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


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## INTRODUCTION

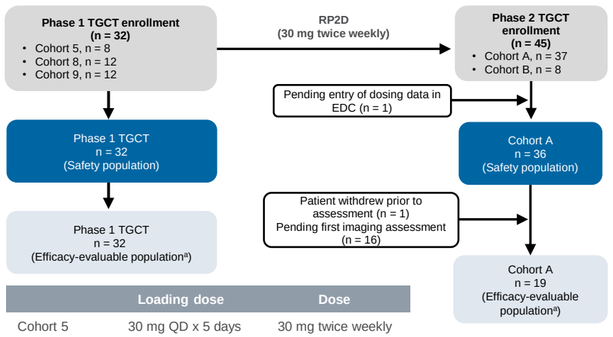
- Tenosynovial giant cell tumor (TGCT) is a rare, locally aggressive neoplasm, where overexpression of colony-stimulating factor 1 (CSF1) drives recruitment of macrophages leading to local inflammation and joint destruction[1,2]
- Patients with TGCT experience debilitating symptoms and significant disease 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




| | Loading dose | Dose |
|---|---|---|
| Cohort 5 | 30 mg QD x 5 days | 30 mg twice weekly |
| Cohort 8 | 30 mg QD x 3 days | 10 mg QD |
| Cohort 9 | 20 mg QD x 3 days | 6 mg QD |
| Phase 2 | NA | 30 mg twice weekly |

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

Data cutoff **7 June 2021**

ClinicalTrials.gov: NCT03069469

- 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) |
| Lacnotuzumab (MCS-110) | 1 (3) | 0 |

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

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

| | Phase 1 | | | | Phase 2 | |
|---|---|---|---|---|---|---|
| | Cohort 5 (n = 8) | | All Patients[a] (n = 32) | | Cohort A[a] (n = 36) | |
| Preferred term, No. (%) | All grades | Grade 3/4 | All grades | Grade 3/4 | All grades | Grade 3/4 |
| **Blood CPK increased** | 7 (88) | 4 (50) | 20 (63) | 10 (31) | 19 (53) | 9 (25) |
| **Periorbital oedema** | 3 (38) | 0 | 17 (53) | 0 | 8 (22) | 0 |
| **Fatigue** | 3 (38) | 0 | 15 (47) | 0 | 6 (17) | 0 |
| **AST increased** | 5 (63) | 1 (13) | 14 (44) | 4 (13) | 12 (33) | 0 |
| **ALT increased** | 2 (25) | 0 | 10 (31) | 1 (3) | 4 (11) | 0 |
| **Myalgia** | 0 | 0 | 9 (28) | 1 (3) | 5 (14) | 0 |
| **Arthralgia** | 2 (25) | 0 | 8 (25) | 1 (3) | 2 (6) | 0 |
| **Face oedema** | 0 | 0 | 8 (25) | 0 | 0 | 0 |
| **Headache** | 3 (38) | 0 | 8 (25) | 0 | 10 (28) | 0 |
| **Lipase increased** | 1 (13) | 0 | 8 (25) | 3 (9) | 4 (11) | 0 |
| **Oedema peripheral** | 1 (13) | 0 | 8 (25) | 0 | 5 (14) | 0 |
| **Pruritus** | 1 (13) | 0 | 8 (25) | 0 | 3 (8) | 0 |
| **Amylase increased** | 1 (13) | 1 (13) | 7 (22) | 2 (6) | 5 (14) | 0 |
| **Diarrhoea** | 1 (13) | 1 (13) | 6 (19) | 1 (3) | 2 (6) | 0 |
| **Generalised oedema** | 2 (25) | 0 | 6 (19) | 0 | 0 | 0 |
| **Hypertension** | 0 | 0 | 6 (19) | 2 (6) | 1 (3) | 0 |
| **Nausea** | 2 (25) | 0 | 6 (19) | 0 | 8 (22) | 0 |
| **Constipation** | 1 (13) | 0 | 5 (16) | 0 | 2 (6) | 0 |
| **Paresthesia** | 0 | 0 | 5 (16) | 0 | 1 (3) | 0 |
| **Rash macular** | 0 | 0 | 5 (16) | 0 | 0 | 0 |
| **Rash maculopapular** | 0 | 0 | 5 (16) | 0 | 5 (14) | 0 |
| **Asthenia** | 1 (13) | 0 | 3 (9) | 0 | 6 (17) | 0 |

