CTNI-66

# IDH-mutant glioma patients treated with vorasidenib: Ongoing data from the vorasidenib expanded access program

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## PLAIN LANGUAGE SUMMARY

### What is an expanded access program (EAP)?

- An EAP allows people to access an investigational treatment outside of clinical trials and before regulatory approval.
- EAPs are most commonly offered for rare diseases or in cancer where treatment options are unavailable or not tolerated or for severe or life-threatening diseases.
- EAPs may be started once an appropriate dose has been established and there is enough evidence of benefit to justify the use of an investigational drug outside of clinical trials.

### Who has access to the EAP?

- Servier started the EAP for oral vorasidenib (VOR) in November 2022 so people in the United States with mutations in the metabolic enzymes isocitrate dehydrogenase 1 or 2 (mIDH1/2) glioma could access this treatment.
  - The FDA approved VOR in August 2024 for certain types of mIDH glioma.
  - Servier designed the EAP along with medical experts, bioethicists, and patients to ensure the program was inclusive.
- The EAP was available to people with mIDH1/2 glioma who are not eligible for other VOR clinical trials and who, in the opinion of their oncologist, may benefit from treatment.
- Following FDA approval in August 2024, enrollment in the EAP is closed and all current patients will transition out of the EAP.

### What are the results of the EAP?

- People taking VOR in the EAP have had similar side effects to people taking VOR in clinical trials.
  - Side effects are generally similar in type and severity.
  - No new significant safety issues have been seen.
- Although patient data are relatively diverse and new in the EAP, initial results are promising in patients with mIDH1/2 glioma.

### Where can I learn more about the EAP?

- You can find more information about the EAP online at https://clinicaltrials.gov/study/NCT05592743.

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## INTRODUCTION

- Gliomas are the most common malignant primary brain tumor found in adults.[1]
- In the United States, gliomas associated with mutations in the genes encoding the metabolic enzymes isocitrate dehydrogenase 1 (mIDH1) or 2 (mIDH2) comprise at least 18% of adult-type diffuse gliomas.[1]
- Active surveillance is a recommended option for patients with grade 2 gliomas with no measurable tumor or for whom immediate chemoradiotherapy is not preferred.[2,3]
- Chemoradiotherapy is the standard care for postoperative treatment of patients with mIDH grade 3/high-risk grade 2 gliomas, but it is not curative and is associated with radiation-induced neurocognitive dysfunction and DNA hypermutation.[3,4]
- There is an unmet need for therapies in this period to postpone the use of radiation therapy and chemotherapy and preserve quality of life.[3]
- Vorasidenib (VOR) is an oral, brain-penetrant dual inhibitor of mIDH1/2 demonstrating clinical efficacy and safety in patients with mIDH1/2 glioma in the phase 3 INDIGO study (NCT04164901).[5]
  - The FDA approved VOR in August 2024 for patients >12 years old with grade 2 astrocytoma or oligodendroglioma with susceptible mIDH1/2 following surgery, including biopsy, subtotal resection, or gross total resection.[6]
- Servier launched an expanded access program (EAP) in November 2022 to provide access to VOR for patients with mIDH1/2 glioma; following FDA approval in August 2024, enrollment is closed, and all current patients will transition out of the EAP.

## AIM

- In November 2022, Servier launched an EAP (NCT05592743) designed to provide access to VOR for patients in the US with mIDH1/2 glioma.
- We present baseline characteristics, safety, and treatment duration data of patients treated in this EAP as of June 2024.

