Long-term efficacy and safety of vimseltinib in patients with tenosynovial giant cell tumor: 2-year results from the MOTION phase 3 trial

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Sebastian Bauer[1], Vivek Bhadri[2], Hans Gelderblom[3], Silvia Stacchiotti[4], Andrew J Wagner[5], Michiel van de Sande[3], Nicholas M Bernthal[6], Antonio López Pousa[7], Albiruni Abdul Razak[8], Antoine Italiano[9], Mahbubl Ahmed[10], Axel Le Cesne[11], Christopher Tait[12], Fiona Zarins[12], Nicholas A Zeringo[12], Brooke Harrow[12], Maitreyi G Sharma[12], Matthew L Sherman[12], Jean-Yves Blay[13], and William D Tap[14]

[1]Department of Medical Oncology, Sarcoma Center, West German Cancer Center, University Hospital Essen, University Duisburg-Essen, and German Cancer Consortium (DKTK), Partner Site University Hospital Essen, Essen, Germany; [2]Chris O'Brien Lifehouse, Camperdown, Australia; [3]Leiden University Medical Center, Leiden, Netherlands; [4]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [5]Dana-Farber Cancer Institute, Boston, MA, USA; [6]University of California Los Angeles, Los Angeles, CA, USA; [7]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [8]Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [9]Institut Bergonié, Bordeaux, France;[10]University College London Hospitals NHS Foundation Trust, London, UK; [11]Gustave Roussy, Villejuif, France; [12]Deciphera Pharmaceuticals, LLC, Waltham, MA, USA; [13]Centre Léon Bérard, Lyon, France; [14]Memorial Sloan Kettering Cancer Center, New York, NY, USA

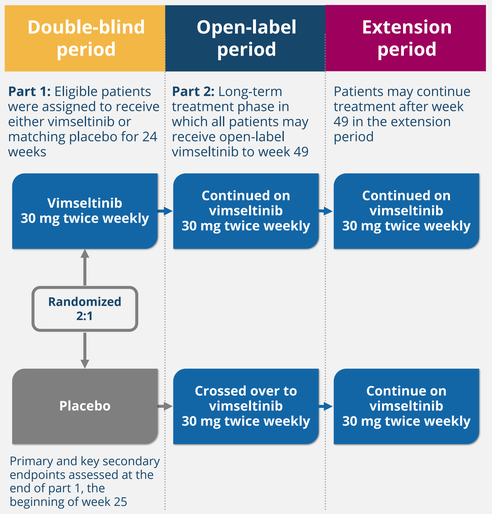
Introduction

- 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[1,2]
- Not all patients have disease that is amenable to surgery, and these patients require systemic therapies with manageable toxicity[1]
- 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 Administration[5]
  - 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 disability[6]
- In part 1 (up to week 25) of the MOTION phase 3 trial, patients receiving vimseltinib experienced robust and statistically significant antitumor activity compared with placebo per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) and per Tumor Volume Score (TVS)[7]
- Here, we report updated efficacy and safety results with 2 years of follow-up from MOTION (data cutoff: February 22, 2025)

Methods

- MOTION is an international, randomized, double-blind, placebo-controlled, phase 3 trial in adults with symptomatic TGCT whose disease is not amenable to surgery (NCT05059262; **Figure 1**)
- Objective response rate (ORR) on study based on best overall response and duration of response (DOR) were assessed by independent radiological review (IRR) per RECIST v1.1 and per TVS
  - Baseline for all patients (including those who crossed over from placebo to vimseltinib) was defined as the last assessment prior to treatment with vimseltinib

Figure 1. MOTION study design



Data cutoff: February 22, 2025.
TGCT, tenosynovial giant cell tumor.

Results

- In total, 118 patients received vimseltinib
  - In the vimseltinib arm, 73/83 patients continued to receive treatment in part 2
  - In the placebo arm, 35/40 patients crossed over to vimseltinib in part 2
- Median (range) treatment duration was 23.6 months (2–36) for patients randomized to vimseltinib and 19.1 months (1–30) for those who crossed over to vimseltinib
- At data cutoff, 51% (60/118) remain on treatment
  - Reasons for treatment discontinuation included withdrawal by patient (n = 29), adverse event (n = 14), physician decision (n = 3), progressive disease by IRR (n = 2), noncompliance with study drug (n = 2), unrelated death (n = 1 [reported reason due to "fall"]), and other (n = 7)
- Patient demographics and baseline characteristics were balanced between treatment arms (**Table 1**)

