

Safety and preliminary efficacy of vimseltinib in tenosynovial giant cell tumor (TGCT)

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Abstract:
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ePoster

INTRODUCTION

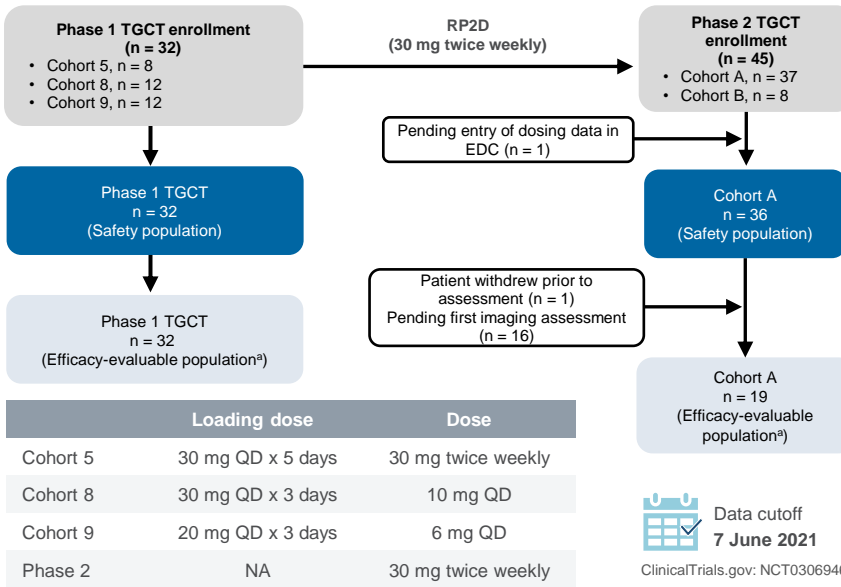
- Tenosynovial giant cell tumor (TGCT) is a rare, locally aggressive neoplasm, where overexpression of colony-stimulating factor 1 (CSF1) drives recruitment of macrophages leading to local inflammation and joint destruction^{1,2}
- Patients with TGCT experience debilitating symptoms and significant disease burden. There remains an unmet need for treatment options for patients with TGCT not amenable to surgery
- Vimseltinib (DCC-3014) is an investigational, oral, highly selective, switch-control kinase inhibitor of CSF1 receptor (CSF1R)³
- We report the safety and preliminary efficacy of patients with TGCT not amenable to surgery receiving vimseltinib in the Phase 1/2 study (NCT03069469)

METHODS

- NCT03069469, an ongoing, multicenter, open-label study of vimseltinib in patients with advanced solid tumors and TGCT consists of 2 phases:
 - Phase 1 (dose escalation) study, a pharmacologically guided 3 + 3 design, to determine the recommended phase 2 dose (RP2D) and the maximum tolerated dose (MTD)
 - Phase 2 (expansion) study to evaluate the safety, tolerability, and preliminary efficacy in 2 TGCT expansion cohorts
 - Cohort A: TGCT patients with no prior anti-CSF1/CSF1R therapy (previous therapy with imatinib or nilotinib is allowed)
 - Cohort B: TGCT patients with prior anti-CSF1/CSF1R therapy (previous therapy with imatinib or nilotinib alone would not be eligible)

RESULTS

Figure 1. TGCT enrollment and disposition in Phase 1/2 Study



^aAt least one post-baseline efficacy assessment.
EDC, electronic data capture; QD, once daily; RP2D, recommended phase 2 dose; TGCT, tenosynovial giant cell tumor.

- Enrollment in phase 1 with dose escalation is complete (n = 32)
- The target enrollment of 40 patients in phase 2 cohort A has been reached as of 13 July 2021
- The results of patients with TGCT in phase 1 (n = 32) and phase 2 Cohort A (n = 36) receiving vimseltinib as of 7 June 2021 are presented

Table 1. Baseline characteristics of patients with TGCT receiving vimseltinib

	Phase 1 TGCT patients n = 32	Phase 2 Cohort A patients n = 36
Age, median (range), years	51 (23-73)	44 (21-71)
Sex		
Female	17 (53)	26 (72)
Male	15 (47)	10 (28)
Race		
White	31 (97)	28 (78)
Asian	1 (3)	2 (6)
Not Reported or Missing	0	6 (17)
Disease location		
Knee	20 (63)	20 (56)
Ankle	5 (16)	5 (14)
Hip	4 (13)	2 (6)
Foot	1 (3)	6 (17)
Other ^a	2 (6)	3 (8)
Patients with at least one prior surgery	12 (38)	32 (89)
Patients with at least one prior systemic therapy	5 (16)	2 (6)
Imatinib or nilotinib	4 (13)	2 (6)
Lacnolutuzumab (MCS-110)	1 (3)	0

Data are presented as n (%) unless otherwise noted. Percentages might not add up to 100% due to rounding.
^aOther locations include wrist, shoulder, and jaw. TGCT, tenosynovial giant cell tumor.