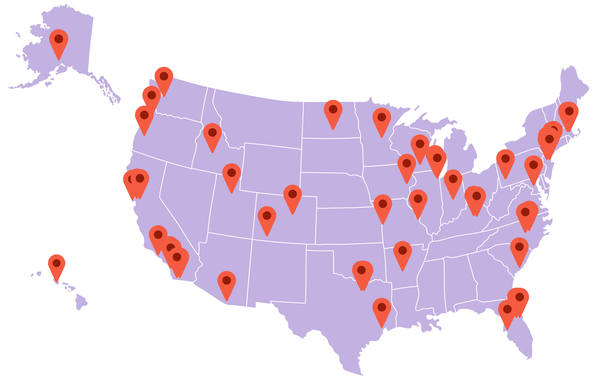
## METHODS

- Key inclusion criteria: aged ≥12 years with mIDH1/2 glioma and, in the opinion of the treating oncologist, would potentially benefit from treatment with VOR.
  - At least one prior surgery for glioma (including biopsy), adequate bone marrow function, hepatic function, and renal function.
- Patients receive either VOR 40 mg orally (PO) once daily (QD) (>40 kg) or 20 mg PO QD (<40 kg).
  - Dosing is initiated at Cycle 1, Day 1 with 28-day treatment cycles, with VOR dosing assessed at each treatment cycle to determine if any dose adjustments are warranted.
  - Safety assessments occur every 2 weeks for the first two 28-day cycles, then monthly for the duration of treatment.
- Measures of interest include frequency and severity of adverse events of special interest (AESIs) and serious adverse events (SAEs), safety laboratory tests, disease and seizure assessment, duration of treatment, and time from surgery to VOR initiation.

## RESULTS

- As of the June 30, 2024 data cutoff, there are 110 participants with mIDH1/2 glioma from 51 sites enrolled in the EAP who have received at least one dose of VOR (**Figure 1**).

### Figure 1. Enrolled sites

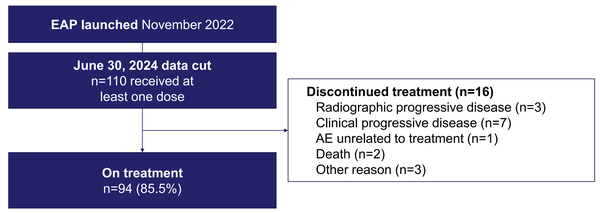


- Patient demographics and baseline characteristics are summarized in **Table 1**.
  - Mean (SD) age was 42.1 (14.7) years; 60 (54.5%) were male; 57 (51.8%) with astrocytoma; and 81 (73.6%) had an IDH1 mutation.
  - The majority of participants had grade 2 gliomas (n=84 [76.4%]) and non-contrast–enhancing disease (n=82 [74.5%]).

**PATIENT DISPOSITION**

- Median duration of treatment was 115 (grade 2), 127 (grade 3), and 121.5 (grade 4) days; overall median (range) duration of treatment was 115 (3–514) days.
- As of the data cutoff, 94 (85.5%) participants remain on treatment, with the majority initiating treatment within the past 6 months (n=77 [70.0%]).
  - 16 (11.2%) participants have discontinued treatment due to: radiographic progressive disease (n=3); clinical progressive disease (n=7); adverse event (AE) unrelated to treatment (n=1); death (n=2); or other reason (n=3).
  - Three participants have died (disease progression, n=2; unrelated infection, n=1) (**Figure 2**).

