Efficacy with vimseltinib in patients with tenosynovial giant cell tumor and prior colony-stimulating factor 1 inhibitor therapy: a phase 2 case series

Abstract: 2110786

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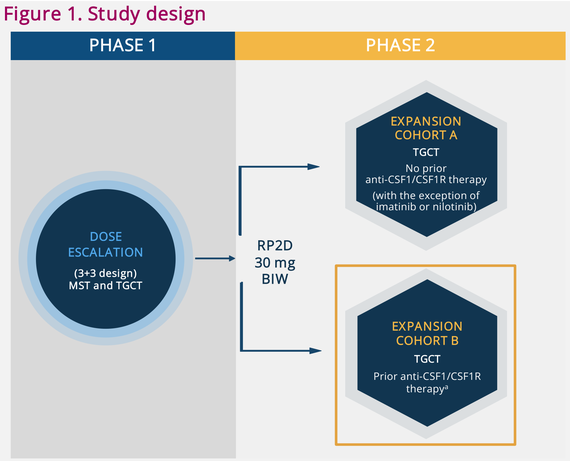
Introduction

- 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[1,2]
- Patients with TGCT require therapies with manageable toxicity,[1] and additional data are needed to inform treatment decisions following discontinuation of systemic therapy
- 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 for the treatment of adult patients with symptomatic TGCT for which surgical resection will potentially cause worsening functional limitation or severe morbidity[5]
  - In September 2025, vimseltinib was also approved by the European Commission for the treatment of TGCT in a similar patient population[6]
- In the phase 2 expansion of a phase 1/2 study (NCT03069469), vimseltinib demonstrated promising antitumor activity, favorable safety, and clinically meaningful improvements in patient-reported outcomes regardless of prior therapy[7,8]
- Here, we report the efficacy of vimseltinib with longer follow-up in patients who received prior anti-CSF1/CSF1R therapy

Methods

- This multicenter, open-label, phase 2 trial is designed to evaluate the safety, tolerability, and efficacy of vimseltinib at the recommended phase 2 dose (30 mg twice weekly)[9] in patients with TGCT not amenable to surgery (**Figure 1**)
  - This analysis only includes patients who received prior anti-CSF1/CSF1R therapy (cohort B)
- Safety assessments included evaluation of treatment-emergent adverse events (TEAEs) using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03
- Antitumor activity was evaluated by independent radiological review (IRR) using Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) and Tumor Volume Score (TVS)[10] via magnetic resonance imaging

Figure 1. Study design



Data cutoff: February 22, 2025.
[a]Patients who received previous imatinib or nilotinib alone were not eligible for cohort B.
BIW, twice weekly; CSF1, colony-stimulating factor 1; CSF1R, CSF1 receptor; MST, malignant solid tumor; RP2D, recommended phase 2 dose; TGCT, tenosynovial giant cell tumor.

Results

- A total of 20 patients were enrolled in cohort B; the median age was 45 years (**Table 1**)
- The most common disease location was the knee, and most patients had ≥1 prior surgery
- Sixteen patients received prior pexidartinib, and 2 received prior vimseltinib
- At data cutoff, 60% (12/20) of patients remain on treatment
  - Reasons for treatment discontinuation included withdrawal by patient (n = 3), adverse event (n = 2), physician decision (n = 1), progressive disease (n = 1), and other (n = 1)

Table 1. Baseline demographics and clinical characteristics

	Cohort B n = 20
Age, median (min, max), years	45 (26, 65)
Sex, n (%)	
Female	10 (50)
Male	10 (50)
Race, n (%)	
White	17 (85)
Black or African American	1 (5)
Pacific Islander	1 (5)
Not reported	1 (5)
Disease location, n (%)	
Knee	11 (55)
Hip	3 (15)
Ankle	2 (10)
Hand	2 (10)
Jaw	2 (10)
Patients with ≥1 prior surgery, n (%)	14 (70)
1 surgery	4 (20)
2–3 surgeries	5 (25)
≥4 surgeries	5 (25)
Patients with ≥1 prior systemic therapy, n (%)	20 (100)
Pexidartinib	16 (80)
Imatinib[a]	3 (15)
Vimseltinib	2 (10)
Other[b]	3 (15)

Data cutoff: February 22, 2025.
[a]Patients received pexidartinib or surufatinib in addition to imatinib. [b]Includes prior cabiralizumab or surufatinib.
max, maximum; min, minimum.

