old with a confirmed diagnosis of symptomatic TGCT for which surgical resection would potentially cause worsening functional limitation or severe morbidity

Previous treatment with imatinib or nilotinib was allowed

Randomization was stratified by geographical region and tumor location



Primary endpoint: ORR by independent radiological review (IRR) using RECIST v1.1 at week 25
Powered to detect a 30% difference between treatment arms

Data cutoff: August 22, 2023.
IRR, independent radiological review; ORR, objective response rate; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TGCT, tenosynovial giant cell tumor.

Key secondary endpoints at week 25

Key secondary endpoints hierarchy:

- ORR by IRR using Tumor Volume Score (TVS)
- Change from baseline in active range of motion (ROM)
  - Measures ability to move the affected joint by goniometry compared to a reference standard
- Patient-reported outcomes:
  - Change from baseline in physical function (PROMIS-physical function; TGCT specific)[1]
    - Questionnaire to assess tumor location–specific physical function
  - Change from baseline in worst stiffness numeric rating scale
    - Participants were asked to assess their worst stiffness in the last 24 hours on a scale of 0 (no stiffness) to 10 (worst imaginable)
  - Change from baseline in health status (EQ-Visual Analogue Scale)
    - Participants were asked "how good or bad is your health today?" on a visual scale of 0 (worst health imaginable) to 100 (best health imaginable)
  - Brief Pain Inventory (BPI) worst pain response rate
    - Participants were asked to rate their worst pain the last 24 hours on a scale of 0 (no pain) to 10 (pain as bad as you can imagine)
    - 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

1) Gelhorn HL, et al. *J Patient Rep Outcomes*. 2019;3:6.

BPI, Brief Pain Inventory; EQ-VAS, EuroQol Visual Analogue Scale; IRR, independent radiological review; ORR, objective response rate; PROMIS, Patient-Reported Outcomes Information System; ROM, range of motion; TGCT, tenosynovial giant cell tumor; TVS, tumor volume score.

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Participant demographics and baseline characteristics

	Vimseltinib n = 83	Placebo n = 40
Age, years, median (IQR)	45 (33–53)	43 (31–53)
Sex		
Female	46 (55)	27 (68)
Male	37 (45)	13 (33)
Race		
White	59 (71)	21 (53)
Asian	1 (1)	4 (10)
Black or African American	4 (5)	0
Other[a]	19 (23)	15 (38)
Affected joint		
Knee	56 (67)	27 (68)
Ankle	9 (11)	6 (15)
Hip	11 (13)	1 (3)
Other[b]	7 (8)	6 (15)
Prior TGCT surgery or procedure[c]	64 (77)	27 (68)
Prior TGCT systemic therapy	19 (23)	9 (23)[d]
Imatinib	16 (19)	7 (18)
Nilotinib	2 (2)	4 (10)
Other[e]	1 (1)	0

- In the vimseltinib arm, 89% (74/83) of participants completed treatment in part 1
  - Reasons for discontinuations were AE (n = 4), withdrawal by participant (n = 3), and other (n = 2)
- In the placebo arm, 1 participant was randomized to placebo but never received treatment; 87% (34/39) completed treatment in part 1
  - Reasons for discontinuations were withdrawal by participant (n = 3), PD by IRR (n = 1), and physician decision (n = 1)

Data cutoff: August 22, 2023. Data shown as n (%) unless otherwise noted.
[a]Includes not reported and unknown. [b]Includes foot, wrist, hand, shoulder, elbow, and temporomandibular joint. [c]All participants had histologically confirmed TGCT per diagnostic biopsy or existing pathology report; diagnostic biopsies were not recorded as a prior surgery or procedure. [d]Two participants in the placebo arm received both imatinib and nilotinib. [e]Includes an investigational agent (BP 27 672).
AE, adverse event; IQR, interquartile range; IRR, independent radiological review; PD, progressive disease; TGCT, tenosynovial giant cell tumor.

