Safety, efficacy, and patient-reported outcomes with vimseltinib in patients with tenosynovial giant cell tumor who received prior anti–colony-stimulating factor 1 therapy: ongoing phase 2 study

Poster: 1770P

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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]
- No systemic agents are approved for the treatment of TGCT in Europe due to safety risks, and only 1 is approved in the US, Taiwan, and South Korea[2-4]
  - There is an unmet need for an effective, CSF1 receptor (CSF1R)-targeted therapy with a favorable safety profile
- Vimseltinib is an investigational, oral, switch-control tyrosine kinase inhibitor specifically designed to selectively and potently inhibit CSF1R[1]
- Here we report updated safety, efficacy, and patient-reported outcome (PRO) results from the phase 2 part (expansion) of an ongoing phase 1/2 study of vimseltinib for patients with TGCT who received prior anti-CSF1/CSF1R therapy (cohort B; NCT03069469)

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)[5] in patients with TGCT not amenable to surgery who received prior specific anti-CSF1/CSF1R agents (cohort B)
- Vimseltinib 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) via magnetic resonance imaging[6]
- Active ROM (in degrees) of the affected joint was normalized to a reference standard value provided by the American Medical Association
- Pain was assessed by 2 items from the brief pain inventory (BPI; worst pain and average pain), with BPI response defined as ≥30% reduction in pain without a ≥30% increase in narcotic analgesic use
- PRO questionnaires were completed electronically and included 15 questions from Patient-Reported Outcomes Measurement Information System Physical Function (PROMIS-PF) and worst stiffness from the numeric rating scale (NRS)
  - Clinically meaningful response for these PROs was defined as a ≥3-point increase or ≥2-point decrease from baseline for PROMIS-PF or NRS stiffness, respectively[7]

Results

- As of March 1, 2024, 20 patients were enrolled in cohort B (enrollment complete); median age was 45 years (**Table 1**)
- The most common disease location was the knee, and most patients had ≥1 prior surgery
- Most patients (80%) previously received pexidartinib and discontinued pexidartinib due to disease progression (n = 5), drug-related toxicity (n = 2), and other (n = 9)

Table 1. Baseline demographics and clinical characteristics

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

Data cutoff: March 1, 2024. Data shown as n (%) unless otherwise noted.
[a]Patients received pexidartinib or surufatinib in addition to imatinib. [b]Includes cabiralizumab and surufatinib.
max, maximum; min, minimum.

Safety

- The majority of treatment-emergent adverse events (TEAEs) were grade 1 or 2; observed aminotransferase elevations were also low grade (**Table 2**)
- Grade 3/4 TEAEs (>5% of patients) were elevated creatine phosphokinase (CPK), hypertension, and eczema
- Enzyme elevations were consistent with the known mechanism of action of CSF1R inhibitors
- There was no evidence of cholestatic hepatotoxicity or drug-induced liver injury
- Overall, 3 patients experienced treatment-related serious TEAEs
  - One patient reported grade 3 eczema and grade 2 edema peripheral
  - One patient reported grade 3 myalgia and grade 4 elevated CPK
  - One patient reported grade 2 squamous cell carcinoma of skin, grade 2 basal cell carcinoma, and grade 4 hypertensive emergency

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]	11 (55)	8 (40)	3 (15)	0
Periorbital edema[a]	9 (45)	7 (35)	2 (10)	0
AST increased	8 (40)	6 (30)	2 (10)	0
Diarrhea	7 (35)	6 (30)	1 (5)	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)	2 (10)	0
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)
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)
Rash[a]	4 (20)	3 (15)	1 (5)	0
Anemia	3 (15)	2 (10)	0	1 (5)
Asthenia[a]	3 (15)	2 (10)	1 (5)	0
Blood creatinine increased	3 (15)	3 (15)	0	0
Dizziness	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: March 1, 2024. 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.

- Median treatment duration was 11.1 months (range, 0.7–36.1; mean, 16.4 months) with 65% (13/20) of patients on treatment at data cutoff
  - Reasons for treatment discontinuation included withdrawal by patient (n = 3), adverse event (n = 2), physician decision (n = 1), and other (n = 1)
- TEAEs led to treatment discontinuation in 10% of patients (**Table 3**)

Table 3. Dose modification due to any TEAEs

	Cohort B (n = 20)
Patients with TEAEs leading to dose modification, n (%)	15 (75)
Dose interruption	13 (65)
Dose reduction	9 (45)
Treatment discontinuation	2 (10)[a]

Data cutoff: March 1, 2024.
[a]G2 rash maculopapular; G2 rash.
G, grade; TEAE, treatment-emergent adverse event.

Efficacy

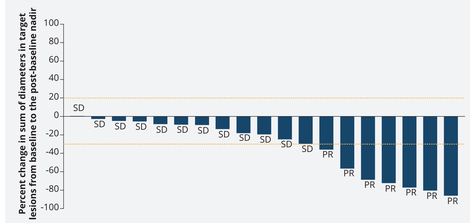
- Best overall responses by IRR were 37% per RECIST v1.1 and 42% per TVS; all patients experienced disease control (partial response or stable disease; **Table 4, Figure 1**)
  - Patients who achieved partial response in cohort B included patients who did not achieve objective response or progressed on/after prior CSF1R-directed therapies
  - Most responses (86%) occurred within 6 months of treatment, with median time to first response of 3.7 months (range, 1.6–8.3; **Figure 2**)
- As of last assessment, no patients had progressive disease by IRR
- Most patients experienced an improvement in active ROM (**Figure 3, Table 5**)

