# SAFETY AND EFFICACY UPDATES FROM A PHASE 1 STUDY OF VIMSELTINIB IN PATIENTS WITH TENOSYNOVIAL GIANT CELL TUMOR

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2023 ctos® ANNUAL MEETING

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# CONFLICT OF INTEREST

- Hans Gelderblom reports institutional research funding from Daiichi Sankyo; Deciphera Pharmaceuticals, LLC; Ipsen; and Novartis



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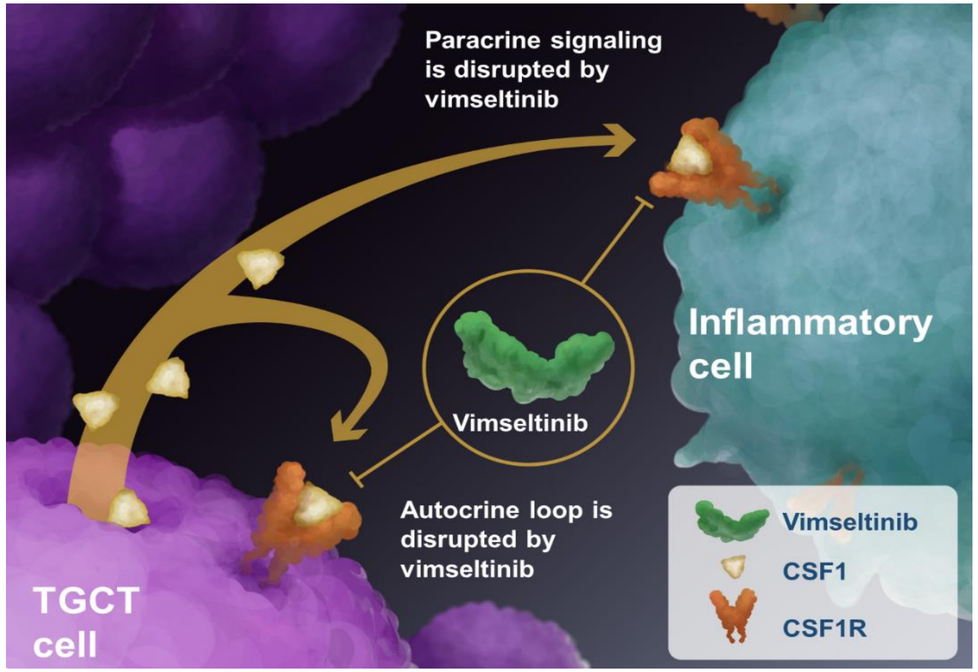
# INTRODUCTION

- TGCT is a rare, locally aggressive neoplasm caused by aberrant expression of the *CSF1* gene[1]
- There is only 1 systemic agent approved by the US Food and Drug Administration for the treatment of patients with TGCT not amenable to surgery, and none by the European Commission or other regulatory agencies, leaving an unmet need for an effective, CSF1R-targeted therapy with a favorable safety profile[2]
- Vimseltinib is an investigational, oral switch-control tyrosine kinase inhibitor specifically designed to selectively and potently inhibit CSF1R[1]

**Objective:**
To report the long-term safety and efficacy of vimseltinib in patients with TGCT not amenable to surgery from the phase 1 dose-escalation part of a phase 1/2 study




1) Smith BD, et al. *Mol Cancer Ther.* 2021;20:2098-109. 2) Pexidartinib (TURALIO®). Prescribing information. Daiichi Sankyo, Inc.; 2022.
CSF1, colony-stimulating factor 1; CSF1R, CSF1 receptor; TGCT, tenosynovial giant cell tumor.

