

# Efficacy and safety of vimseltinib in tenosynovial giant cell tumor (TGCT): Phase 2 expansion

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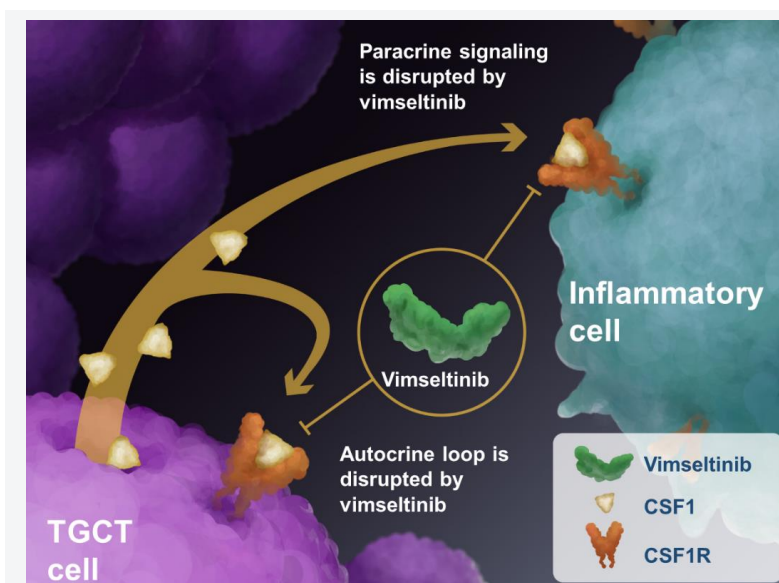
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## INTRODUCTION

- 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 the safety, efficacy, and preliminary patient-reported outcome data in patients with TGCT treated with vimseltinib at the recommended phase 2 dose (RP2D; 30 mg twice weekly) from phase 2 (expansion) of the ongoing, multicenter, open-label study (NCT03069469)

Figure 1. Vimseltinib inhibition of CSF1R



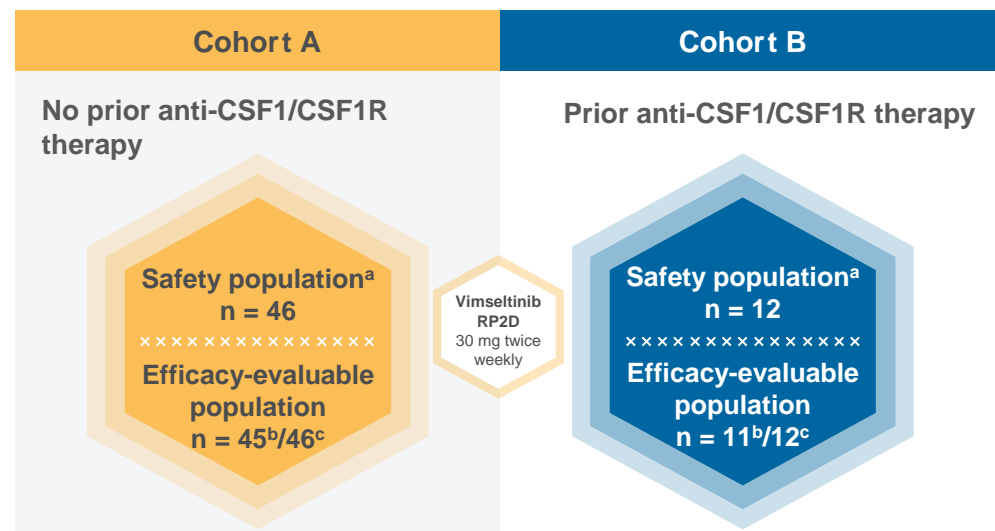
CSF1, colony-stimulating factor 1; CSF1R, CSF1 receptor; TGCT, tenosynovial giant cell tumor.