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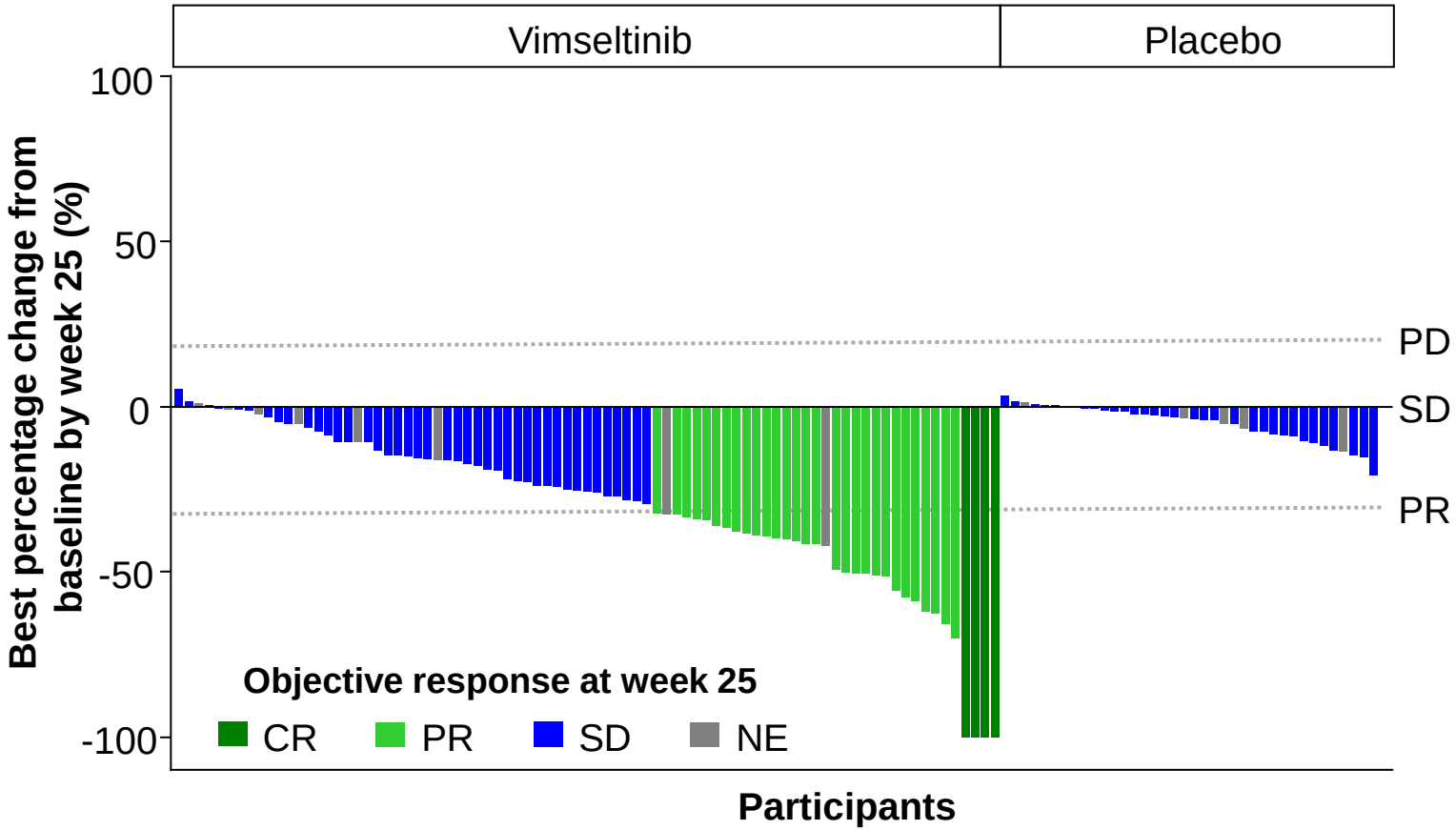
Vimseltinib demonstrated robust and statistically significant antitumor activity by RECIST v1.1



At week 25	Vimseltinib n = 83	Placebo n = 40
Overall response using RECIST v1.1		
CR	4 (5)	0
PR	29 (35)	0
SD	42 (51)	33 (83)
NE	8 (10)	7 (18)
ORR using RECIST v1.1	33 (40)	0
Treatment difference, % (95% CI), *P*-value[a]	40 (29 to 51), ***P* <0.0001**	
DOR using RECIST v1.1, months, median[b] (min, max)	NR (0.03+,11.7+)	N/A