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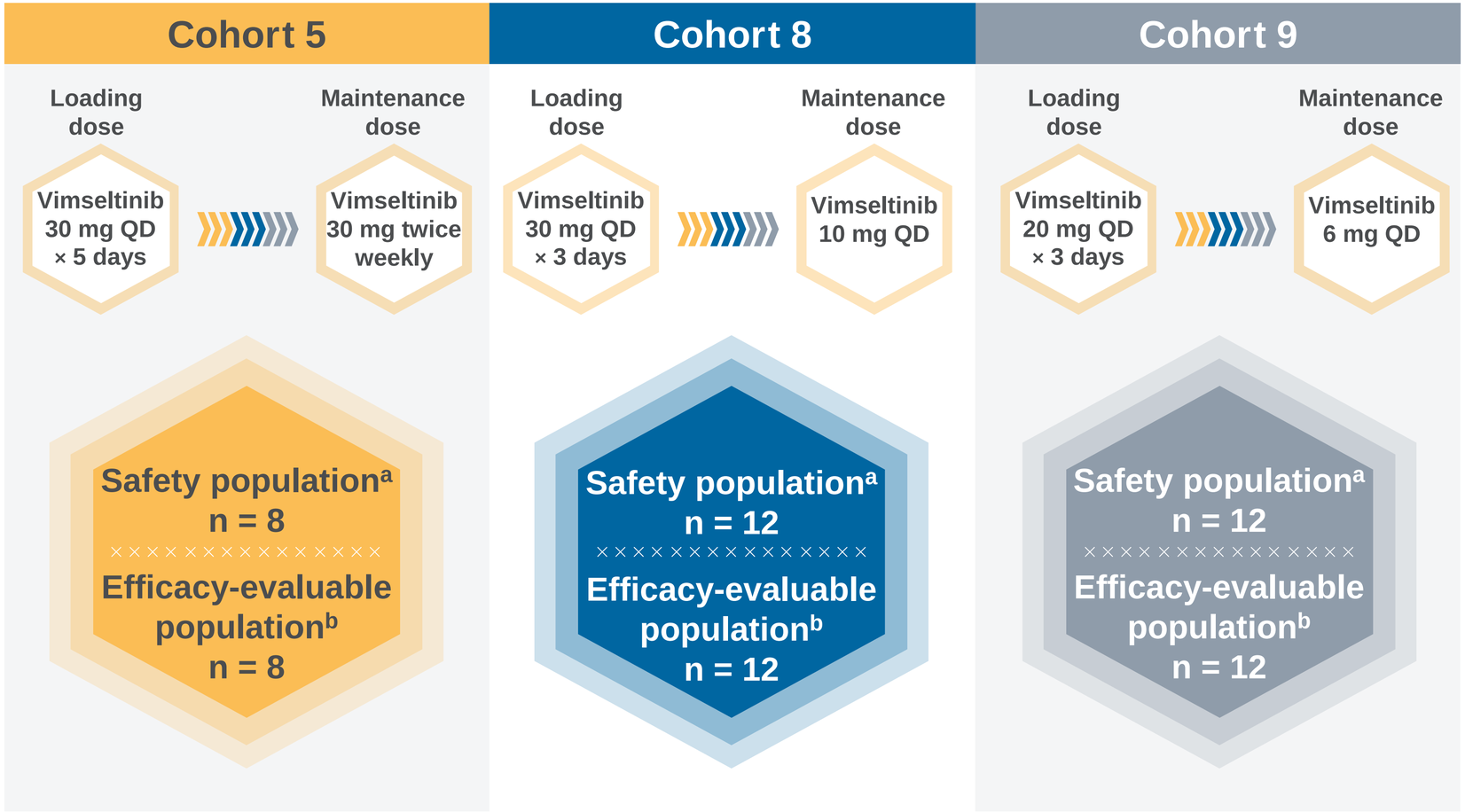
# METHODS AND STUDY DESIGN




- This first-in-human phase 1 trial was designed to evaluate the safety and tolerability, as well as to determine the RP2D of vimseltinib (NCT03069469)
- Three TGCT-specific cohorts were evaluated in the trial
  - RP2D was determined to be 30 mg twice weekly (no loading dose)
- Antitumor activity was evaluated by IRR using RECIST v1.1

**Data cutoff**
**June 27, 2023**

[a]Includes patients who received at least one dose of the study drug. [b]Patients with ≥1 post-baseline imaging assessment, obtained via IRR or local imaging; one patient (cohort 5) had a local assessment for efficacy, but no IRR was performed.
IRR, independent radiological review; QD, once daily; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; RP2D, recommended phase 2 dose; TGCT, tenosynovial giant cell tumor.

