TIP-09

A Phase 2 Study Evaluating the Efficacy and Safety of Safusidenib in Grade 2 or 3 Isocitrate Dehydrogenase 1 (*IDH1*)-Mutant Glioma After Disease Progression on Vorasidenib

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Background

- *IDH*-mutant gliomas are a distinct category of adult-type diffuse glioma per WHO CNS 2021 criteria[1]
- The standard-of-care treatment is maximal safe resection; in patients with Grade 2 and some patients with Grade 3 *IDH1*-mutant glioma, surgery may be followed by treatment with vorasidenib (an IDH1/2 inhibitor)[2–6]
  - Although vorasidenib has been shown to improve PFS and time to next intervention compared with placebo in the Phase 3 INDIGO trial, patients eventually experience PD[7]
  - Treatment options for recurrent glioma are generally limited to re-resection or RT/CT,[8] which can be associated with substantial, long-term detrimental impacts for patients[9]
  - There is, therefore, an unmet need for effective targeted therapies that continue to delay PD and the need for RT/CT after PD on vorasidenib

Rationale

- Safusidenib is an investigational mutant-IDH1 inhibitor with high potency, selectivity, and blood-brain barrier permeability,[10] that has recently been granted fast track designation by the US FDA for treatment of *IDH1*-mutant glioma[11]
  - Safusidenib demonstrated encouraging clinical activity and a favorable risk-benefit profile in patients with *IDH1*-mutant glioma in Phase 1 (NCT03030066) and Phase 2 (NCT04458272) studies, including responses across histological grades and risk groups[12,13]
  - Safusidenib has also demonstrated encouraging clinical activity in patients with RT/CT-naïve *IDH1*-mutant glioma in the Phase 2 study (**Table 1**)[11,13]
  - Safusidenib remains active in models resistant to ivosidenib,[14] supporting sequential IDH inhibition as a potential treatment strategy; in addition, safusidenib binds mutant IDH1 differently compared with vorasidenib and may work through a distinct mechanism of action[10,15]
  - Together, these findings support further evaluation of safusidenib for patients who experience PD on vorasidenib

Study Aim

- This ongoing, Phase 2, multicenter study (NCT07703436) is evaluating the **efficacy and safety** of **safusidenib** in patients with **Grade 2 or 3 *IDH1*-mutant glioma** who experienced PD following vorasidenib treatment and do not require immediate RT/CT[16]

Table 1. Phase 2, Open-Label Study of Safusidenib in Patients With RT/CT-Naïve Grade 2 *IDH1*-Mutant Glioma (NCT04458272)[11]

Endpoint	N=27
Confirmed ORR, %	51.9
Median PFS, months	NR
36-month PFS rate, %	79.1

Median PFS follow-up: 38.8 months

See poster CTNI-11 at this meeting for updated data from this Phase 2 study

Study Design (NCT07703436)

Key Eligibility Criteria

Inclusion Criteria

- Histologically confirmed Grade 2 or 3 *IDH1*-mutant glioma, per WHO CNS 2021 criteria[1]
- Age ≥18 years
- KPS ≥60
- ≥1 surgery for glioma
- Prior vorasidenib treatment discontinued due to radiographic PD during treatment, confirmed by BICR
- Measurable disease per modified RANO 2.0, confirmed by BICR
- Not in need of immediate RT/CT

Exclusion Criteria

- Vorasidenib discontinued due to toxicity or any reason other than radiographic PD
- Prior treatment for glioma with anti-angiogenic or investigational agents
- Other prior anticancer therapy for glioma except surgery

Treatment

Patients with Grade 2 or 3 ***IDH1*-mutant glioma** who have discontinued vorasidenib due to PD **(N≈40)**

Open Label

Safusidenib
250 mg PO BID

28-day continuous cycles until PD or discontinuation

Study Endpoints

Primary Endpoint

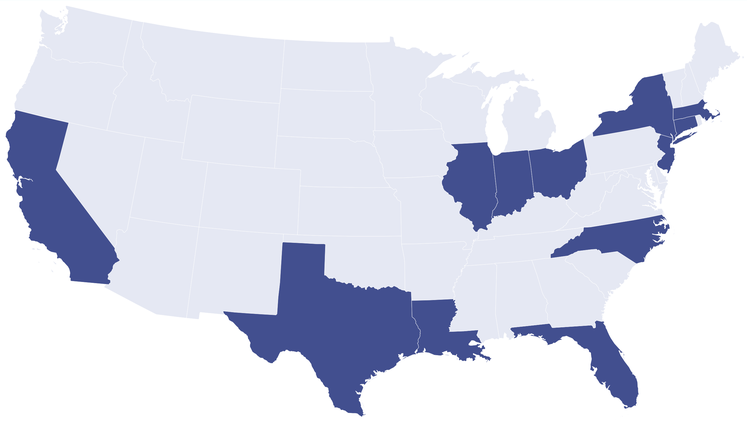
- ORR per modified RANO 2.0 by BICR

Secondary Endpoints

- ORR per modified RANO 2.0 by INV
- Volumetric tumor growth rate by BICR
- Duration of response[a]
- Time to response[a]
- PFS[a]
- Time to next intervention
- Overall survival
- Safety
- Seizure activity

[a]BICR and investigator assessed, per modified RANO 2.0.

Trial Progress



- This Phase 2, multicenter study (NCT07703436) is ongoing, with 18 US sites selected as of October 2026

Summary

- For patients with Grade 2 or 3 *IDH1*-mutant glioma who experience PD on vorasidenib, there is an unmet need for effective targeted therapies that continue to delay the need for RT/CT
- Safusidenib is an investigational mutant-IDH1 inhibitor with high potency, selectivity, and blood-brain barrier permeability that has shown encouraging efficacy in patients with *IDH1*-mutant glioma[10,12,13]
- This ongoing, Phase 2, multicenter study (NCT07703436) is evaluating the efficacy and safety of safusidenib in patients with Grade 2 or 3 *IDH1*-mutant glioma who experienced PD following vorasidenib treatment

Abbreviations

BICR, blinded independent central review; BID, twice daily; CNS, central nervous system; CT, chemotherapy; FDA, Food and Drug Administration; IDH1/2, isocitrate dehydrogenase 1/2; INV, investigator; KPS, Karnofsky Performance Status; NR, not reached; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PO, orally; RANO, Response Assessment in Neuro-Oncology; RT, radiotherapy; WHO, World Health Organization; US, United States.

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