Data cutoff: August 22, 2023. Dotted line at 20% represents threshold for PD; dotted line at −30% represents threshold for PR. The plot shows individual values from participants with evaluable post-baseline scans; 2 participants receiving placebo did not have post-baseline scans. Participants who did not have an assessment at the end of part 1 for any reason or whose week 25 assessment after the first dose in the open-label period or outside of the visit window of ±14 days were assessed as NE and a nonresponder. [a]An unstratified exact CI was utilized. [b]Based on Kaplan-Meier estimate. DOR is defined as time from first imaging result showing response to disease progression or death by any cause.
CI, confidence interval; CR, complete response; DOR, duration of response; IRR, independent radiological review; NE, not evaluable; NR, not reached; min, minimum; max, maximum; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

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Vimseltinib demonstrated robust and statistically significant antitumor activity by Tumor Volume Score

- The irregular growth and shape of TGCT can make measurement with linear methods, like RECIST, difficult[1]
- Tumor Volume Score (TVS) is a TGCT-specific semiquantitative MRI scoring system that estimates tumor volume[1]
- TVS response corresponds to ≥50% reduction in tumor volume
- Response by TVS at week 25 may predict long-term response by RECIST

At week 25	Vimseltinib n = 83	Placebo n = 40
Overall response using TVS		
CR	4 (5)	0
PR	52 (63)	0
SD	19 (23)	34 (85)
PD	0	1 (3)
NE	8 (10)	5 (13)
ORR using TVS	56 (67)	0
Treatment difference, % (95% CI), *P*-value	67 (56 to 77) ***P* <0.0001**	
DOR using TVS, months, median[a] (min, max)	NR (0.03+, 13.9+)	N/A

Data cutoff: August 22, 2023. Data shown as n (%) unless otherwise noted. Participants who did not have an assessment at the end of part 1 for any reason or whose week 25 assessment after the first dose in the open-label period or outside of the visit window of ±14 days were assessed as NE and a nonresponder.
[a]Based on Kaplan-Meier estimate. DOR is defined as time from first imaging result showing response to disease progression or death by any cause.
1) Peterfy C, et al. *Future Oncol*. 2022;18(12):1449-59.
CI, confidence interval; CR, complete response; DOR, duration of response; IRR, independent radiological review; max, maximum; min, minimum; MRI, magnetic resonance imaging; N/A not applicable; NE, not evaluable; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TGCT, tenosynovial giant cell tumor; TVS, tumor volume score.

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Vimseltinib provided statistically significant and clinically meaningful improvements versus placebo

At week 25	Vimseltinib n = 83	Placebo n = 40	*P*-values	Statistically significant	Clinically meaningful
Active Range of Motion					
% Mean change from baseline (SE)	18.4 (6.5)	3.8 (7.2)			
% Difference (95% CI), *P*-value	14.6 (4.0 to 25.3)		***P* = 0.0077**	✓	✓
PROMIS-Physical Function					
Mean change from baseline (SE)	4.6 (1.0)	1.3 (0.9)			
Difference (95% CI), *P*-value	3.3 (1.4 to 5.2)		***P* = 0.0007**	✓	✓
Worst stiffness Numeric Rating Scale					
Mean change from baseline (SE)	−2.1 (0.2)	−0.3 (0.3)			
Difference (95% CI), *P*-value	−1.8 (−2.5 to −1.1)		***P* <0.0001**	✓	✓
EQ-Visual Analogue Scale					
Mean change from baseline (SE)	13.5 (2.4)	6.1 (2.9)			
Difference (95% CI), *P*-value	7.4 (1.4 to 13.4)		***P* = 0.0155**	✓	✓
BPI worst pain					
n (% Response rate[a])	40 (48)	9 (23)			
% Difference (95% CI), *P*-value[b]	26 (4 to 42)		***P* = 0.0056**	✓	✓

[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. [b]An unstratified exact CI was utilized.
BPI, Brief Pain Inventory; CI, confidence interval; EQ-VAS, EuroQol Visual Analogue Scale; PROMIS-PF, Patient-Reported Outcomes Information System Physical Function; ROM, range of motion; SE, standard error.