Safety

- The majority of TEAEs were grade 1 or 2; observed aminotransferase elevations (aspartate aminotransferase, alanine aminotransferase) were also of low grade (**Table 2**)
- Grade 3/4 TEAEs (>5% of patients) were elevated creatine phosphokinase, hypertension, and eczema
- Liver enzyme elevations were consistent with the known mechanism of action of CSF1R inhibitors[11,12]
- There was no evidence of cholestatic hepatotoxicity or drug-induced liver injury
- For patients who received prior pexidartinib, the median treatment duration was longer with vimseltinib than with pexidartinib (**Table 3**)
  - Reasons for pexidartinib discontinuation were not known for some patients

Table 2. TEAEs in ≥15% of patients

	Cohort B n = 20			
Preferred term, n (%)	All grades	Grade 1	Grade 2	Grade 3/4
Blood CPK increased	12 (60)	2 (10)	3 (15)	7 (35)
Fatigue[a]	11 (55)	9 (45)	1 (5)	1 (5)
Headache[a]	10 (50)	8 (40)	2 (10)	0
Periorbital edema[a]	9 (45)	7 (35)	2 (10)	0
AST increased	8 (40)	6 (30)	2 (10)	0
Diarrhea	8 (40)	6 (30)	2 (10)	0
Nausea[a]	6 (30)	5 (25)	1 (5)	0
Rash maculopapular[a]	6 (30)	2 (10)	4 (20)	0
Amylase increased	5 (25)	3 (15)	1 (5)	1 (5)
Arthralgia[a]	5 (25)	2 (10)	2 (10)	1 (5)
Hypertension	5 (25)	0	2 (10)	3 (15)
Myalgia[a]	5 (25)	4 (20)	0	1 (5)
Rash[a]	5 (25)	4 (20)	1 (5)	0
ALT increased	4 (20)	2 (10)	2 (10)	0
Eczema[a]	4 (20)	0	2 (10)	2 (10)
Edema peripheral[a]	4 (20)	3 (15)	1 (5)	0
Pain in extremity[a]	4 (20)	2 (10)	1 (5)	1 (5)
Anemia	3 (15)	2 (10)	0	1 (5)
Asthenia[a]	3 (15)	1 (5)	2 (10)	0
Blood creatinine increased	3 (15)	3 (15)	0	0
Dizziness	3 (15)	3 (15)	0	0
Dry skin	3 (15)	3 (15)	0	0
Hypercholesterolemia	3 (15)	1 (5)	2 (10)	0
Hypophosphatemia	3 (15)	3 (15)	0	0
Pruritus[a]	3 (15)	1 (5)	2 (10)	0
Weight increased[a]	3 (15)	2 (10)	0	1 (5)

Data cutoff: February 22, 2025. Safety population includes patients who received ≥1 dose of study drug. Severity was assessed by the investigator according to the toxicity grade described in the National Cancer Institute CTCAE v4.03 (grade 1 [mild] to grade 5 [death]). Two of 3 patients with grade 3/4 hypertension had prior history of hypertension.
[a]Denotes events without a grade 4 severity category in the CTCAE v4.03.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; CTCAE v4.03, Common Terminology Criteria for Adverse Events version 4.03; TEAE, treatment-emergent adverse event.

Table 3. Treatment duration for patients who received prior pexidartinib

	On prior pexidartinib n = 16	On vimseltinib n = 16
Treatment duration, median (Q1, Q3), months	10.0 (5.6, 17.3)	21.8 (4.1, 34.6)

Data cutoff: February 22, 2025.
Q1, lower quartile (25th percentile); Q2, upper quartile (75th percentile).

