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.
• 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 (GDC-341) is an investigational, orally selective, switch-controlled kinase inhibitor of CSF1 receptor (CSF1R).
• 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 is an ongoing, multicenter, open-label study of vimseltinib in patients with advanced tenosynovial and TGCT consistent of 2 phases:
  - Phase I (dose escalation) study, a pharmacologically guided 3 + 3 design, to determine the maximum tolerated dose (MTD) and the maximum recommended dose (MRD).
  - Phase II (expansion) study to evaluate the safety, tolerability, and preliminary efficacy in ≥2 TGCT patient cohorts.
• Phase I patient cohorts:
  - Cohort A: TGCT patients with no prior anti-CSF1R/GSK2338496 therapy (previous therapy with mitotane or rituximab allowed).
  - Cohort B: TGCT patients with prior anti-CSF1R/GSK2338496 therapy (previous therapy with mitotane or rituximab not allowed).
• Phase II TGCT patient cohorts:
  - Cohort 1: TGCT patients with ≥1 prior resection or relapse, no prior anti-CSF1R/GSK2338496 therapy (previous therapy with mitotane or rituximab allowed).
  - Cohort 2: TGCT patients with ≥1 prior resection or relapse, prior anti-CSF1R/GSK2338496 therapy (previous therapy with mitotane or rituximab not allowed).

RESULTS

• Of the 32 patients in Phase 1, ORR of 50% with durable responses observed across all dose cohorts, including 1 complete response.
• The target enrollment of 40 patients in Phase 2 cohort A has been reached as of 13 July 2021.
• Vimseltinib was well tolerated in both phase 1 and phase 2 Cohort A. The safety profile remains manageable with longer follow-up.

SAFETY

• Grade 3/4 TEAEs in ≥15% of patients with TGCT receiving vimseltinib:
  - Nausea
  - Diarrhoea
  - Oral ulcers
  - Generalised oedema
  - Gr2 rash maculopapular
  - Gr3 CPK increased and Gr2 AST increased
• Dose reductions were made for 6 (19%) patients with TGCT receiving vimseltinib.

EFFICACY

• Best overall response in patients with TGCT:
  - CR, complete response; NE, not evaluable; PR, partial response; SD, stable disease; TGCT, tenosynovial giant cell tumor.
  - Table 3: Dose modifications due to any TEAEa

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 follow-up across all phase 1 dose cohorts.
  - Vimseltinib demonstrated encouraging preliminary efficacy.
• Of the 32 patients in phase 1, 20 in phase 2, with 14% 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 timepoints. 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.

*Please note this is the corrected version of the poster that is published on the ESMO website.

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ePoster

Table 1. Baseline characteristics of patients with TGCT receiving vimseltinib

| Stage | Age, median (range), years | Sex | Race | Prior‡ | History of prior treatment with CSF1R inhibitor or anti-CSF1R/GSK2338496 therapy | Prior‡ | Grade 3/4 TEAEs | Prior CSF1R inhibitor or anti-CSF1R/GSK2338496
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<td>56 (20 - 77)</td>
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Table 2. TEAEs in ≥10% of patients with TGCT receiving vimseltinib

Table 3. Dose modifications due to any TEAEa

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<td>Any TEAEs leading to dose modification</td>
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<td>9 (30)</td>
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<tr>
<td>Dose escalation</td>
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<td>9 (30)</td>
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<td>Dose reduction</td>
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<tr>
<td>Treatment discontinuation</td>
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