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

Preferred term, No. (%)	Phase 1		Phase 2	
	Cohort 5 (n = 8)	All Patients ^a (n = 32)	Cohort A ^a (n = 36)	
	All grades	Grade 3/4	All grades	Grade 3/4
Blood CPK increased	7 (88)	4 (50)	19 (53)	9 (25)
Periorbital oedema	3 (38)	0	8 (22)	0
Fatigue	3 (38)	0	6 (17)	0
AST increased	5 (63)	1 (13)	12 (33)	0
ALT increased	2 (25)	0	4 (11)	0
Myalgia	0	0	5 (14)	0
Arthralgia	2 (25)	0	2 (6)	0
Face oedema	0	0	0	0
Headache	3 (38)	0	10 (28)	0
Lipase increased	1 (13)	0	4 (11)	0
Oedema peripheral	1 (13)	0	5 (14)	0
Pruritus	1 (13)	0	3 (8)	0
Amylase increased	1 (13)	1 (13)	5 (14)	0
Diarrhoea	1 (13)	1 (13)	2 (6)	0
Generalised oedema	2 (25)	0	0	0
Hypertension	0	0	1 (3)	0
Nausea	2 (25)	0	8 (22)	0
Constipation	1 (13)	0	2 (6)	0
Parosmia	0	0	1 (3)	0
Rash macular	0	0	0	0
Rash maculopapular	0	0	5 (14)	0
Asthenia	1 (13)	3 (9)	6 (17)	0

^aTEAEs cutoff of >15% based on all grades for total phase 1 and phase 2 cohort A.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; TEAE, treatment-emergent adverse event.

Table 3. Dose modifications due to any TEAEs

	Phase 1		Phase 2
	Cohort 5 (n = 8)	All patients (n = 32)	Cohort A (n = 36)
Any TEAEs leading to dose modification, n (%)	5 (63)	19 (59)	10 (28)
Dose interruption	5 (63)	18 (56)	9 (25)
Dose reduction	4 (50)	13 (41) ^a	3 (8) ^b
Treatment discontinuation	1 (13)	2 (6) ^c	1 (3) ^d

^aCohort 5: Gr3 urticaria (n = 1), Gr3 diarrhoea (n = 1), Gr2 AST increase (n = 1), Gr3 amylase, Gr3 CPK, and Gr3 LDH increased (n = 1); Cohort 8: Gr2 fatigue, Gr2 edema peripheral, and Gr2 rash maculopapular (n = 1), Gr2 rash macular (n = 1), Gr2 joint swelling and Gr1 pyrexia (n = 1), Gr3 CPK increased and Gr2 myalgia (n = 1), Gr3 pruritic rash (n = 1); Cohort 9: Gr1 generalised oedema and Gr1 periorbital oedema (n = 1), Gr1 rash maculopapular (n = 1), Gr3 AST increased (n = 1).
^bCohort A: Gr1 periorbital oedema and Gr1 rash maculopapular (n = 1); Gr1 headache (n = 1), Gr2 headache, Gr2 nausea, and Gr2 vomiting (n = 1).
^cCohort 5: Gr3 metabolic encephalopathy (n = 1); Cohort 8: Gr3 AST increase (DLT, n = 1); Gr1 periorbital oedema and Gr1 rash maculopapular (n = 1).
AST, aspartate aminotransferase; CPK, creatine phosphokinase; DLT, dose-limiting toxicity; Gr, Grade; LDH, lactate dehydrogenase; TEAE, treatment-emergent adverse event.

Table 4. Best overall response in patients with TGCT

	Phase 1 ^a		Phase 2 ^a
	Cohort 5 (n = 8) ^b	All patients (n = 32) ^b	Cohort A (n = 19)
Best overall response, n (%)			
Complete response	1 (13)	1 (3)	0
Partial response	3 (38)	15 (47)	8 (42)
Stable disease	4 (50)	16 (50)	11 (58)
ORR, %	4 (50)	16 (50)	8 (42)

^aOf the 51 efficacy-evaluable patients in phase 1 across all dose cohorts and phase 2 cohort A, 24 patients had a response resulting in an ORR of 47%.
^b1 patient had a local assessment for efficacy, but no central assessment was performed.
ORR, objective response rate; QD, once daily.