[a] TEAEs 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] |

[a] Cohort 5: Gr3 uricaria (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 (n = 1), Gr3 CPK increased and Gr2 myalgia (n = 1), Gr3 pruritic rash (n = 1); Cohort 9: Gr1 generalized oedema and Gr1 periorbital oedema (n = 1), Gr1 rash maculopapular (n = 1), Gr3 AST increased (n = 1).
[b] Cohort A: Gr1 periorbital oedema and Gr1 rash maculopapular (n = 1); Gr1 headache (n = 1), Gr2 headache, Gr2 nausea, and Gr2 vomiting (n = 1).
[c] Cohort 5: Gr3 metabolic encephalopathy (n = 1); Cohort 8: Gr3 AST increase (DLT, n = 1). [d] 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) |

[a] Of 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%.
[b] 1 patient had a local assessment for efficacy, but no central assessment was performed.
ORR, objective response rate; QD, once daily.

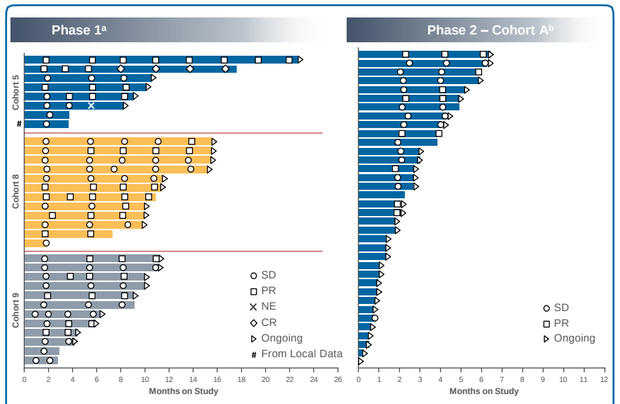
## SAFETY

- 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

## EFFICACY

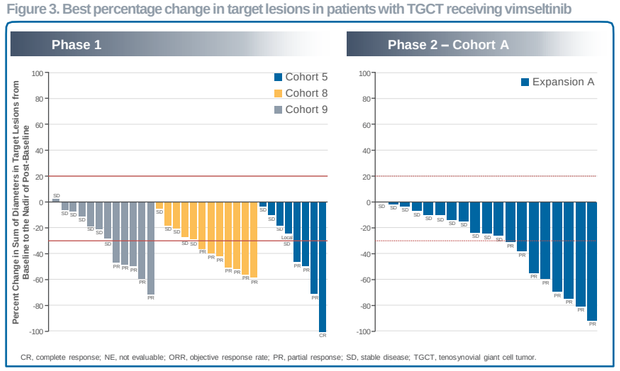
- Phase 1: ORR of 50%; responses observed across all dose cohorts (**Table 4, Figure 2, Figure 3**)
- Phase 2 Cohort A: ORR of 42% (all partial responses; **Table 4, Figure 2, Figure 3**)

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




[a] 1 patient had a local assessment for efficacy, but no central assessment was performed. [a] Median duration of treatment of 10.1 months across all phase 1 dose cohorts.
[b] Median 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.

## 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

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### References

**1)** Staals EL, et al. *Eur J Cancer*. 2016;63:34-40; **2)** West RB, et al. *Proc Natl Acad Sci USA*. 2006;103:690-695; **3)** Smith BD, et al. *Mol Cancer Ther*. 2021 Aug 25. doi:10.1158/1535-7163.MCT-21-0361.


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