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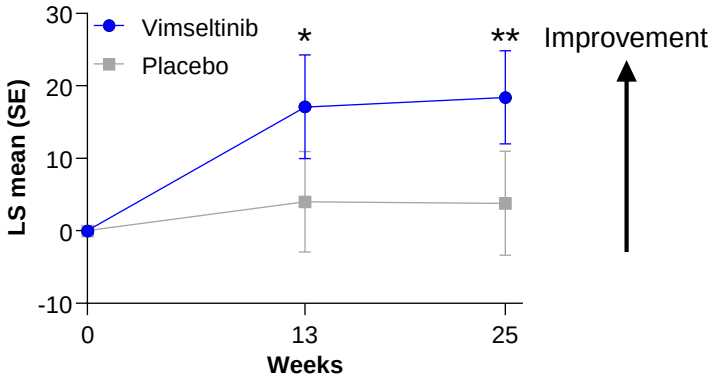
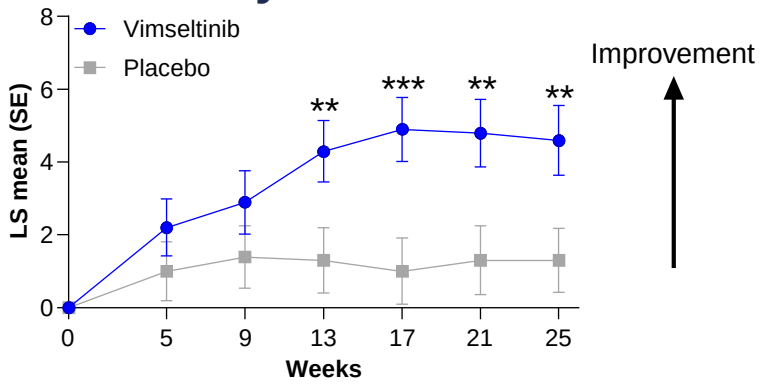
Vimseltinib provided early and durable functional and symptomatic improvements versus placebo

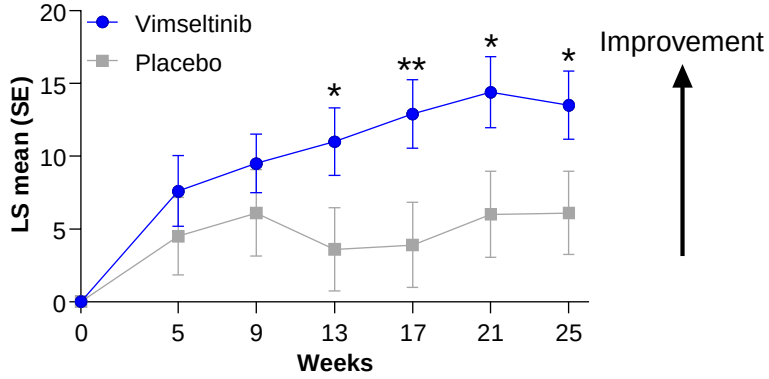
Active Range of Motion



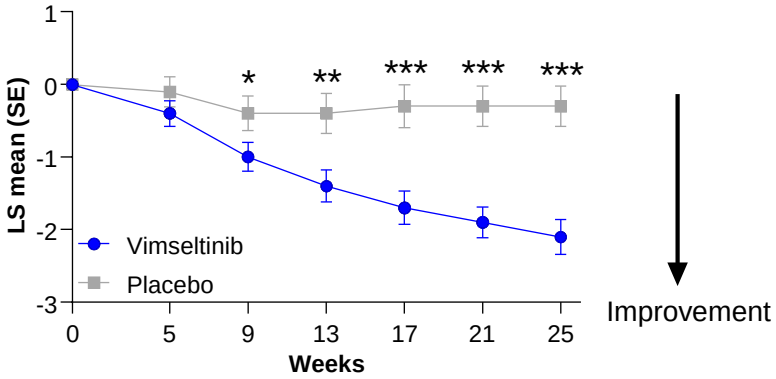
Physical Function†1



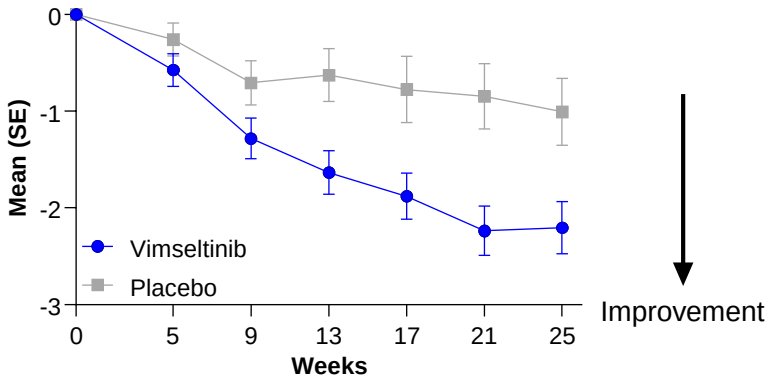
Health Status‡



Worst Stiffness



Worst Pain



Regardless of objective tumor response by IRR using RECIST v1.1, approximately 40% of participants receiving vimseltinib achieved a response in ≥3 clinical outcomes vs 6% of participants receiving placebo