SAFETY

- Majority of the common (≥15%) TEAEs were ≤Grade 2 (Table 2)
- Observed transaminase, pancreatic, and CPK enzyme elevations were mostly low grade and not associated with symptoms; are consistent with the mechanism of action of CSF1R inhibitors
- No abnormalities in bilirubin levels reported
- In phase 1, 2 patients had TEAEs leading to treatment discontinuation (Table 3) and 2 patients had treatment-related grade 3 serious AEs (SAE): metabolic encephalopathy (possibly related) and vaginal hemorrhage (probably related)
- In phase 2 Cohort A, 1 patient had a TEAE leading to treatment discontinuation (Table 3) and no treatment-related SAEs were reported

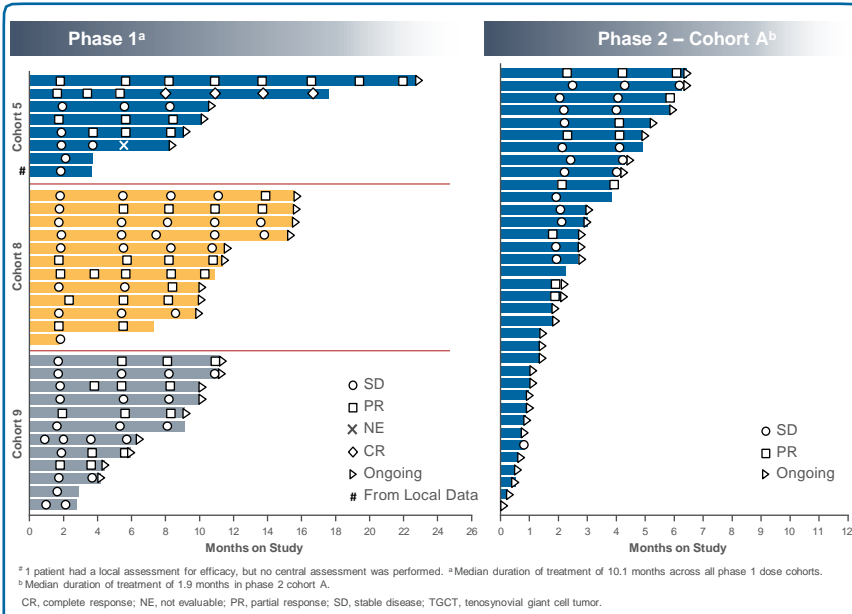
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- Phase 1: ORR of 50%; responses observed across all dose cohorts (Table 4, Figure 2, Figure 3)
- Phase 2 Cohort A: ORR of 42% (all partial responses; Table 4, Figure 2, Figure 3)

CONCLUSIONS

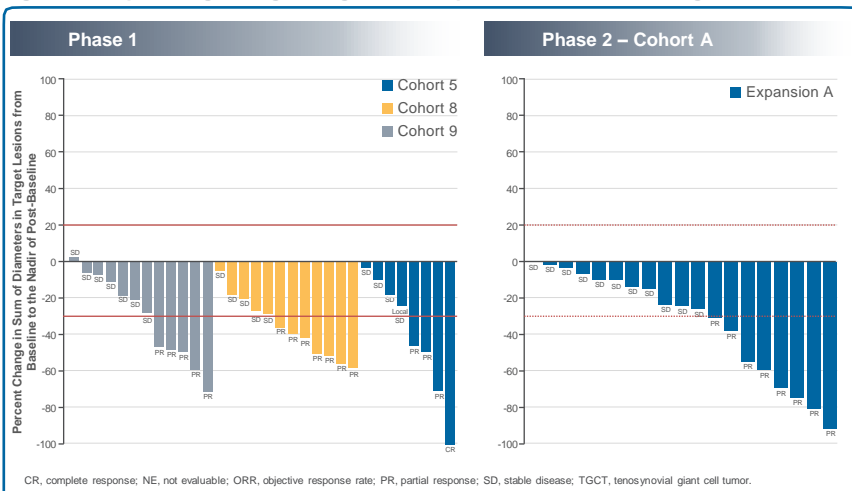
- In patients with TGCT not amenable to surgical resection,
 - Vimseltinib was well tolerated in both phase 1 and phase 2 Cohort A. The safety profile remains manageable with longer-term follow-up across all phase 1 dose cohorts
 - Vimseltinib demonstrated encouraging preliminary efficacy
 - Of the 32 patients in phase 1, ORR of 50% with durable responses observed across all dose cohorts, including 1 complete response in Cohort 5
 - Of the 36 patients enrolled in phase 2 Cohort A, 19 patients were evaluable for efficacy and had an ORR of 42%. Of the 19 patients, 10 had >1 follow-up imaging assessment and 2 responses occurred at later scans. The study is ongoing and follow-up evaluation is continuing
- These results support further evaluation of vimseltinib in the MOTION study, a randomized, placebo-controlled, phase 3 trial in patients with TGCT not amenable to surgical resection

Figure 2. Duration of treatment and response in patients with TGCT receiving vimseltinib



^a1 patient had a local assessment for efficacy, but no central assessment was performed. ^bMedian duration of treatment of 10.1 months across all phase 1 dose cohorts.
^cMedian duration of treatment of 1.9 months in phase 2 cohort A.
CR, complete response; NE, not evaluable; PR, partial response; SD, stable disease; TGCT, tenosynovial giant cell tumor.

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



CR, complete response; NE, not evaluable; ORR, objective response rate; PR, partial response; SD, stable disease; TGCT, tenosynovial giant cell tumor.

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