Efficacy

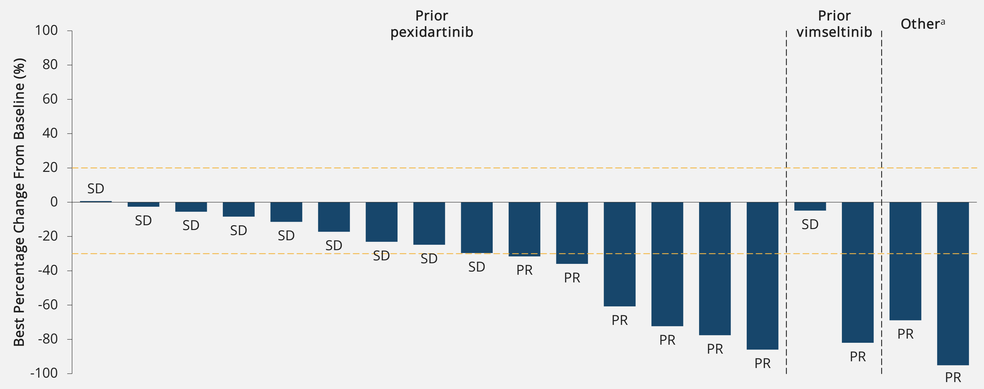
- Objective response rate (ORR) on study by IRR for all patients in cohort B was 47% (9/19) per RECIST v1.1 and 42% (8/19) per TVS (**Table 4**)
- For patients who received prior pexidartinib and had a post-baseline scan, the ORR on study per RECIST v1.1 on vimseltinib was 40% (6/15)
- All patients experienced disease control per RECIST v1.1 (partial response or stable disease; **Figure 2**)
  - Most responses per RECIST v1.1 (67%) occurred within the first 6 months of treatment with median time to first response of 5.3 months (range, 1.6–16.2; **Figure 3**)

Table 4. Response assessed by IRR per RECIST v1.1 and TVS

	RECIST v1.1 n = 19	TVS n = 19
ORR on study, n (%)	9 (47)	8 (42)
Partial response	9 (47)	8 (42)
Stable disease, n (%)	10 (53)	11 (58)
Duration of response, median[a] (min, max), months	NR (2.8 to 41.4+)	NR (8.6+ to 42.3+)

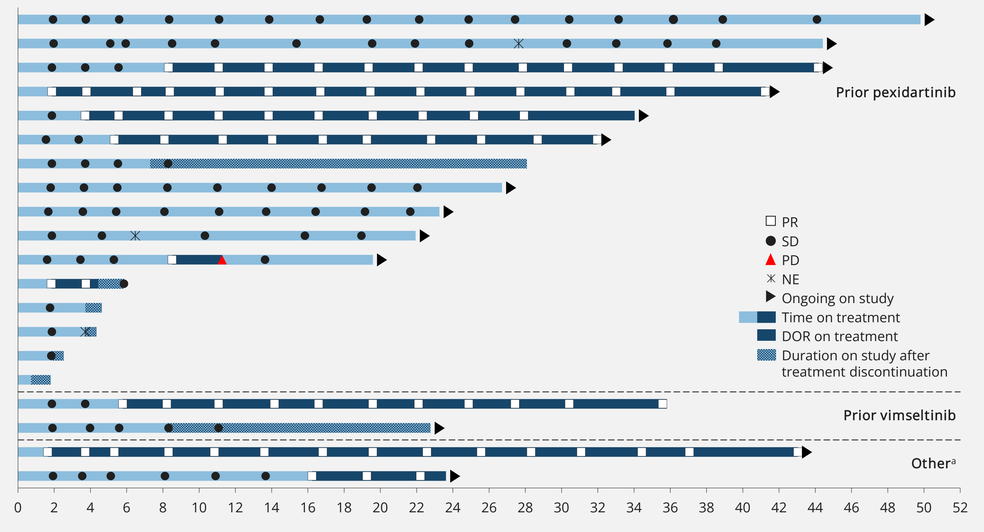
Data cutoff: February 22, 2025; 19/20 patients had ≥1 post-baseline imaging assessment at data cutoff (efficacy-evaluable population). + indicates that response was ongoing at last assessment.
[a]Based on Kaplan-Meier estimate. Duration of response is defined as time from first imaging result showing response to progressive disease.
IRR, independent radiological review; max, maximum; min, minimum; NR, not reached; ORR, objective response rate; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TVS, Tumor Volume Score.

