

# Safety and efficacy of vimseltinib in tenosynovial giant cell tumor (TGCT): Long-term phase 1 update

Hans Gelderblom<sup>1</sup>, Albiruni Abdul Razak<sup>2</sup>, Javier Martín-Broto<sup>3</sup>, Breelyn A Wilky<sup>4</sup>, Piotr Rutkowski<sup>5</sup>, Supraja Narasimhan<sup>6</sup>, Marc Vallee<sup>6</sup>, Maitreyi G Sharma<sup>6</sup>, Rodrigo Ruiz-Soto<sup>6</sup>, Matthew L Sherman<sup>6</sup>, William D Tap<sup>7</sup>

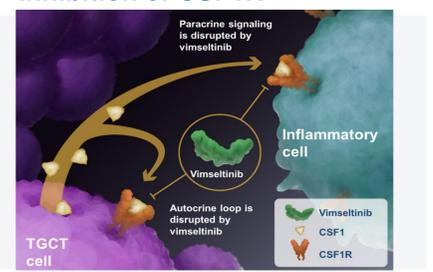
<sup>1</sup>Leiden University Medical Center, Leiden, Netherlands; <sup>2</sup>Princess Margaret Cancer Center, Toronto, Ontario, Canada; <sup>3</sup>University Hospital Fundación Jiménez Díaz, Madrid, Spain; <sup>4</sup>University of Colorado Cancer Center, Aurora, CO, USA; <sup>5</sup>Maria Skłodowska-Curie National Research Institute of Oncology, Warszawa, Poland; <sup>6</sup>Deciphera Pharmaceuticals, LLC, Waltham, MA, USA; <sup>7</sup>Memorial Sloan Kettering Cancer Center, New York, NY, USA

FPN: 475P

## INTRODUCTION

- Tenosynovial giant cell tumor (TGCT) is a rare, locally aggressive neoplasm caused by upregulation of the colony-stimulating factor 1 (CSF1) gene<sup>1</sup>
  - The CSF1 receptor (CSF1R) is a receptor tyrosine kinase implicated in the recruitment and survival of tumor-associated macrophages, which contribute to angiogenesis, tumor growth, and metastasis<sup>1</sup>
- Surgery is the standard of care for most patients with TGCT, but a number of patients are not amenable to surgery<sup>2</sup>
- There is only one systemic agent approved by the US Food and Drug Administration for the treatment of patients with TGCT not amenable to surgery and none in Europe, leaving an unmet need for an effective, CSF1R-targeted therapy with a favorable safety profile<sup>3</sup>
- Vimseltinib is an oral switch-control tyrosine kinase inhibitor specifically designed to selectively and potently inhibit CSF1R (Figure 1)
- Here, we report long-term safety and efficacy of vimseltinib in patients with TGCT not amenable to surgery from phase 1 (dose escalation) of the ongoing, multicenter, open-label study of vimseltinib in patients with advanced solid tumors and TGCT (NCT03069469)

Figure 1. Vimseltinib inhibition of CSF1R

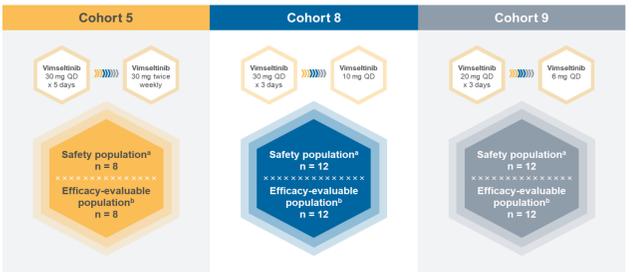


## METHODS

- This phase 1 trial is designed to determine the recommended phase 2 dose (RP2D) and the maximum tolerated dose using a pharmacologically guided 3 + 3 design (Figure 2)
  - Cohort 5: 30 mg once-daily (QD) loading dose for 5 days and 30 mg twice weekly thereafter
  - Cohort 8: 30 mg QD loading dose for 3 days and 10 mg QD thereafter
  - Cohort 9: 20 mg QD loading dose for 3 days and 6 mg QD thereafter
- Vimseltinib antitumor activity was evaluated using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 by blinded independent radiological review (IRR)

## RESULTS

Figure 2. TGCT enrollment and disposition in phase 1 study



<sup>a</sup>Includes patients who received at least one dose of study drug. <sup>b</sup>Patients with at least one post-baseline imaging assessment; one patient (Cohort 5) had local assessment for efficacy, but no independent radiological review was performed. QD, once daily; TGCT, tenosynovial giant cell tumor.