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

	RECIST v1.1		TVS	
	BOR (n = 19)	**Week 25[a] (n = 19)**	**BOR (n = 19)**	**Week 25[a] (n = 19)**
ORR, n (%)	7 (37)	5 (26)	8 (42)	5 (26)
Complete response	0	0	0	0
Partial response	7 (37)	5 (26)	8 (42)	5 (26)
Stable disease	12 (63)	9 (47)	11 (58)	10 (53)
Duration of response, median[b] (min, max), months	NR (4.0+, 29.5+)		NR (0.03+, 34.1+)	

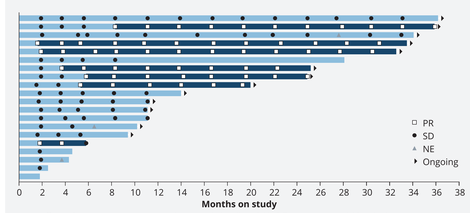
Data cutoff: March 1, 2024; 19/20 patients had ≥1 post-baseline imaging assessment as of the data cutoff (efficacy evaluable population); + indicates that response was ongoing at last assessment.
[a]Patients that either reached week 25 or discontinued treatment or study prior to week 25 were included. [b]Based on Kaplan-Meier estimate. Duration of response is defined as time from first imaging result showing response to progressive disease.
BOR, best overall response; 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 1. Best percent change in target lesions



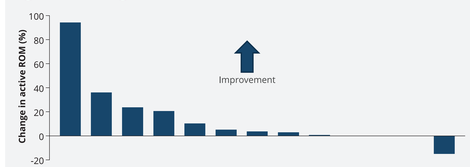
Data cutoff: March 1, 2024. Using RECIST v1.1 by IRR; includes all available follow-up visits. Dotted line at 20% represents threshold for PD; dotted line at −30% represents threshold for PR. Graph shows individual patient values.
IRR, independent radiological review; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Figure 2. Duration of treatment and response



Data cutoff: March 1, 2024. Using RECIST v1.1 by IRR; includes all available follow-up visits. Dark blue shading represents duration of response.
IRR, independent radiological review; NE, not evaluable; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Figure 3. Change in active ROM at week 25



Data cutoff: March 1, 2024. Graph shows individual patient values. Increase from baseline: n = 9; no change: n = 3; decrease: n = 1. ROM, range of motion.

Table 5. Active ROM change from baseline to week 25

	Cohort B (n = 13)
Active ROM of the affected joint, mean (SD), %	
Baseline	51.1 (35.9)
Week 25	65.2 (37.5)
Change from baseline to week 25, mean (SD), percentage points	14.1 (27.4)

Data cutoff: March 1, 2024. Analysis only includes patients with active ROM assessments at baseline and week 25.
ROM, range of motion; SD, standard deviation.

Patient-reported outcomes

- At week 25, 55% (11/20) of patients experienced BPI response for both worst pain and average pain
- Two patients (40%) with objective responses per RECIST v1.1 at week 25 were also BPI responders (**Table 6**)
  - Most patients (78%) with stable disease at week 25 were also BPI responders
- At week 25, 80% and 71% of patients had clinically meaningful improvements in PROMIS-PF and NRS stiffness, respectively (**Table 7**)

Table 6. BPI worst pain response by objective response per RECIST v1.1 at week 25

	RECIST v1.1 at week 25 by IRR[a]	
	Partial response (n = 5)	**Stable disease (n = 9)**
Worst pain responder, n (%)	2 (40)	7 (78)

Data cutoff: March 1, 2024.
[a]Includes patients with both BPI and efficacy data available at week 25 (n = 14); percentages represent proportion of patients with partial response or stable disease with ≥30% pain reduction.
BPI, Brief Pain Inventory; IRR, independent radiological review; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Table 7. PROMIS-PF and NRS worst stiffness at week 25

	PROMIS-PF (n = 15)		NRS stiffness (n = 14)	
	Baseline	**Week 25**	**Baseline**	**Week 25**
Mean (SD)	43.3 (8.0)	49.5 (7.8)	4.7 (2.4)	2.6 (2.2)
Change from baseline, mean (SD)	6.2 (8.0)		−2.2 (3.0)	
Response, n (%)	12 (80)		10 (71)	

Data cutoff: March 1, 2024.
NRS, numeric rating scale; PROMIS-PF, Patient-Reported Outcomes Measurement Information System Physical Function; SD, standard deviation.

CONCLUSIONS

- Vimseltinib demonstrated promising antitumor activity in this population who previously received anti-CSF1/CSF1R therapy, with best overall responses of 37% per RECIST v1.1 and 42% per TVS
  - Nearly all patients experienced a reduction in tumor size, and no patients had progressive disease by IRR
- Longer follow-up showed that vimseltinib continued to be well tolerated with a manageable safety profile in patients with TGCT who were previously treated with anti-CSF1/CSF1R therapy
  - At data cutoff, 65% of patients remained on treatment
- Patients experienced clinically meaningful improvements in pain, physical function, and stiffness at week 25
  - Patients had clinically meaningful reductions in pain regardless of objective response; patients with stable disease also experienced clinically meaningful reductions in pain
  - Most patients experienced clinically meaningful improvements in physical function and stiffness
- Despite being in patients pretreated with anti-CFS1/CSF1R therapy, these results are consistent with results from the MOTION phase 3 trial in which vimseltinib provided statistically significant and clinically meaningful improvements for patients with TGCT vs placebo[7]

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DISCLOSURES

Gina D'Amato reports consulting/advisory roles for Blueprint Medicines, Deciphera Pharmaceuticals, LLC, Daiichi Sankyo, Epizyme, and Lilly.

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