Figure 2. Best percent change from baseline in target lesions by IRR per RECIST v1.1



Data cutoff: February 22, 2025; 19/20 patients had ≥1 post-baseline imaging assessment at data cutoff (efficacy-evaluable population). Includes all available follow-up visits. Dotted line at 20% represents the threshold for PD; dotted line at −30% represents threshold for PR. Graph shows individual patient values. [a]Other includes prior cabiralizumab or surufatinib.
IRR, independent radiological review; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Figure 3. Duration on study and duration of response

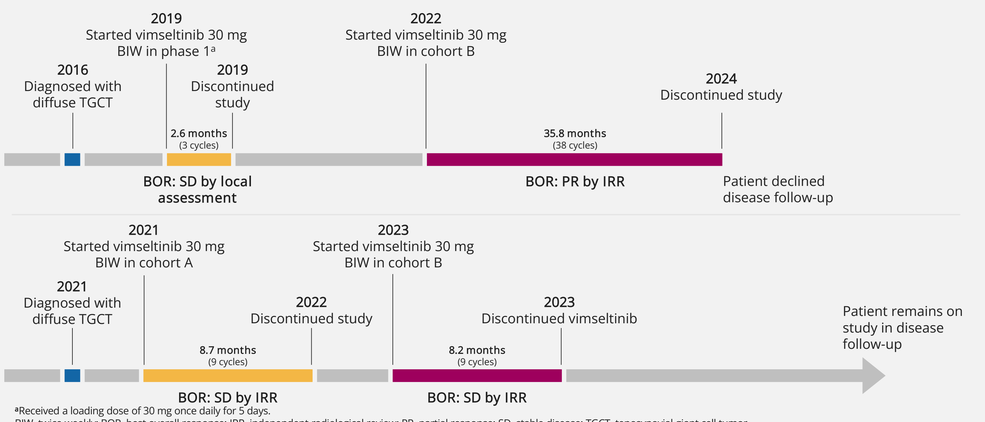


Data cutoff: February 22, 2025; n = 20. Using RECIST v1.1 by IRR; Includes all available follow-up visits. Dark blue shading represents the DOR.
[a]Other includes prior cabiralizumab or surufatinib.
DOR, duration of response; IRR, independent radiological review; NE, not evaluable; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Case series: prior exposure to vimseltinib

- Two patients in cohort B received vimseltinib prior to enrolling in cohort B (**Figure 4**)
- The first patient received vimseltinib in the phase 1 portion of this study and enrolled in cohort B approximately 2.5 years posttreatment
  - Best overall response (BOR) was stable disease by local assessment (IRR not available) in phase 1 and partial response by IRR in cohort B
- The second patient received vimseltinib in cohort A and enrolled in cohort B approximately 1 year posttreatment
  - BOR in both cohorts was stable disease by IRR, which has been maintained for approximately 8 months in cohort B
  - After the last response assessment by IRR in cohort B, there was no subsequent radiologically confirmed disease progression based on review of medical records for approximately 12 additional months in disease follow-up

Figure 4. Patients who received prior vimseltinib



[a]Received a loading dose of 30 mg once daily for 5 days.
BIW, twice weekly; BOR, best overall response; IRR, independent radiological review; PR, partial response; SD, stable disease; TGCT, tenosynovial giant cell tumor.

CONCLUSIONS

- Longer follow-up showed that vimseltinib has a manageable safety profile in patients who previously received anti-CSF1/CSF1R therapy
- Vimseltinib continued to demonstrate promising antitumor activity in these patients, with ORR on study of 47% per RECIST v1.1 and 42% per TVS, and nearly all patients experienced a reduction in tumor size
- For patients who received prior pexidartinib, the treatment duration with vimseltinib was longer than with prior pexidartinib
- Vimseltinib offers an effective systemic treatment that provides clinical benefit for people with TGCT living with substantial morbidity and limited treatment options, including those who received prior vimseltinib or other anti-CSF1/CSF1R therapies

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