### Figure 2. Disposition



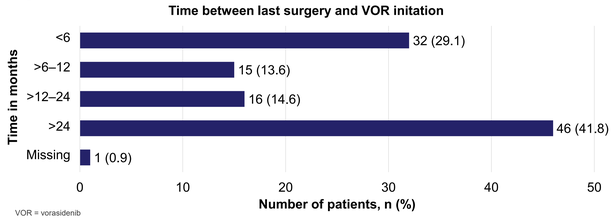

AE = adverse event; EAP = expanded access program

### Table 1. Patient demographics and baseline characteristics

| | EAP patients (N=110) |
|---|---|
| **Age in years, mean (SD)** | 42.1 (14.7) |
| **Sex, n (%)** | |
| Male | 60 (54.5) |
| Female | 50 (45.5) |
| **Race, n (%)** | |
| White | 84 (76.4) |
| Asian | 5 (4.5) |
| Native Hawaiian or other Pacific Islander | 3 (2.7) |
| Black or African American | 2 (1.8) |
| American Indian or Alaska Native | 1 (0.9) |
| Other | 1 (0.9) |
| Unknown/not reported | 14 (12.7) |
| **Ethnicity, n (%)** | |
| Hispanic | 10 (9.1) |
| Non-Hispanic | 60 (54.5) |
| Unknown/not reported | 40 (36.4) |
| **IDH mutation type, n (%)** | |
| 1 | 81 (73.6) |
| 2 | 28 (25.5) |
| Both | 1 (0.9) |
| **Grade reported at screening, n (%)** | |
| 2 | 84 (76.4) |
| 3 | 19 (17.3) |
| 4 | 7 (6.4) |
| **Prior treatment, n (%)** | |
| RT only | 1 (0.9) |
| RT/chemotherapy | 35 (31.8) |
| Chemotherapy only | 8 (7.3) |
| None | 66 (60.0) |
| **Prior IDH inhibitor, n (%)** | |
| Ivosidenib | 28 (25.5) |
| Enasidenib | 3 (2.7) |
| Vorasidenib | 2 (1.8) |
| None | 77 (70.0) |
| **Last surgery, n (%)** | |
| Biopsy | 17 (15.5) |
| Gross total resection | 41 (37.3) |
| Subtotal resection | 52 (47.3) |
| **Histological subtype, n (%)** | |
| Astrocytoma | 57 (51.8) |
| Oligodendroglioma | 53 (48.2) |

EAP = expanded access program; IDH = isocitrate dehydrogenase; RT = radiotherapy

### Figure 3. Time between last surgery and VOR initiation




VOR = vorasidenib

**SAFETY**

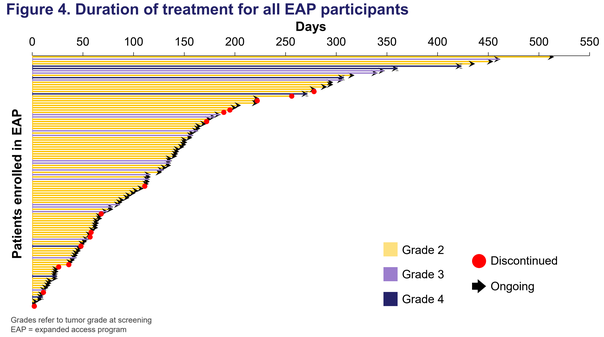
- At least one AE of any grade was seen in 38 (26.6%) participants (**Table 2**).
- 12 (8.4%) patients had AESIs (defined as grade 2 or higher alanine aminotransferase/aspartate aminotransferase elevations).
- 5 (3.5%) patients had unrelated SAEs (as determined by the investigator).
- 17 (11.9%) patients had AEs that led to dose interruption and 7 (4.9%) patients had dose reduction.

### Table 2. Treatment-related AEs

| AEs | n (%) |
|---|---|
| Elevated LFTs G1 | 14 (10) |
| Low ANC | 3 (2) |
| Nausea G1 | 3 (2) |
| Fatigue G1 | 2 (1) |
| Headache | 1 (1) |
| Hyponatremia | 1 (1) |
| QTc prolongation | 1 (1) |
| Low CL | 1 (1) |
| Low Hgb | 1 (1) |
| Left lower back pain | 1 (1) |
| Low Na | 1 (1) |
| Vomiting | 1 (1) |

AE = adverse events; ANC = absolute neutrophil count; CL = chloride; Hgb = hemoglobin; LFT, liver function test; Na = sodium; QTc = corrected QT interval

### Figure 4. Duration of treatment for all EAP participants




Grades refer to tumor grade at screening
EAP = expanded access program

## CONCLUSIONS

- The safety profile of VOR in the EAP is comparable with the profile reported in clinical trials, and no new safety concerns have been identified.
- VOR was well tolerated in a heterogeneous population, including patients with grade 3 and 4 gliomas, as well as patients who received prior anti-cancer treatment.
- Data continue to mature and future publications will analyze efficacy.
- Enrollment in the EAP has closed post FDA approval (August 2024), and all current patients will transition out of the EAP.