## METHODS

- This phase 2 trial is designed to evaluate the safety, tolerability, and efficacy of vimseltinib at the RP2D in patients with TGCT not amenable to surgery enrolled in 2 cohorts (Figure 2)
  - Cohort A: No prior anti-CSF1/CSF1R therapy (previous therapy with imatinib or nilotinib is allowed)
  - Cohort B: Prior anti-CSF1/CSF1R therapy (previous therapy with imatinib or nilotinib alone would not be eligible)
- 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 2 study



<sup>1</sup>Includes patients who received at least one dose of study drug. <sup>2</sup>Patients with at least one post-baseline imaging assessment. <sup>3</sup>At least one post-baseline efficacy assessment for patient-reported outcomes. CSF1, colony-stimulating factor 1; CSF1R, CSF1 receptor; RP2D, recommended phase 2 dose; TGCT, tenosynovial giant cell tumor.

## RESULTS

Table 1. Baseline demographics and clinical characteristics

	Cohort A (n = 46)	Cohort B (n = 12)	Total (N = 58)
Age, median (min, max), years	44 (21, 71)	47 (26, 65)	45 (21, 71)
Sex			
Female	31 (67)	7 (58)	38 (66)
Male	15 (33)	5 (42)	20 (35)
Race			
White	36 (78)	9 (75)	45 (78)
Asian	2 (4)	0	2 (3)
Black or African American	0	1 (8)	1 (2)
Pacific Islander	0	1 (8)	1 (2)
Not reported or missing	8 (17)	1 (8)	9 (16)
Disease location			
Knee	26 (57)	7 (58)	33 (57)
Ankle	9 (20)	1 (8)	10 (17)
Foot	6 (13)	0	6 (10)
Hand	0	1 (8)	1 (2)
Other <sup>a</sup>	5 (11)	3 (25)	8 (14)
Tumor type			
Diffuse TGCT	23 (50)	9 (75)	32 (55)
Localized TGCT	23 (50)	3 (25)	26 (45)
Patients with ≥1 prior surgery	31 (67)	10 (83)	41 (71)
2–3 prior surgeries	11 (24)	7 (58)	18 (31)
≥4 prior surgeries	1 (2)	1 (8)	2 (3)
Patients with ≥1 prior systemic therapy	3 (7)	12 (100)	15 (26)
Imatinib	3 (7)	0	3 (5)
Pexidartinib	NA	7 (58)	7 (12)
Imatinib and pexidartinib	NA	2 (17)	2 (3)
Cabiralizumab and pexidartinib	NA	1 (8)	1 (2)
Cabiralizumab	NA	1 (8)	1 (2)
Vimseltinib	NA	1 (8)	1 (2)

Data shown as n (%). Unless otherwise noted, percentages are rounded. <sup>a</sup>Other includes jaw, hip, shoulder, and thigh. NA, not applicable; TGCT, tenosynovial giant cell tumor.

- As of May 6, 2022, 58 patients with TGCT were enrolled—46 in Cohort A (enrollment complete; Dec 8, 2020–Sept 6, 2021) and 12 in Cohort B (enrollment ongoing; first patient enrolled: Dec 22, 2020); the median age was 45 years (Table 1)
- The most common disease location was the knee (33 [57%])
- Overall, 22 (38%) patients discontinued the study treatment; the most common reasons for treatment discontinuation were withdrawal of consent (13 [22%]), physician decision (5 [9%]), and adverse event (4 [7%])

## SAFETY

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

Preferred term, n (%)	Cohort A (n = 46)		Cohort B (n = 12)		Total (N = 58)	
	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4
Blood CPK increased	30 (65)	20 (44)	4 (33)	2 (17)	34 (59)	22 (38)
Headache	19 (41)	0	8 (67)	0	27 (47)	0
Periorbital edema	16 (35)	0	6 (50)	0	22 (38)	0
Nausea	14 (30)	0	5 (42)	0	19 (33)	0
Fatigue	9 (20)	0	7 (58)	0	16 (28)	0
Asthenia	14 (30)	1 (2)	1 (8)	0	15 (26)	1 (2)
Myalgia	13 (28)	0	2 (17)	0	15 (26)	0
Arthralgia	10 (22)	0	3 (25)	1 (8)	13 (22)	1 (2)
Rash maculopapular	10 (22)	1 (2)	3 (25)	0	13 (22)	1 (2)
AST increased	8 (17)	0	2 (17)	0	10 (17)	0
Face edema	8 (17)	0	2 (17)	0	10 (17)	0
Diarrhea	6 (13)	0	3 (25)	0	9 (16)	0
Edema peripheral	7 (15)	0	2 (17)	0	9 (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]). 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