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# BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

| | Cohort 5 (n = 8) | Cohort 8 (n = 12) | Cohort 9 (n = 12) | Total (N = 32) |
|---|---|---|---|---|
| **Age, median (min, max), years** | 44 (23, 66) | 50 (24, 73) | 52 (29, 73) | 51 (23, 73) |
| **Sex** | | | | |
| Female | 3 (38) | 7 (58) | 7 (58) | 17 (53) |
| Male | 5 (63) | 5 (42) | 5 (42) | 15 (47) |
| **Race** | | | | |
| White | 8 (100) | 12 (100) | 11 (92) | 31 (97) |
| Asian | 0 | 0 | 1 (8) | 1 (3) |
| **Disease location** | | | | |
| Knee | 5 (63) | 9 (75) | 6 (50) | 20 (63) |
| Ankle | 0 | 2 (17) | 3 (25) | 5 (16) |
| Hip | 2 (25) | 1 (8) | 1 (8) | 4 (13) |
| Wrist | 1 (13) | 0 | 1 (8) | 2 (6) |
| Foot | 0 | 0 | 1 (8) | 1 (3) |
| **Patients with ≥1 prior surgery** | 7 (88) | 3 (25) | 3 (25) | 13 (41) |
| 1 prior surgery | 4 (50) | 2 (17) | 1 (8) | 7 (22) |
| 2–3 prior surgeries | 2 (25) | 1 (8) | 1 (8) | 4 (13) |
| ≥4 prior surgeries | 1 (13) | 0 | 1 (8) | 2 (6) |
| **Patients with ≥1 prior systemic therapy**[a] | 0 | 4 (33) | 1 (8) | 5 (16) |
| TKI | 0 | 3 (25) | 1 (8) | 4 (13) |
| Monoclonal antibody | 0 | 1 (8) | 0 | 1 (3) |

- As of June 27, 2023, 32 patients with TGCT were enrolled
- The most common disease location was the knee (20 patients, 63%)

Data shown as n (%) unless otherwise noted. The safety population includes patients who received ≥1 dose of the study drug. Data cutoff: June 27, 2023. First patient in: February 2019.
[a]TKIs included imatinib and nilotinib; monoclonal antibody included lacnotuzumab (MCS-110).
max, maximum; min, minimum; TGCT, tenosynovial giant cell tumor; TKI, tyrosine kinase inhibitor.



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# TEAEs IN ≥15% OF TOTAL PATIENTS