Data cutoff: August 22, 2023. **P* <0.05; ***P* <0.01; ****P* <0.0001. †) Physical function as assessed by PROMIS-PF (TGCT specific) . ‡) Health status as assessed by EQ-VAS. 1) Gelhorn HL, et al. *J Patient Rep Outcomes*. 2019;3:6.
BPI, brief pain inventory; EQ-VAS, EuroQol Visual Analogue Scale; IRR, independent radiological review; LS, least squares; PROMIS-PF, Patient-Reported Outcomes Measurement Information System Physical Function; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; ROM, range of motion; SD, standard deviation; SE, standard error; TGCT, tenosynovial giant cell tumor.

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Vimseltinib was generally well tolerated with few discontinuations due to TEAEs

TEAEs in ≥15% of participants in either treatment arm	Vimseltinib n = 83		Placebo n = 39[a]	
Preferred term, n (%)	All grades	Grade 3/4	All grades	Grade 3/4
Periorbital edema	37 (45)	3 (4)	5 (13)	0
Fatigue	27 (33)	0	6 (15)	0
Face edema	26 (31)	1 (1)	3 (8)	0
Pruritus	24 (29)	2 (2)	3 (8)	0
Headache	23 (28)	1 (1)	10 (26)	0
Asthenia	22 (27)	1 (1)	9 (23)	1 (3)
Nausea	21 (25)	0	8 (21)	1 (3)
Blood CPK increased	20 (24)	8 (10)	0	0
AST increased	19 (23)	0	1 (3)	0
Arthralgia	16 (19)	0	6 (15)	1 (3)
Rash	16 (19)	0	2 (5)	0
Rash maculopapular	16 (19)	1 (1)	0	0
Edema peripheral	15 (18)	0	3 (8)	0
Hypertension	14 (17)	4 (5)	4 (10)	1 (3)
Diarrhea	10 (12)	0	8 (21)	1 (3)

- Most TEAEs were grade 1/2
- Serum enzyme elevations were consistent with the known mechanism of action of CSF1R inhibitors[1,2]
- TEAEs led to treatment discontinuation in 6% of participants receiving vimseltinib[b]
- There was no evidence of cholestatic hepatotoxicity, drug-induced liver injury, or hair/skin hypopigmentation

[a]One participant randomized to placebo never received treatment. [b]Reflects treatment discontinuations at data cutoff; AEs are attributed to part 1 or part 2 based on AE start date and may have occurred in part 2 for some participants.

1) Pognan F, et al. *Curr Res Toxicol*. 2022;3:100091. 2) Radi ZA, et al. *Am J Pathol*. 2011;179(1):240-7.

AE, adverse event; AST, aspartate aminotransferase; CSF1R, colony-stimulating factor 1 receptor; CPK, creatine phosphokinase; TEAE, treatment-emergent AE.

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MOTION primary results demonstrated the clinical and functional benefits of vimseltinib in participants with TGCT

- Vimseltinib provided statistically significant and clinically meaningful improvements versus placebo for the primary and all 6 key secondary endpoints at week 25
- Significantly more participants receiving vimseltinib experienced objective tumor response by IRR using RECIST v1.1 or TVS than placebo
- Participants experienced clinically meaningful improvement in active ROM, which could provide relief from mobility-related limitations
- Participants reported statistically significant and clinically meaningful improvements in physical function, stiffness, health status, and pain
  - Functional and symptomatic benefit was achieved regardless of objective tumor response
- Vimseltinib was well tolerated with no evidence of cholestatic hepatotoxicity, drug-induced liver injury, or hair hypopigmentation
- If approved, vimseltinib offers an effective systemic treatment to people with TGCT and provides proven functional health and symptomatic benefit to a population living with substantial morbidity and limited treatment options

IRR, independent radiological review; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; ROM, range of motion; TGCT, tenosynovial giant cell tumor; TVS, tumor volume score.

