Safety and efficacy with vimseltinib in patients with tenosynovial giant cell tumor who received no prior anti–colony-stimulating factor 1 therapy: ongoing phase 2 study

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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 long-term safety and efficacy results from the phase 2 part (expansion) of an ongoing phase 1/2 study of vimseltinib for patients with TGCT (cohort A; 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 did not receive prior specific anti-CSF1/CSF1R agents (cohort A; previous therapy with imatinib or nilotinib is allowed)
- 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]

Results

- As of March 1, 2024, 46 patients were enrolled in cohort A (enrollment complete); the median age was 44 years (**Table 1**)
- The most common disease location was the knee, and most patients had ≥1 prior surgery

Table 1. Baseline demographics and clinical characteristics

	Cohort A (n = 46)
Age, median (min, max), years	44 (21, 71)
Sex	
Female	31 (67)
Male	15 (33)
Race	
White	36 (78)
Asian	2 (4)
Not reported	5 (11)
Missing	3 (7)
Disease location	
Knee	26 (57)
Ankle	9 (20)
Foot	6 (13)
Hip	3 (7)
Shoulder	1 (2)
Jaw	1 (2)
Patients with ≥1 prior surgery	31 (67)
1 surgery	18 (39)
2–3 surgeries	11 (24)
≥4 surgeries	2 (4)
Patients with ≥1 prior systemic therapy	3 (7)
Imatinib	3 (7)

Data cutoff: March 1, 2024. Data shown as n (%) unless otherwise noted.
max, maximum; min, minimum.

Safety

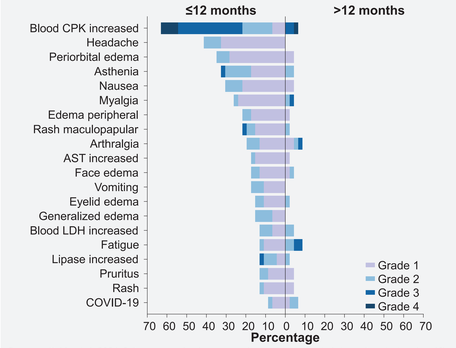
- The majority of treatment-emergent adverse events (TEAEs) were grade 1 or 2; observed aminotransferase elevations were also low grade (**Table 2**)
  - The safety profile remains consistent with continued vimseltinib treatment, and the majority of the most severe events occurred within the first 12 months (**Figure 1**)
- Grade 3/4 TEAEs (>5% of patients) were elevated creatine phosphokinase and hypertension
- Enzyme elevations were consistent with the known mechanism of action of CSF1R inhibitors
- There were no treatment-related serious adverse events and no evidence of cholestatic hepatotoxicity or drug-induced liver injury

Table 2. TEAEs in ≥15% of patients

	Cohort A (n = 46)			
Preferred term, n (%)	**All grades**	**Grade 1**	**Grade 2**	**Grade 3/4**
Blood CPK increased	32 (70)	3 (7)	7 (15)	22 (48)
Headache[a]	19 (41)	15 (33)	4 (9)	0
Periorbital edema[a]	18 (39)	15 (33)	3 (7)	0
Asthenia[a]	17 (37)	8 (17)	8 (17)	1 (2)
Nausea[a]	16 (35)	12 (26)	4 (9)	0
Myalgia[a]	14 (30)	11 (24)	2 (4)	1 (2)
Arthralgia[a]	13 (28)	8 (17)	4 (9)	1 (2)
Edema peripheral[a]	11 (24)	9 (20)	2 (4)	0
Rash maculopapular[a]	11 (24)	7 (15)	3 (7)	1 (2)
Face edema[a]	10 (22)	7 (15)	3 (7)	0
Fatigue[a]	10 (22)	5 (11)	3 (7)	2 (4)
AST increased	9 (20)	8 (17)	1 (2)	0
Blood LDH increased	8 (17)	3 (7)	5 (11)	0
Eyelid edema[a]	8 (17)	5 (11)	3 (7)	0
Pruritus[a]	8 (17)	6 (13)	2 (4)	0
Rash[a]	8 (17)	7 (15)	1 (2)	0
Vomiting	8 (17)	5 (11)	3 (7)	0
COVID-19	7 (15)	4 (9)	3 (7)	0
Generalized edema[a]	7 (15)	3 (7)	4 (9)	0
Lipase increased	7 (15)	2 (4)	4 (9)	1 (2)

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]). Grade 3/4 hypertension was observed in 9% (4/46) of patients; 3 of 4 patients had prior history of hypertension.
[a]Denotes events without a grade 4 severity category in the CTCAE v4.03.
AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; CPK, creatine phosphokinase; CTCAE v4.03, Common Terminology Criteria for Adverse Events version 4.03; LDH, lactate dehydrogenase; TEAE, treatment-emergent adverse event.