Table 1. Patient demographics and baseline characteristics

	Vimseltinib n = 83	Placebo n = 40
Age, median (IQR), years	45 (33–53)	43 (31–53)
Sex, n (%)		
Female	46 (55)	27 (68)
Male	37 (45)	13 (33)
Race, n (%)		
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, n (%)		
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], n (%)	64 (77)	27 (68)
Prior TGCT systemic therapy, n (%)	19 (23)	9 (23)[d]
Imatinib	16 (19)	7 (18)
Nilotinib	2 (2)	4 (10)
Other[e]	1 (1)	0

Results from Gelderblom H, et al. *Lancet*. 2024.[7] Total percentages may be >100 due to rounding. [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]Two patients in the placebo arm received both imatinib and nilotinib. [e]Includes an investigational agent (BP 27 672).
IQR, interquartile range; TGCT, tenosynovial giant cell tumor.

Efficacy

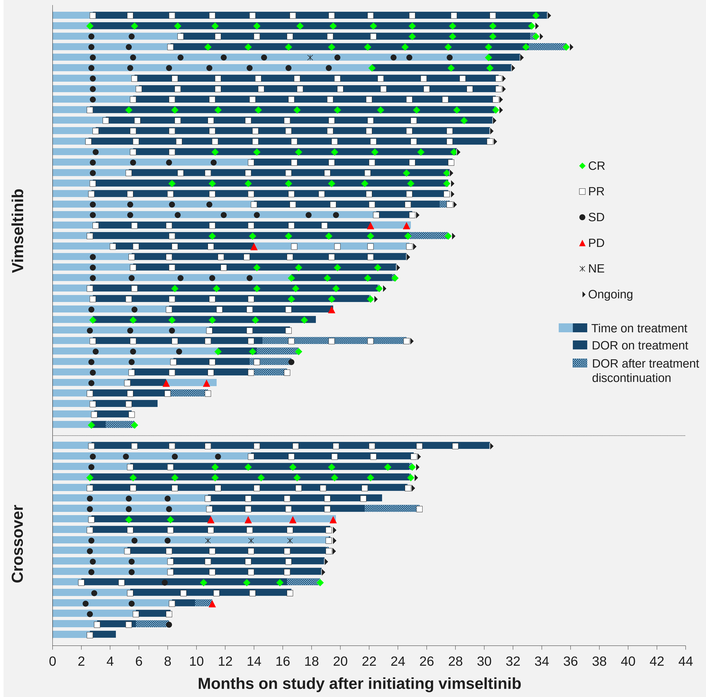
- ORR on study per RECIST v1.1 was 48% (40/83) for patients randomized to vimseltinib and 54% (19/35) for those who crossed over to vimseltinib (**Table 2**); ORR on study per TVS was 81% (67/83) for patients randomized to vimseltinib and 71% (25/35) for those who crossed over to vimseltinib (**Table 3**)
  - Median DOR per RECIST v1.1 (**Figure 2**) and TVS was still not reached for both groups

Table 2. Response assessed by IRR per RECIST v1.1

	Week 25		≥2 years on study[b]	
	Vimseltinib n = 83	Placebo n = 40	Vimseltinib n = 83	Crossover n = 35
ORR, n (%) (95% CI)	33 (40)[a] (29 to 51)	0 (0 to 9)	40 (48) (37 to 59)	19 (54) (37 to 71)
Complete response	4 (5)	0	19 (23)	4 (11)
Partial response	29 (35)	0	21 (25)	15 (43)
DOR, median (range), months	NR[b] (2.5+ to 30.9+)	N/A	NR (0.03+ to 30.9+)	NR (0.03+ to 25.4+)

+ denotes response was ongoing at the last assessment.
[a]Data cutoff: August 22, 2023, from Gelderblom H, et al. *Lancet.* 2024.[7]
[b]Data cutoff: February 22, 2025.
CI, confidence interval; DOR, duration of response; IRR, independent radiological review; N/A, not applicable; NR, not reached; ORR, objective response rate; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Figure 2. Time on treatment and DOR in patients receiving vimseltinib with objective responses per RECIST v1.1



Data cutoff: February 22, 2025. Dark blue and patterned shading represents the DOR.
CR complete response; DOR, duration of response; NE, not evaluable; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Table 3. Response assessed by IRR per TVS

	Week 25		≥2 years on study[b]	
	Vimseltinib n = 83	Placebo n = 40	Vimseltinib n = 83	Crossover n = 35
ORR, n (%) (95% CI)	56 (67)[a] (56 to 77)	0 (0 to 9)	67 (81) (71 to 89)	25 (71) (54 to 85)
Complete response	4 (5)	0	20 (24)	4 (11)
Partial response	52 (63)	0	47 (57)	21 (60)
DOR, median (range), months	NR[b] (2.5+ to 33.1+)	N/A	NR (2.4+ to 33.1+)	NR (1.9+ to 25.4+)