| | Cohort 5 (n = 8) | | Cohort 8 (n = 12) | | Cohort 9 (n = 12) | | Total (N = 32) | |
|---|---|---|---|---|---|---|---|---|
| **Preferred term, n (%)** | All grades | Grade 3/4 | All grades | Grade 3/4 | All grades | Grade 3/4 | All grades | Grade 3/4 |
| Blood CPK increased | 7 (88) | 4 (50) | 8 (67) | 4 (33) | 6 (50) | 2 (17) | 21 (66) | 10 (31) |
| Periorbital edema[a] | 3 (38) | 0 | 10 (83) | 0 | 6 (50) | 0 | 19 (59) | 0 |
| Fatigue[a] | 3 (38) | 0 | 6 (50) | 0 | 7 (58) | 0 | 16 (50) | 0 |
| AST increased | 5 (63) | 1 (13) | 4 (33) | 2 (17) | 2 (17) | 1 (8) | 11 (34) | 4 (13) |
| Arthralgia[a] | 3 (38) | 0 | 3 (25) | 0 | 5 (42) | 1 (8) | 11 (34) | 1 (3) |
| COVID-19 | 1 (13) | 0 | 4 (33) | 0 | 5 (42) | 0 | 10 (31) | 0 |
| Face edema[a] | 1 (13) | 0 | 6 (50) | 0 | 3 (25) | 0 | 10 (31) | 0 |
| Pruritus[a] | 1 (13) | 0 | 4 (33) | 0 | 4 (33) | 0 | 9 (28) | 0 |
| Myalgia[a] | 0 | 0 | 5 (42) | 1 (8) | 4 (33) | 0 | 9 (28) | 1 (3) |
| Edema peripheral[a] | 1 (13) | 0 | 5 (42) | 0 | 3 (25) | 0 | 9 (28) | 0 |
| Headache[a] | 3 (38) | 0 | 3 (25) | 0 | 2 (17) | 0 | 8 (25) | 0 |
| Lipase increased | 1 (13) | 0 | 5 (42) | 3 (25) | 1 (8) | 0 | 7 (22) | 3 (9) |
| Diarrhea | 1 (13) | 1 (13) | 4 (33) | 0 | 2 (17) | 0 | 7 (22) | 1 (3) |
| ALT increased | 2 (25) | 0 | 3 (25) | 0 | 2 (17) | 1 (8) | 7 (22) | 1 (3) |
| Generalized edema[a] | 2 (25) | 0 | 2 (17) | 0 | 2 (17) | 0 | 6 (19) | 0 |
| Nausea[a] | 2 (25) | 0 | 3 (25) | 0 | 1 (8) | 0 | 6 (19) | 0 |
| Constipation | 1 (13) | 0 | 1 (8) | 0 | 4 (33) | 0 | 6 (19) | 0 |
| Rash[a] | 1 (13) | 0 | 2 (17) | 0 | 3 (25) | 0 | 6 (19) | 0 |
| Hypertension | 0 | 0 | 3 (25) | 2 (17) | 3 (25) | 0 | 6 (19) | 2 (6) |
| Amylase increased | 1 (13) | 1 (13) | 4 (33) | 1 (8) | 0 | 0 | 5 (16) | 2 (6) |
| Paresthesia[a] | 0 | 0 | 5 (42) | 0 | 0 | 0 | 5 (16) | 0 |
| Dry skin[a] | 1 (13) | 0 | 2 (17) | 0 | 2 (17) | 0 | 5 (16) | 0 |
| Rash maculopapular[a] | 0 | 0 | 4 (33) | 0 | 1 (8) | 0 | 5 (16) | 0 |

- The majority of common (≥15%) TEAEs were low grade
- Grade 3/4 TEAEs in >5% of patients included increases in blood CPK, AST, lipase, amylase, and hypertension
  - Grade 3/4 AST, lipase, and amylase elevations were not associated with pancreatitis or liver damage
  - Both patients with grade 3/4 hypertension had a prior history of hypertension
- Enzyme elevations were consistent with the known mechanism of action of CSF1R inhibitors
- No evidence of cholestatic hepatotoxicity
- No new treatment-related SAEs were reported since the previous data cutoff date
  - Treatment-related SAEs of grade 3 metabolic encephalopathy (n = 1; possibly related) and grade 3 vaginal hemorrhage (n = 1; probably related) were previously reported[1]

The safety population includes patients who received ≥1 dose of the study drug. Severity was assessed by the investigator according to the toxicity grade described in the NCI-CTCAE v4.03 (grade 1 [mild] to grade 5 [death]).
Data cutoff: June 27, 2023.
[a]Denotes terms that do not have a specified grade 4 category in the NCI-CTCAE v4.03.
1. Gelderblom et al. Poster presented at ESMO 2022: September 9–13, 2022; Paris, France. FPN 475P.
AST, aspartate aminotransferase; ALT, alanine aminotransferase; COVID-19, coronavirus disease 19; CPK, creatine phosophokinase; CSF1R, CSF1 receptor; NCI-CTCAE v4.03, National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03; SAE, serious adverse event; TEAE, treatment-emergent adverse event.