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We thank the **participants and their families and caregivers**, the investigators, and the investigational site staff for the MOTION study

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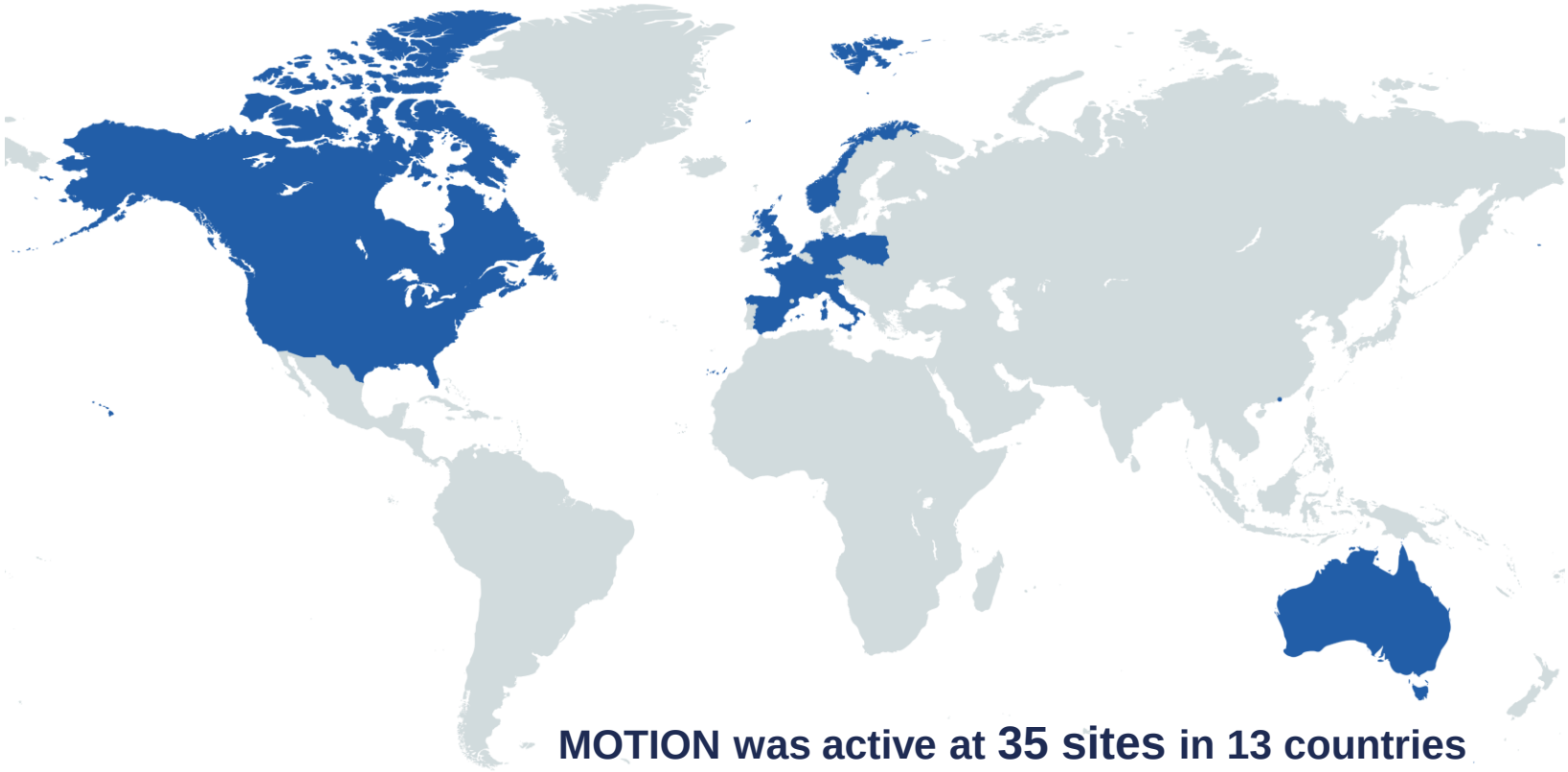

MOTION was active at 35 sites in 13 countries

Full article published online today!

- The publication of these results is available at *The Lancet* by scanning the QR code

Vimseltinib versus placebo for tenosynovial giant cell tumour (MOTION): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial

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