	Cohort A (n = 46)	Cohort B (n = 12)	Total (N = 58)
Patients with TEAEs leading to dose modification	33 (72)	7 (58)	40 (69)
Dose interruption	29 (63)	6 (50)	35 (60)
Dose reduction	21 (46) <sup>a</sup>	3 (25) <sup>b</sup>	24 (41)
Treatment discontinuation	3 (7) <sup>c</sup>	2 (17) <sup>d</sup>	5 (9)

Percentages are rounded. A patient may be counted in more than one category. <sup>a</sup>G1 periorbital edema and G1 rash maculopapular; G1 skin hypopigmentation; G3 CPK increase; G2 rash maculopapular; G1 headache; G2 CPK increase, G2 erythema, and G3 pain in extremity; G1 eyelid edema; G2 asthenia and musculoskeletal pain; G2 asthenia, generalized edema, and G1 troponin I increase; G3 asthenia and G2 rash; G2 eyelid edema; G1 hypertension; G1 CPK increase; G2 CPK increase and G1 periorbital edema; G1 erythema; G2 headache, nausea, and vomiting; G2 CPK elevation and ejection fraction decrease; G2 CPK increase; G2 asthenia and G1 headache, rash, and swelling face; G1 migraine; G3 CPK increase. <sup>b</sup>G2 rash; G1 swelling face; G2 eczema. <sup>c</sup>G1 rash maculopapular and periorbital edema; G1 chapped lips, G2 rash papular, and G1 swelling face; G2 myalgia. <sup>d</sup>G2 rash maculopapular; G2 rash, CPK, creatine phosphokinase; G, grade; TEAE, treatment-emergent adverse event; TGCT, tenosynovial giant cell tumor.

- Mean treatment duration was 9.1 months (Cohort A) and 7.5 months (Cohort B) (median treatment duration, 9.8 months in Cohort A and 5.9 months in Cohort B)
- Most nonlaboratory treatment-emergent adverse events (TEAEs) were low grade (Table 2)
- The only Grade 3/4 TEAE observed in >5% of patients was blood creatine phosphokinase (CPK) increase; most treatment-related TEAEs were Grade 1/2
- In Cohort B, one patient had post-baseline Grade 1 bilirubin elevation
- In Cohort A, no treatment-related serious adverse events (SAEs) were reported
- In Cohort B, one patient experienced treatment-related SAEs of Grade 3 eczema (possibly related) and Grade 2 edema peripheral (probably related)
- Post-data cut, an SAE of Grade 4 blood CPK increase and Grade 3 myalgia was reported in Cohort B; treatment was interrupted and adverse events resolved. Patient discontinued study due to reasons unrelated to adverse events