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# DOSE MODIFICATIONS DUE TO ANY TEAEs

| | Cohort 5 (n = 8) | Cohort 8 (n = 12) | Cohort 9 (n = 12) | Total (N = 32) |
|---|---|---|---|---|
| **TEAEs leading to dose modification, n (%)** | 6 (75) | 11 (92) | 8 (67) | 25 (78) |
| Dose interruption | 6 (75) | 10 (83) | 8 (67) | 24 (75) |
| Dose reduction | 5 (63) | 9 (75) | 6 (50) | 20 (63) |
| Treatment discontinuation | 1 (13)[a] | 1 (8)[b] | 0 | 2 (6) |

- Overall, 17 (53%) patients discontinued the study treatment for any reason
  - Only 2 patients discontinued due to an AE
  - Other reasons for treatment discontinuation included withdrawal by patient (n = 10), physician decision (n = 3), and progressive disease (per RECIST v1.1 by local read[c], n = 2)

The safety population includes patients who received ≥1 dose of the study drug. Data cutoff: June 27, 2023.
Dose modification groups are not mutually exclusive.
[a]G3 metabolic encephalopathy (SAE, possibly related). [b]G3 AST increase (DLT). [c]No patients progressed as assessed per RECIST v1.1 by IRR.
AE, adverse event; AST, aspartate aminotransferase; CPK, creatine phosphokinase; DLT, dose-limited toxicity; G, grade; IRR, independent radiological review; LDH, lactate dehydrogenase; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SAE, serious adverse event; TEAE, treatment-emergent adverse event.



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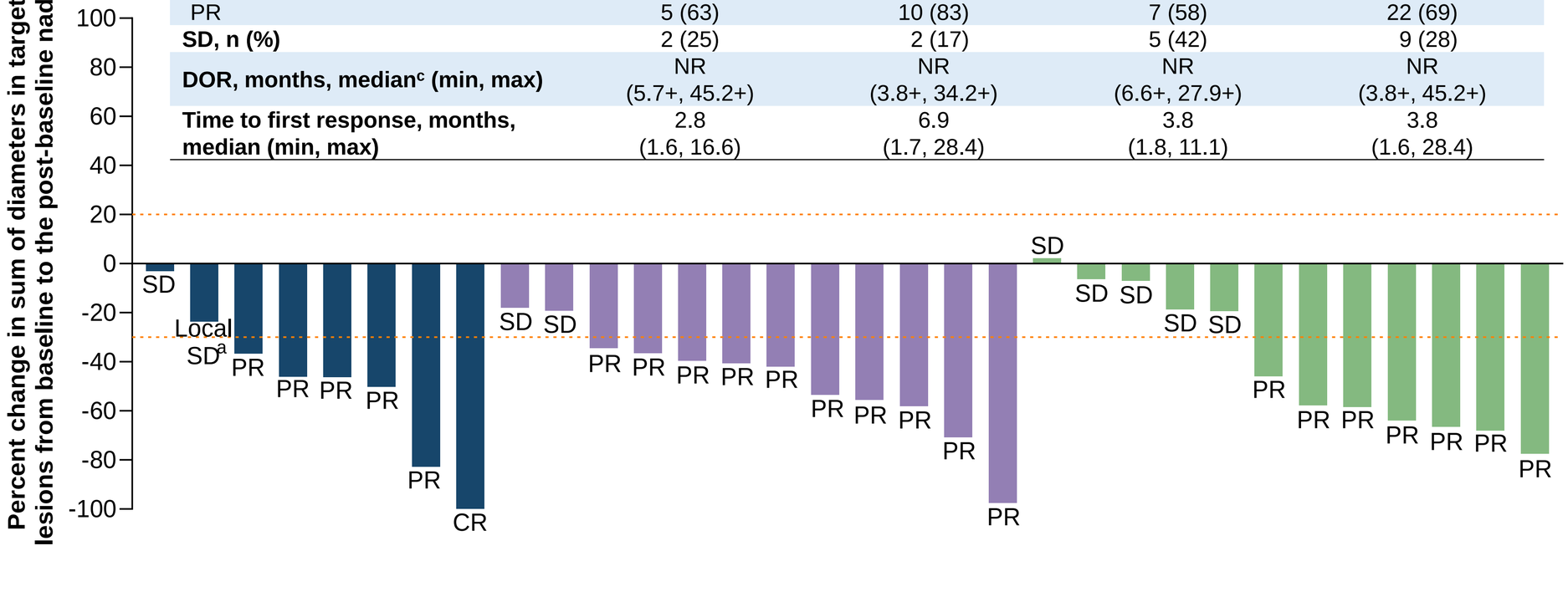
# BEST OVERALL RESPONSE ASSESSED USING RECIST v1.1 BY IRR