## RESULTS

Table 1. Baseline demographics and clinical characteristics

	Cohort 5 (n = 8)	Cohort 8 (n = 12)	Cohort 9 (n = 12)	Total (N = 32)
Age, median (min, max), years	44 (23, 66)	50 (24, 73)	52 (29, 73)	51 (23, 73)
Sex				
Female	3 (38)	7 (58)	7 (58)	17 (53)
Male	5 (63)	5 (42)	5 (42)	15 (47)
Race				
White	8 (100)	12 (100)	11 (92)	31 (97)
Asian	0	0	1 (8)	1 (3)
Disease location				
Knee	5 (63)	9 (75)	6 (50)	20 (63)
Ankle	0	2 (17)	3 (25)	5 (16)
Hip	2 (25)	1 (8)	1 (8)	4 (13)
Wrist	1 (13)	0	1 (8)	2 (6)
Foot	0	0	1 (8)	1 (3)
Patients with ≥1 prior surgery	6 (75)	3 (25)	3 (25)	12 (38)
2–3 prior surgeries	2 (25)	1 (8)	1 (8)	4 (13)
≥4 prior surgeries	1 (13)	0	1 (8)	2 (6)
Patients with ≥1 systemic therapy	0	4 (33)	1 (8)	5 (16)
Imatinib	0	3 (25)	0	3 (9)
Nilotinib	0	0	1 (8)	1 (3)
Lacrotuzumab (MSC-110)	0	1 (8)	0	1 (3)

Data shown as n (%) unless otherwise noted. Percentages are rounded.

- As of 6 May 2022, 32 patients with TGCT were enrolled (19 Feb 2019–01 Feb 2021; Table 1)
- The most common disease location was the knee (20 [63%])
- Overall, 15 (47%) patients discontinued the study treatment; the most common reasons for treatment discontinuation were withdrawal of consent (9 [28%]), physician decision (3 [9%]), adverse event (2 [6%]), and progressive disease (1 [3%]; local assessment)

## SAFETY

Table 2. TEAEs in ≥15% of patients with TGCT receiving vimseltinib

Preferred term, n (%)	Cohort 5 (n = 8)		Cohort 8 (n = 12)		Cohort 9 (n = 12)		Total (N = 32)	
	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4
Blood CPK increased	7 (88)	4 (50)	8 (67)	4 (33)	5 (42)	2 (17)	20 (63)	10 (31)
Periorbital edema	3 (38)	0	9 (75)	0	5 (42)	0	17 (53)	0
Fatigue	3 (38)	0	6 (50)	0	7 (58)	0	16 (50)	0
AST increased	5 (63)	1 (13)	4 (33)	2 (17)	2 (17)	1 (8)	11 (34)	4 (13)
Arthralgia	4 (50)	0	2 (17)	0	4 (33)	1 (8)	10 (31)	1 (3)
Face edema	0	0	6 (50)	0	3 (25)	0	9 (28)	0
Myalgia	0	0	5 (42)	1 (8)	4 (33)	0	9 (28)	1 (3)
Edema peripheral	1 (13)	0	5 (42)	0	3 (25)	0	9 (28)	0
Pruritus	1 (13)	0	4 (33)	0	4 (33)	0	9 (28)	0
Headache	3 (38)	0	3 (25)	0	2 (17)	0	8 (25)	0
ALT increased	2 (25)	0	3 (25)	0	2 (17)	1 (8)	7 (22)	1 (3)
Diarrhea	1 (13)	1 (13)	4 (33)	0	2 (17)	0	7 (22)	1 (3)
Lipase increased	1 (13)	0	5 (42)	3 (25)	1 (8)	0	7 (22)	3 (9)
Generalized edema	2 (25)	0	2 (17)	0	2 (17)	0	6 (19)	0
Hypertension	0	0	3 (25)	2 (17)	3 (25)	0	6 (19)	2 (6)
Nausea	2 (25)	0	3 (25)	0	1 (8)	0	6 (19)	0
Rash	1 (13)	0	3 (25)	0	2 (17)	0	6 (19)	0
Amylase increased	1 (13)	1 (13)	4 (33)	1 (8)	0	0	5 (16)	2 (6)
Constipation	1 (13)	0	1 (8)	0	3 (25)	0	5 (16)	0
Dry skin	1 (13)	0	2 (17)	0	2 (17)	0	5 (16)	0
Paresthesia	0	0	5 (42)	0	0	0	5 (16)	0
Rash maculopapular	0	0	4 (33)	0	1 (8)	0	5 (16)	0

Percentages are rounded. Safety population includes patients who received at least one dose of study drug. Severity was assessed by the investigator according to the toxicity grade described in the National Cancer Institute Common Terminology Criteria for Adverse Events v4.03 (Grade 1 [mild] to Grade 5 [death]). ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; TEAE, treatment-emergent adverse event; TGCT, tenosynovial giant cell tumor.