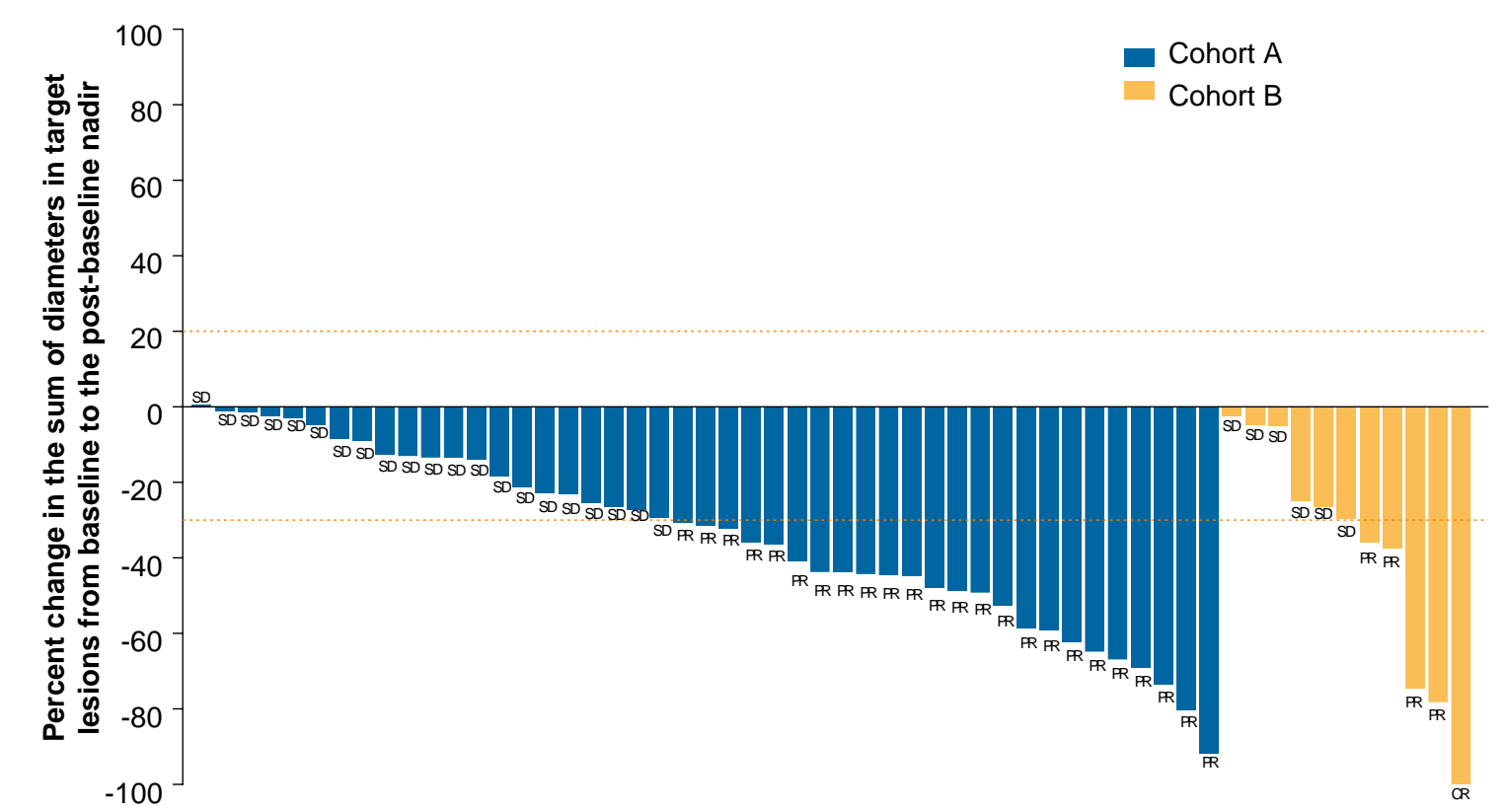
## EFFICACY

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

	Cohort A (n = 45)	Cohort A (n = 45)	Cohort B (n = 11)
	Best overall response <sup>a</sup>	Week 25 <sup>b</sup>	Best overall response <sup>a</sup>
ORR <sup>c</sup>	24 (53)	17 (38)	5 (46)
Complete response	0	0	1 (9)
Partial response	24 (53)	17 (38)	4 (36)
Stable disease	21 (47)	22 (49)	6 (55)
Duration of response, median <sup>d</sup> (min, max), months	NR (0.03, 12.0)		NR (0.03, 9.2)