| | Cohort 5 (n = 8)[a] | Cohort 8 (n = 12) | Cohort 9 (n = 12) | Total (N = 32) |
|---|---|---|---|---|
| **ORR[b], n (%)** | 6 (75) | 10 (83) | 7 (58) | 23 (72) |
| CR | 1 (13) | 0 | 0 | 1 (3) |
| PR | 5 (63) | 10 (83) | 7 (58) | 22 (69) |
| **SD, n (%)** | 2 (25) | 2 (17) | 5 (42) | 9 (28) |
| **DOR, months, median[c] (min, max)** | NR (5.7+, 45.2+) | NR (3.8+, 34.2+) | NR (6.6+, 27.9+) | NR (3.8+, 45.2+) |
| **Time to first response, months, median (min, max)** | 2.8 (1.6, 16.6) | 6.9 (1.7, 28.4) | 3.8 (1.8, 11.1) | 3.8 (1.6, 28.4) |




- Vimseltinib demonstrated robust antitumor activity with an ORR of 72% (23/32 patients) across all cohorts
  - The ORR at 6 months was 47% across all cohorts (15/32 patients)

Data cutoff: June 27, 2023.

+ denotes that response is ongoing at last assessment. The dotted line at 20% represents the threshold for progressive disease; the dotted line at −30% represents the threshold for PR.

[a]One patient had a local assessment for efficacy but will never have IRR data. This patient has been included in the SD assessment (cohort 5). [b]Best overall response of target lesions assessed using RECIST v1.1 by IRR; includes all available follow-ups. [c]Based on the Kaplan-Meier estimate. DOR is defined as the time from the first imaging results showing response to progressive disease.

CR, complete response; DOR, duration of response; IRR, independent radiological review; max, maximum; min, minimum; NR, not reached; ORR, objective response rate; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.



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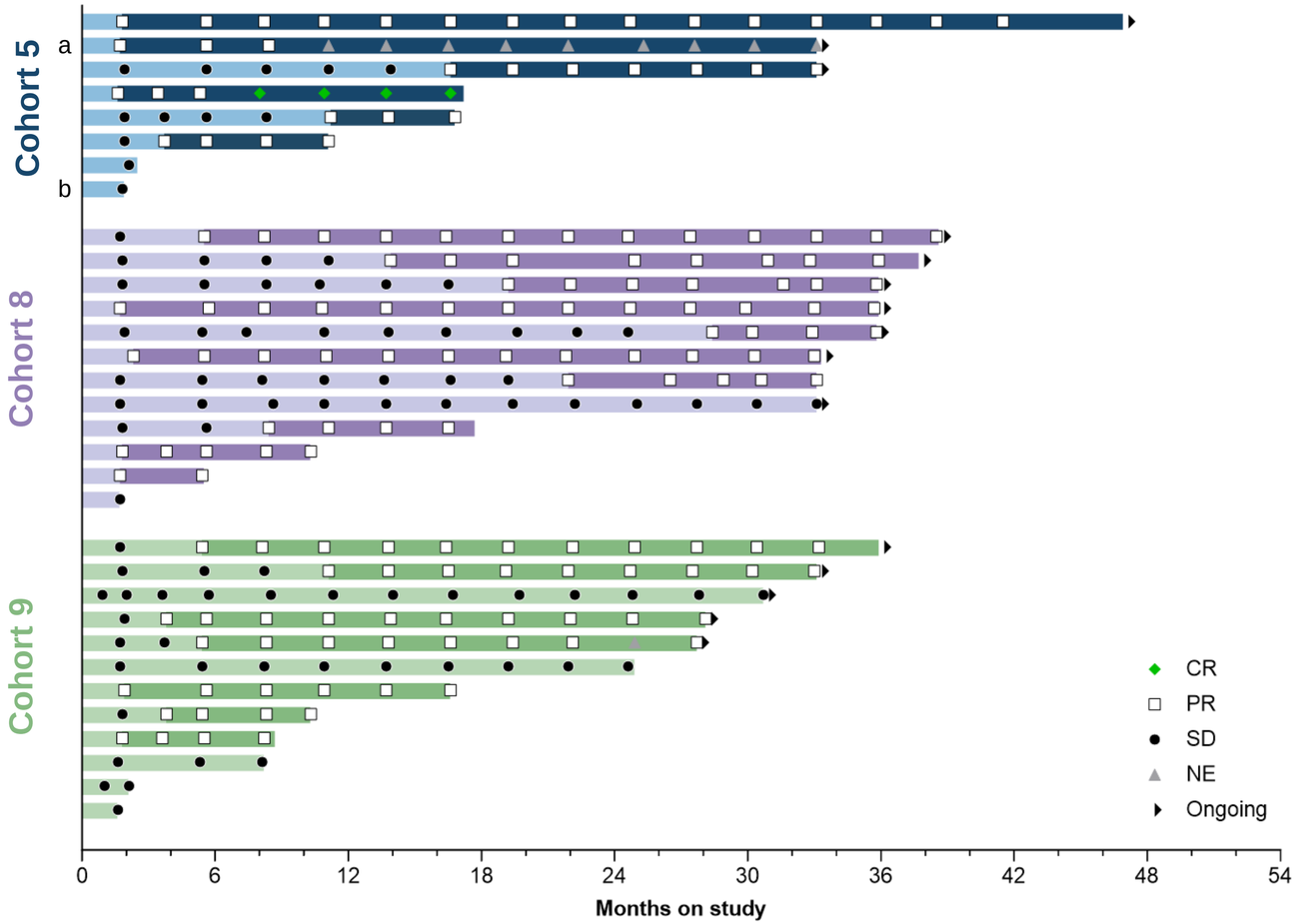
# DURATION OF TREATMENT AND RESPONSE