+ denotes response was ongoing at the last assessment. TVS response corresponds to ≥50% reduction in estimated tumor volume.[8]
[a]Data cutoff: August 22, 2023, from Gelderblom H, et al. *Lancet.* 2024.[7]
[b]Data cutoff: February 22, 2025.
CI, confidence interval; DOR, duration of response; IRR, independent radiological review; N/A, not applicable; NR, not reached; ORR, objective response rate; TVS, Tumor Volume Score.

Safety

- Most treatment-emergent adverse events (TEAEs) were grade 1/2, and grade 3/4 TEAEs were similar between randomized vimseltinib and crossover groups (**Table 4**)
- There were no new TEAEs (preferred terms) in ≥15% of patients receiving vimseltinib and no new serious adverse events in more than 1 patient
- Serum enzyme elevations were consistent with the known mechanism of action of CSF1R inhibition,[9,10] and there was no evidence of cholestatic hepatotoxicity or drug-induced liver injury
- TEAEs led to dose interruption in 63% (74/118) and dose reduction in 58% (68/118) of patients, and 12% (14/118) of patients discontinued due to TEAEs
  - TEAEs that led to treatment discontinuation in >1 patient were periorbital edema (n = 3), pruritus (n = 3), and rash (n = 2)

Table 4. TEAEs in ≥15% of patients receiving vimseltinib

	Vimseltinib n = 83		Crossover n = 35		Vimseltinib total n = 118	
Preferred term n (%)	**All Grades**	**Grade 3/4**	**All Grades**	**Grade 3/4**	**All Grades**	**Grade 3/4**
Periorbital edema[a]	40 (48)	4 (5)	17 (49)	1 (3)	57 (48)	5 (4)
Pruritus[a]	31 (37)	3 (4)	11 (31)	2 (6)	42 (36)	5 (4)
Face edema[a]	28 (34)	1 (1)	9 (26)	0	37 (31)	1 (1)
Arthralgia	27 (33)	0	9 (26)	0	36 (31)	0
Blood CPK increased	26 (31)	12 (14)	10 (29)	7 (20)	36 (31)	19 (16)
Asthenia[a]	27 (33)	1 (1)	8 (23)	1 (3)	35 (30)	2 (2)
Fatigue	30 (36)	1 (1)	5 (14)	0	35 (30)	1 (1)
AST increased	23 (28)	1 (1)	11 (31)	0	34 (29)	1 (1)
Headache[a]	25 (30)	1 (1)	9 (26)	1 (3)	34 (29)	2 (2)
Rash	27 (33)	0	6 (17)	0	33 (28)	0
Hypertension	18 (22)	6 (7)	11 (31)	4 (11)	29 (25)	10 (8)
Edema peripheral	21 (25)	0	8 (23)	0	29 (25)	0
Nausea	22 (27)	0	6 (17)	0	28 (24)	0
Rash maculopapular[a]	20 (24)	2 (2)	6 (17)	0	26 (22)	2 (2)
Diarrhea	15 (18)	1 (1)	8 (23)	0	23 (19)	1 (1)
ALT increased	13 (16)	0	8 (23)	0	21 (18)	0
COVID-19	16 (19)	1 (1)	3 (9)	0	19 (16)	1 (1)
Generalized edema	15 (18)	1 (1)	4 (11)	0	19 (16)	1 (1)

Data cutoff: February 22, 2025.
[a]Denotes AEs without grade 4 criteria per Common Terminology Criteria for AEs version 5.0.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, coronavirus disease-2019; CPK, creatine phosphokinase; TEAE, treatment-emergent AE.

CONCLUSIONS

- With at least 2 years of follow-up, results demonstrate robust and durable antitumor activity with vimseltinib per RECIST v1.1 and per TVS, including in patients who crossed over to vimseltinib in part 2
- Vimseltinib continued to have a manageable safety profile that was consistent with prior reports with no new safety signals
- Most TEAEs were grade 1/2, and there was no evidence of cholestatic hepatotoxicity or drug-induced liver injury
- Vimseltinib offers an effective systemic treatment for people with TGCT and provides proven functional health and symptomatic benefits[5,6] to a population living with substantial morbidity and limited treatment options

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CORRESPONDING AUTHOR
Sebastian Bauer, MD
sebastian.bauer@uk-essen.de

DISCLOSURES

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