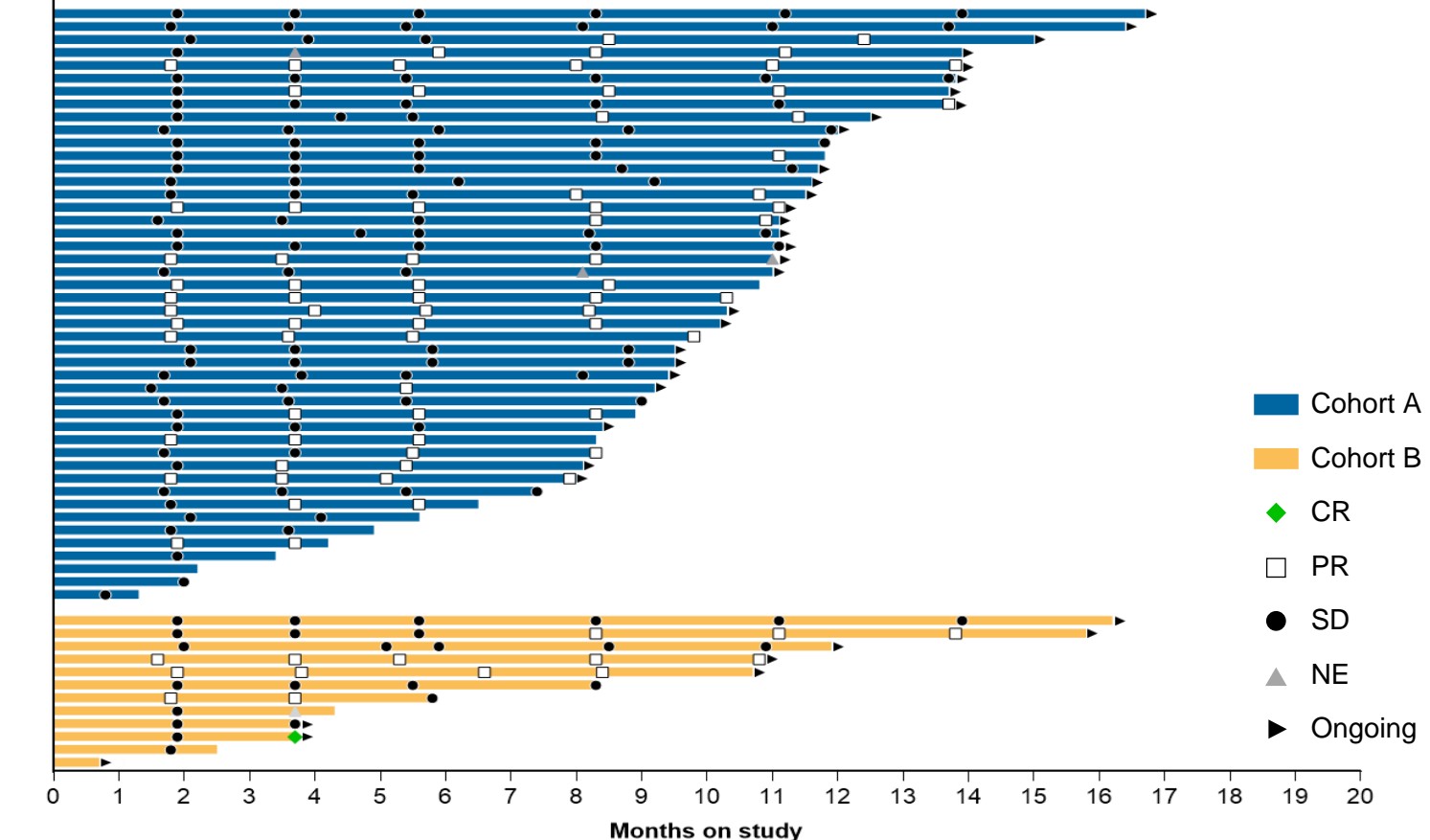
Data shown as n (%). Unless otherwise indicated, percentages are rounded. <sup>a</sup>Includes all available follow-ups. <sup>b</sup>Patients that either reached week 25 or discontinued treatment or study prior to week 25 were included. <sup>c</sup>Based on Kaplan-Meier estimates. Duration of response 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.

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



Using RECIST v1.1 by IRR; includes all available follow-ups. 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. 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.