- The median treatment duration was 25.1 months (range, 0.7–46.9 months; mean, 21.8 months)
- Fifteen (47%) patients remain on treatment and have received vimseltinib for 2 or more years, with the longest time on treatment being approximately 4 years at the time of data cutoff
- Responses (n = 23) were durable and were observed before and after 6 months, demonstrating continued clinical benefit with prolonged treatment
  - By 6 months: 15/23
  - By 12 months: 18/23
  - By 24 months: 22/23
  - By 36 months: 23/23

Response was analyzed using RECIST v1.1 by IRR; includes all available follow-up visits. Dark shading represents the duration of response. Data cutoff: June 27, 2023.
[a]One patient had metallic artifacts at baseline; as the tumor reduced, metallic artifacts prevented accurate tumor measurements by IRR, resulting in NE assessments beyond 10 months in the study (cohort 5).
[b]One patient had a local assessment for efficacy but will never have IRR data. This patient has been included in the SD assessment (Cohort 5).
CR, complete response; IRR, independent radiological review; NE, not evaluable; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

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# CONCLUSIONS

- Vimseltinib demonstrated long-term tolerability and a manageable safety profile in patients with TGCT not amenable to surgery, which remained consistent with longer follow-up
  - Only 2 patients discontinued treatment due to AEs, and no new treatment-related SAEs were observed
- Nearly 50% of patients were on treatment for more than 2 years at the time of this analysis, with the longest time on treatment being approximately 4 years
- Vimseltinib demonstrated robust antitumor activity with an ORR of 72% across all cohorts
  - The ORR at 6 months was 47% and additional responses occurred after 6 months, demonstrating continued clinical benefit with prolonged treatment
  - No patients progressed on treatment, as assessed by IRR
- Vimseltinib could fulfill the unmet need for an effective systemic therapy with a favorable safety profile for patients with TGCT not amenable to surgery
- These results support continued evaluation of vimseltinib in the ongoing phase 2 part of this study (NCT03069469) and in the phase 3 MOTION trial (NCT05059262)

AE, adverse event; IRR, independent radiological review; ORR, objective response rate; SAE, serious AE; TGCT, tenosynovial giant cell tumor.



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