Table 3. Dose modification due to any TEAEs in patients with TGCT receiving vimseltinib

n, (%)	Cohort 5 (n = 8)	Cohort 8 (n = 12)	Cohort 9 (n = 12)	Total (N = 32)
Patients with TEAEs leading to dose modification	5 (63)	10 (83)	8 (67)	23 (72)
Dose interruption	5 (63)	9 (75)	7 (58)	21 (66)
Dose reduction	4 (50) <sup>a</sup>	7 (58) <sup>b</sup>	4 (33) <sup>c</sup>	15 (47)
Treatment discontinuation	1 (13) <sup>d</sup>	1 (8) <sup>e</sup>	2 (17) <sup>f</sup>	4 (13)

Percentages are rounded. A patient may be counted in more than one category. <sup>a</sup>G3 diarrhea; G3 urticaria; G2 AST increase; G3 amylase, CPK, and LDH increase. <sup>b</sup>G1 face edema; G2 fatigue, edema peripheral, and rash maculopapular; G2 rash macular; G2 joint swelling and G1 pyrexia (SAE, not related); G3 CPK increase; G3 CPK increase and G2 myalgia; G3 rash pruritic. <sup>c</sup>G1 generalized edema and periorbital edema; G1 rash maculopapular; G1 periorbital edema; G3 AST increase. <sup>d</sup>G3 metabolic encephalopathy (SAE, possibly related). <sup>e</sup>G3 AST increase (DLT). <sup>f</sup>G2 arthralgia, G1 myalgia. AST, aspartate aminotransferase; CPK, creatine phosphokinase; DLT, dose-limiting toxicity; G, grade; LDH, lactate dehydrogenase; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TGCT, tenosynovial giant cell tumor.

- Long-term safety data from phase 1 demonstrates continued tolerability of vimseltinib with a mean treatment duration of 15.8 months (median 17.5 months)
- The majority of common (≥15%) treatment-emergent adverse events (TEAEs) were ≤Grade 2 (Table 2)
- Grade 3/4 TEAEs in >5% of patients included increases in blood creatine phosphokinase, aspartate aminotransferase, lipase, amylase, and hypertension (Table 2)
- No post-baseline bilirubin elevations were observed
- No new treatment-related serious adverse events in phase 1 since the 07 June 2021 data cut
- Overall, two patients (6%), both in Cohort 5, had treatment-related Grade 3/4 serious adverse events of metabolic encephalopathy (possibly related) and vaginal hemorrhage (probably related)
  - No recurrence of vaginal hemorrhage occurred after rechallenge with study drug

## EFFICACY

Table 4. Response assessed by RECIST v1.1 by IRR in patients with TGCT receiving vimseltinib

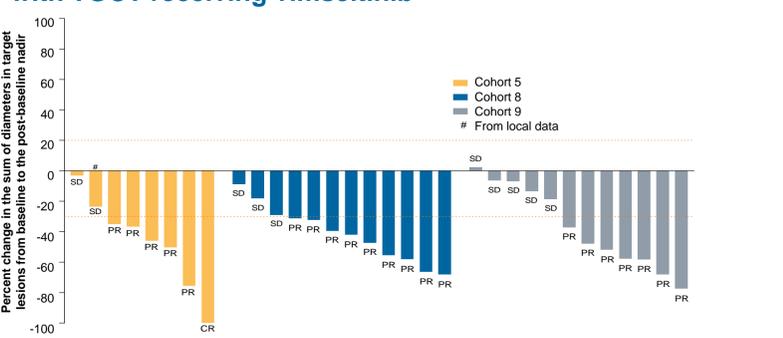
	Cohort 5 (n = 8) <sup>a</sup>	Cohort 8 (n = 12)	Cohort 9 (n = 12)	Total (N = 32) <sup>a</sup>
ORR <sup>b</sup>	6 (75)	9 (75)	7 (58)	22 (69)
Complete response	1 (13)	0	0	1 (3)
Partial response	5 (63)	9 (75)	7 (58)	21 (66)
Stable disease	2 (25)	3 (25)	5 (42)	10 (31)
Duration of response, median <sup>c</sup> (min, max), months	NR (2.8, 31.4)	NR (2.9, 20.4)	NR (6.4, 16.8)	NR (2.8, 31.4)

Data shown as n (%) unless otherwise noted. Percentages are rounded. <sup>a</sup>One patient had a local assessment for efficacy but will never have IRR data. This patient has been included in the SD assessment. <sup>b</sup>Includes all available follow-ups. <sup>c</sup>Based on Kaplan-Meier estimate. Duration of response is defined as time from first imaging result showing response to progressive disease. IRR, independent radiological review; NR, not reached; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid tumors; TGCT, tenosynovial giant cell tumor.