- Cohort A: Best overall response was 53%; overall response rate at week 25 was 38% (Table 4)
  - In Cohort A, out of the 24 responders, 18 (75%) responses were achieved within 6 months (1 responder discontinued prior to 6 months) and 6 (25%) after 6 months on treatment (Figure 4)
- Cohort B: Best overall response was 46% (Table 4)
  - In Cohort B, out of the 5 responders, 4 (80%) responses were achieved within 6 months and 1 (20%) after 6 months on treatment (Figure 4)
  - Patients who achieved a partial response (PR) or complete response (CR) in Cohort B included patients who did not achieve a PR/CR or progressed on/after prior CSF1R-directed therapies
- As of the data cutoff date (May 6, 2022), no patients progressed as assessed by IRR

## PATIENT-REPORTED OUTCOMES

Table 5. Pain and stiffness in patients with TGCT receiving vimseltinib

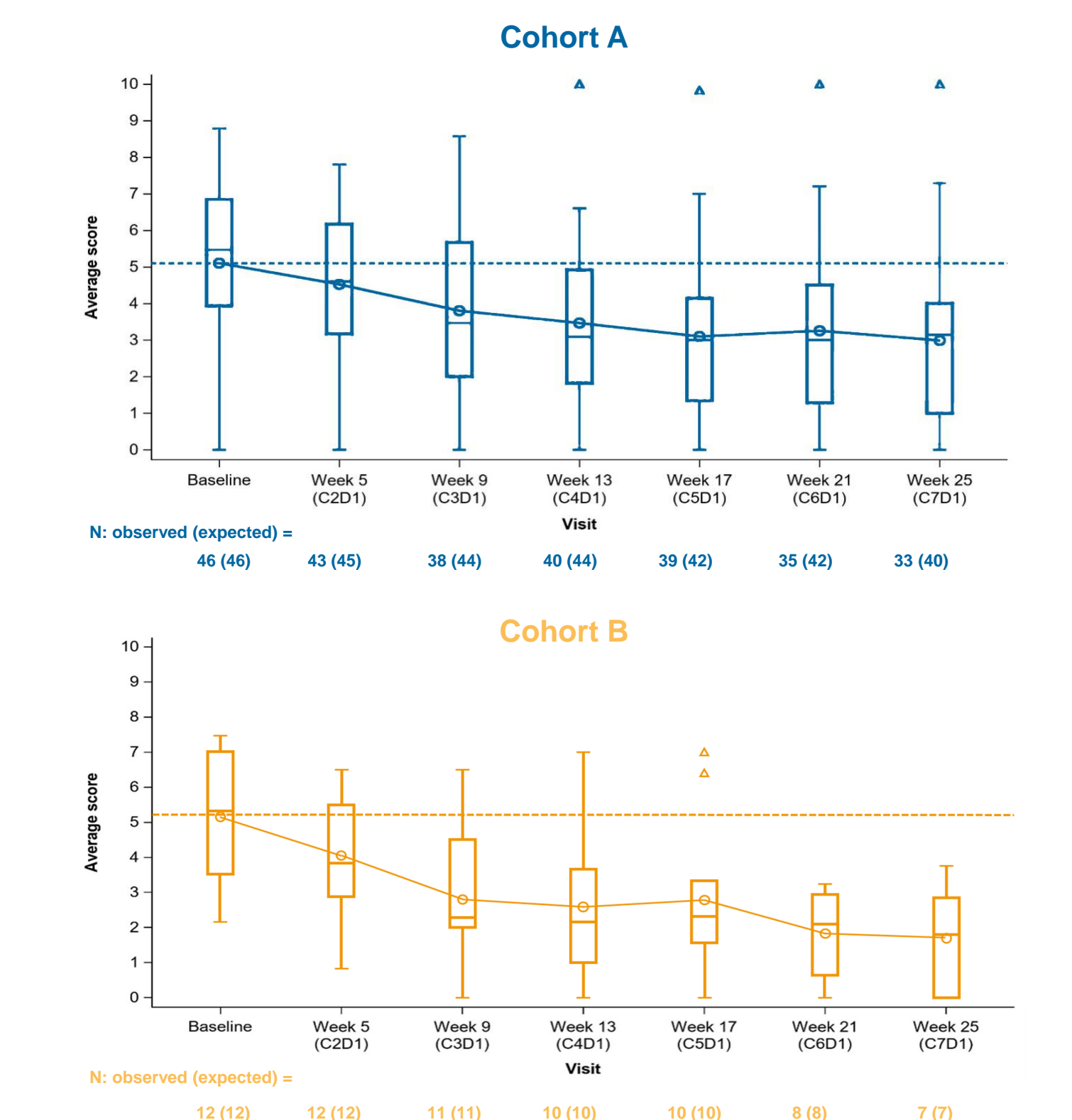
	Cohort A (n = 46) <sup>a</sup>	Cohort B (n = 9) <sup>a</sup>
BPI response <sup>b</sup> , n (%)	22 (48) <sup>b</sup>	5 (56)
Stiffness NRS, mean change from baseline to week 25 (SD) <sup>c</sup>	-2.0 (3)	-2.7 (2)