**ACKNOWLEGMENTS**

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## DISCLOSURES

**TFC:** Katmai – cofounder, major stock holder, consultant, and board member; 501c3 Global Coalition for Adaptive Research – membership of the board and paid consultancy; Chimerix – stockholder, receiving milestone payments and possible future royalties; Erasca – stockholder; Break Through Cancer and Cure Brain Cancer Foundation – membership of the scientific advisory boards; AbbVie, Agios, Amgen, Bayer, Boehringer Ingelheim, Boston, BrainStorm, Bristol Myers Squibb, Celgene, Clinical Care Options, Cortice, Deciphera, DNAtrix, Eli Lilly and Company, Gan & Lee, Genocea, GW, Human Longevity, Ideology Health, Immvira, Inovio, Insys, Jubilant, Karyopharm, Katmai, Kintara, Kiyatec, Medefield, Medqia Trizel, Merrimack, Merck, Novartis, Novocure, Novogen, Notable Labs, Odonate Therapeutics QED, Pascal, Pfizer, ProNai, Puma, Roche, Sagimet, Sapience, SDP, Servier, Sunovion, Tocagen, Tyme, VBI, VBL, Vigeo, and Wellcome Trust – providing paid consulting services; AbbVie, Agios, Amgen, AstraZeneca, Beigene, Boston, Bristol Myers Squibb, Decipherea, DNAtrix, Karyopharm, Kazia, Merck, Novartis, Oncoceutics, Orbus, Tocagen, and UCLA for the Brain Tumor Program with Oncovir – providing paid consulting services; the Regents of the University of California (TFC's employer) – licensed intellectual property co-invented by TFC to Katmai. **KBP:** AbbVie, Servier – consultant/advisor and research funding; Bayer, Boehringer Ingelheim, Eisai – consultant/advisor; BioMimetix, Bristol Myers Squibb, Novocure – research funding. **HC:** Best Doctors/Teladoc, Orbus, PPD, Chimerix, ArriHeart, Alpha Biopharma, Sumitomo Pharma Oncology, Novartis, Servier – advisory board/consultant; Orbus, GCAR, Bayer, CNS Pharma, Sumitomo Dainippon Pharma Oncology, Samus, Erasca, ArriHeart, Novartis – research funding (site PI/institutional contract). **JWT:** Bristol Myers Squibb, Navio, AbbVie – principal investigator, data collection and analysis, manuscript preparation for clinical trials within past 5 years. **IKM:** Puma, Servier, Voyager – consultant/advisor and travel expenses; Amgen, Eli Lilly and Company, General Electric – research funding; AstraZeneca – travel expenses; Black Diamond, Debiopharm – consultant/advisor; Roche – honoraria and travel expenses. **HAS:** Advanced Accelerator Applications – scientific advisory board; AbbVie – received institutional research funding (to MGH). **CC, JD:** Servier – employment. **PYW:** AstraZeneca, Bayer, Servier, Vascular Biogenics, VBI Vaccines – consultant/advisor and research funding; AbbVie, BeiGene, Celgene, Kazia, Lilly, MediciNova, Merck, Novartis, Oncoceutics, Puma – research funding; Blue Earth Diagnostics, Decipherea, Elevate Bio, Immunomonic, Imvax, Integral Health, Karyopharm, Kayatec, Puma, QED, Taiho, Tocagen, Voyager – consultant/advisor; Merck – speakers' bureau and research funding; Prime Oncology – speakers' bureau and research funding.

Audio/video narration

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