## CONCLUSIONS

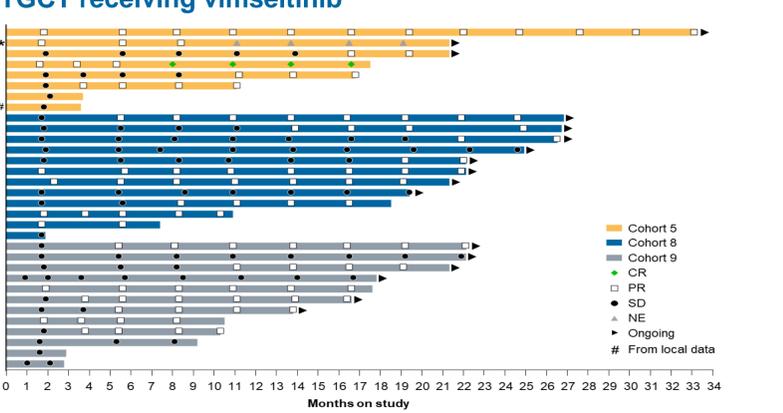
- The RP2D was determined as 30 mg twice weekly (no loading dose)
- Vimseltinib continues to demonstrate long-term tolerability and a manageable safety profile in patients with TGCT not amenable to surgery
- Vimseltinib demonstrated robust antitumor activity with an objective response rate (69% across all cohorts) that continues to improve with longer follow-up
  - Responses were observed across all cohorts, both within and after 6 months, demonstrating continued benefit with prolonged treatment
- These results support continued evaluation of vimseltinib in the actively enrolling phase 3 MOTION trial (NCT05059262)

Figure 3. Best percentage change in target lesions in patients with TGCT receiving vimseltinib



Using RECIST v1.1 by IRR; includes all available follow-ups. # Cohort 5: One patient had a local assessment for efficacy but will never have IRR data. This patient has been included in the SD assessment. Dotted line at 20% represents threshold for progressive disease; dotted line at -30% represents threshold for PR. CR, complete response; IRR, independent radiological review; PR, partial response; RECIST, Response Evaluation Criteria in Solid tumors; SD, stable disease; TGCT, tenosynovial giant cell tumor.

Figure 4. Duration of treatment and response in patients with TGCT receiving vimseltinib



Using RECIST v1.1 by IRR; includes all available follow-ups. # Cohort 5: one patient had a local assessment for efficacy but will never have IRR data. This patient has been included in the SD assessment. CR, complete response; IRR, independent radiological review; NE, not evaluable; PR, partial response; RECIST, Response Evaluation Criteria in Solid tumors; SD, stable disease; TGCT, tenosynovial giant cell tumor.

- Across all cohorts, 22/32 (69%) patients showed objective response (1 complete response and 21 partial responses; Table 4, Figure 3, Figure 4)
  - Responses were durable across cohorts (Figure 4 and Table 4)
  - Of the responses, 68% (15/22) were achieved within 6 months on treatment and 32% (7/22) were achieved beyond 6 months on treatment (Figure 4)
- As of the data cutoff date (6 May 2022), no patients progressed as assessed by IRR

### Acknowledgements

We thank the patients and their families and caregivers, the investigators, and the investigational site staff of the study. The study was sponsored by Deciphera Pharmaceuticals, LLC (Waltham, MA, USA). Medical writing was provided by Elisabetta Lauretti, PhD, of AlphaBioCom, LLC (King of Prussia, PA, USA), and funded by Deciphera Pharmaceuticals, LLC.

### Corresponding Author

Hans Gelderblom (a.j.gelderblom@lumc.nl). HG reports invited speaker roles for Daiichi Sankyo, Inc.; Deciphera Pharmaceuticals, LLC; Novartis; Boehringer Ingelheim; AmMax Bio; Debiopharm; and Cytovation.

### References

- Smith BD, et al. *Mol Cancer Ther*. 2021;20:2098–109.
- Lin F, et al. *JHEOR*. 2022;9:68–74.
- Pexidartinib (TURALIO®) prescribing information. Basking Ridge, NJ: Daiichi Sankyo, Inc. 2020.