<sup>a</sup>Applicable to BPI response only. Ns for stiffness NRS are available in Figure 5. Percentages are rounded. <sup>b</sup>BPI worst pain responder is defined as a patient who experiences a decrease of ≥30% in the mean BPI worst pain NRS item without experiencing a ≥30% increase in narcotic analgesic use at week 25, comparing data collected at the same time as the pain questionnaire was completed, with baseline values collected prior to the first dose of the study treatment. <sup>c</sup>Additional analysis showed that only 1/46 (2.1%) patient had a clinically meaningful increase in worst pain in Cohort A. No increase for Cohort B was observed. <sup>d</sup>In terms of data completeness, 75% and 100% NRS stiffness data were available at week 25 for Cohorts A and B, respectively. BPI, Brief Pain Inventory; NRS, numeric rating scale; SD, standard deviation; TGCT, tenosynovial giant cell tumor.

## CONCLUSIONS

- Vimseltinib was well tolerated with a manageable safety profile (mean treatment duration 9.1 months [Cohort A] and 7.5 months [Cohort B]) in patients with TGCT not amenable to surgery at the RP2D dose of 30 mg twice weekly, with or without prior anti-CSF1/CSF1R therapy
- Vimseltinib demonstrated promising antitumor activity in patients with and without prior anti-CSF1/CSF1R therapy, with best overall response of 53% in Cohort A and 46% in Cohort B, and 100% clinical response benefit (CR, PR, and stable disease) without disease progression observed in any patient
- Preliminary patient-reported outcomes indicate that vimseltinib provides clinically meaningful symptomatic benefit for patients with respect to both pain and stiffness at week 25
- These results support continued evaluation of vimseltinib in the actively enrolling phase 3 MOTION trial (NCT05059262)

Figure 5. Worst stiffness NRS in patients with TGCT



Worst stiffness NRS average score at site of tumor in the last 24 hours. The item has a response scale of 0–10, where 0 is “no stiffness” and 10 is “stiffness as bad as you can imagine.” Threshold for meaningful change is considered as half of the SD of the baseline value.<sup>4</sup> For Cohort A, half of the SD of baseline (2.1) is 1.1. In terms of data completeness, 75% NRS stiffness data were available at week 25. For Cohort B, half of the SD of baseline (1.8) is 0.9. In terms of data completeness, 100% NRS stiffness data were available at week 25. The box represents the range from the 1st (bottom) to the 3rd (top) quartile. The circle in the box represents the mean and the horizontal line represents the median. The endpoint of the upper whisker represents the highest observation contained within 1.5 × IQR from the 3rd quartile. The end point of the lower whisker represents the lowest observation contained within 1.5 × IQR from the 1st quartile. The triangles represent any observation outside of the interval defined above as 1.5 × IQR from the 3rd quartile or 1.5 × IQR from the 1st quartile, referred to as outliers. C, cycle; D, day; IQR, interquartile range; NRS, numeric rating scale; SD, standard deviation; TGCT, tenosynovial giant cell tumor.

- In Cohorts A and B, 48% and 56% of patients had a Brief Pain Inventory response at week 25, respectively (Table 5)
- Between baseline and week 25, progressive improvements in stiffness were observed in patients treated with vimseltinib (Figure 5)
  - In Cohorts A and B, mean change from baseline was -2.0 and -2.7, respectively (Table 5)
  - Improvements observed were considered clinically meaningful changes, as the threshold for meaningful change is estimated to be 1.4<sup>5</sup>

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