Figure 1. Percentage of TEAEs by maximum grade in ≥15% of patients occurring before and after 12 months on treatment



Data cutoff: March 1, 2024. Safety population includes patients who received ≥1 dose of study drug (n = 46). 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]). Time denotes the earliest start date of the worst grade for each TEAE.
AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; CPK, creatine phosphokinase; CTCAE v4.03, Common Terminology Criteria for Adverse Events version 4.03; LDH, lactate dehydrogenase; TEAE, treatment-emergent adverse event.

- Median treatment duration was 22.2 months (range, 0.2–36.6; mean 20.1 months) with 41% (19/46) of patients on treatment at data cutoff
  - Reasons for treatment discontinuation included withdrawal by patient (n = 15), adverse event (n = 7), and physician decision (n = 5)
- TEAEs led to treatment discontinuation in 13% of patients (**Table 3**)

Table 3. Dose modification due to any TEAEs

	Cohort A (n = 46)
Patients with TEAEs leading to dose modification, n (%)	36 (78)
Dose interruption	32 (70)
Dose reduction	28 (61)
Treatment discontinuation	6 (13)[a]

Data cutoff: March 1, 2024.
[a]G1 dermatitis acneiform; G1 rash maculopapular and G1 periorbital edema; G2 eczema; G2 eyelid edema and G2 asthenia; G3 mixed connective tissue disease; G3 breast cancer. One patient discontinued treatment due to an unrelated adverse event which started approximately 3 months after date of last dose and was therefore not deemed to be treatment-emergent.
G, grade; TEAE, treatment-emergent adverse event.

Efficacy

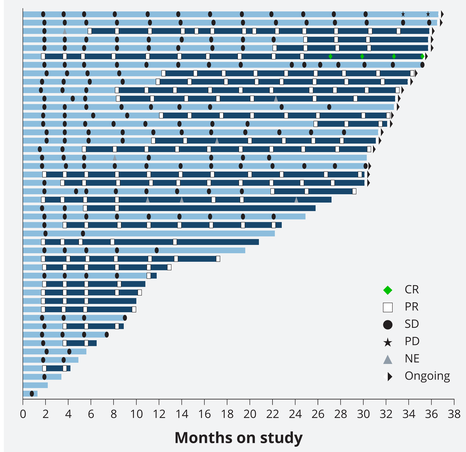
- Longer follow up demonstrated the best overall responses per RECIST v1.1 (64%) and per TVS (62%) were maintained and durable over time; the week 25 objective response rate was 38% per RECIST v1.1 and 51% per TVS (**Table 4, Figure 2**)
  - The majority of responses (62%, 18/29) were achieved within 6 months of treatment, with a median time to first response of 3.7 months (range, 1.8–25.8)
  - Responses also occurred beyond 6 months, with 1 complete response by RECIST v1.1 achieved after >2 years on treatment (**Figure 2**)
- As of last assessment, all responses were ongoing

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

	RECIST v1.1		TVS	
	BOR (n = 45)	**Week 25 (n = 45)[a]**	**BOR (n = 45)**	**Week 25 (n = 45)[a]**
ORR, n (%)	29 (64)	17 (38)[b]	28 (62)	23 (51)
Complete response	1 (2)	0	0	0
Partial response	28 (62)	17 (38)	28 (62)	23 (51)
Stable disease	16 (36)	22 (49)	17 (38)	16 (36)
Duration of response, median[c] (min, max), months	NR (0.03+, 33.4+)		NR (0.03+, 33.4+)	

Data cutoff: March 1, 2024; 45/46 patients had at ≥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]One of the 18 responders had a response prior to week 25 but discontinued the study before the week 25 scan and was considered a nonresponder at week 25.
[c]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 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.
CR, complete 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.

CONCLUSIONS

- Vimseltinib demonstrated promising antitumor activity with best overall responses of 64% per RECIST v1.1 and 62% per TVS
  - Objective responses with vimseltinib were maintained and durable over time
- Longer follow-up showed that vimseltinib continued to be well tolerated with a manageable safety profile in patients with TGCT whose disease is not amenable to surgery and who received no prior anti-CSF1/CSF1R therapy
- The median treatment duration increased to 22.2 months, with 41% of patients remaining on treatment at data cutoff
- These results are consistent with 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

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