Explore updated outcomes from the INDIGO extended analysis, including tumor growth rate and seizure activity

In patients with Grade 2 m*IDH1/2* astrocytoma or oligodendroglioma

# HALT PROGRESSION WITH PRECISION


## See VORANIGO® extended analysis results from the INDIGO trial—

6 months additional data for progression-free survival (PFS), tumor growth rate (TGR), and seizure activity[1,2,a]

## Major efficacy outcome: Progression-free survival (PFS)

**61% reduced risk of disease progression or death in the primary analysis** compared to placebo (HR=0.39; 95% CI, 0.27-0.56; *P*<0.0001).[1]

**65%** **reduced risk of disease progression or death vs placebo in the extended analysis[2]**

**HR=0.35 (95% CI, 0.25-0.49)**

**Median PFS was not reached for VORANIGO (95% CI, 22.1-NE) vs** 11.4 months for placebo (95% CI, 11.1-13.9).

[a]The extended analysis includes an additional 6 months of data from the primary analysis data cutoff date of September 6, 2022, to the date of unblinding on March 7, 2023.[2]
HR, hazard ratio; mIDH, mutant isocitrate dehydrogenase; NE, not estimable.

## INDICATION

VORANIGO (40 mg tablets) is indicated for the treatment of adult and pediatric patients 12 years and older with Grade 2 astrocytoma or oligodendroglioma with a susceptible isocitrate dehydrogenase-1 (IDH1) or isocitrate dehydrogenase-2 (IDH2) mutation, as detected by an FDA-approved test, following surgery including biopsy, sub-total resection, or gross total resection.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

**Hepatotoxicity**: VORANIGO can cause hepatic transaminase elevations, which can lead to hepatic failure, hepatic necrosis, and autoimmune hepatitis. Monitor liver laboratory tests (AST, ALT, GGT, total bilirubin, and alkaline phosphatase) prior to the start of VORANIGO, every 2 weeks during the first 2 months of treatment, then monthly for the first 2 years of treatment, and as clinically indicated, with more frequent testing in patients who develop transaminase elevations. Reduce the dose, withhold, or permanently discontinue VORANIGO based on severity.

**Please see additional Important Safety Information throughout and accompanying Full Prescribing Information.**

Voranigo®
vorasidenib tablets

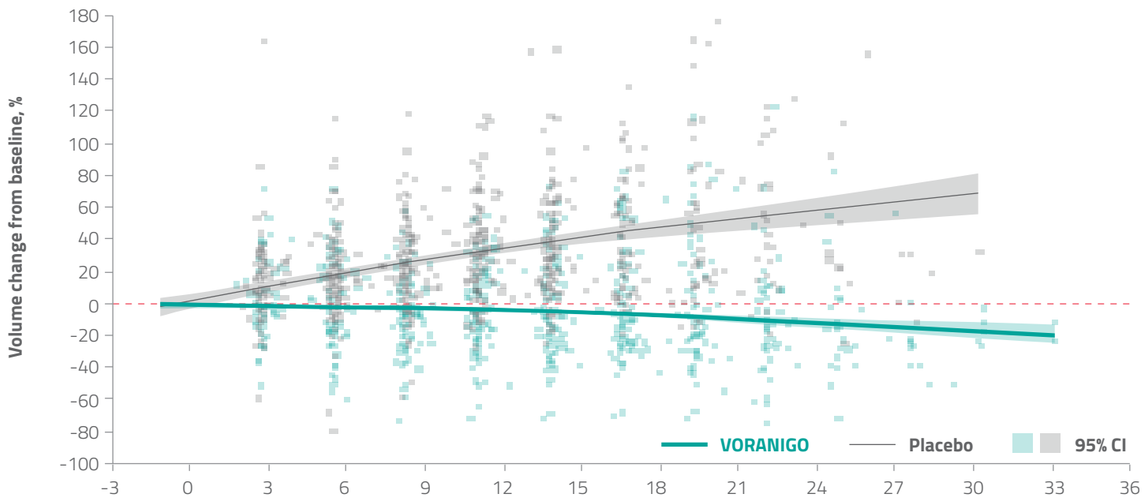
# Secondary outcome: Tumor growth rate (TGR)[2]

## In the extended analysis, TGR in the VORANIGO® arm was -1.3% vs 14.4% in the placebo arm

**Percent change in tumor volume every 6 months[a,b]**

| | **VORANIGO** (n=167) | **Placebo** (n=161) |
|---|---|---|
| Tumor growth rate per BIRC | **-1.3%** (95% CI, -3.2 to 0.7) | **14.4%** (95% CI, 12.0 to 16.8) |
| Difference between slopes | **15.9%** (95% CI, 12.6 to 19.3) | |

**On-treatment TGR[c]**




**Number of patients with tumor volume assessments:**

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **VORANIGO** | 167 | 149 | 154 | 144 | 138 | 128 | 91 | 70 | 46 | 25 | 13 | 6 | 2 |
| **Placebo** | 163 | 148 | 154 | 139 | 122 | 96 | 61 | 42 | 25 | 9 | 4 | 1 | |

The TGR endpoint has not been validated and the clinical significance of the changes observed is not known. This outcome was not controlled for multiplicity.

[a]n was the number of patients who had at least one volume record during the corresponding period.
[b]The table depicts the TGR estimated from the linear mixed effect model, for which the treatment group, time, treatment group by time interaction, log of tumor volume at baseline, and codeletion randomization stratification stratum are fixed effects. Tumor volume was measured per BIRC using modified RANO-LGG criteria at baseline and after randomization following a schedule of tumor assessments.
[c]The figure shows the percent change of volume from baseline plotted against time from randomization based on nonparametric LOESS regression.
BIRC, blinded independent review committee; LOESS, locally estimated scatterplot smoothing.

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS (cont'd)

**Embryo-Fetal Toxicity:** Based on findings from animal studies, VORANIGO can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective nonhormonal contraception during treatment with VORANIGO and for 3 months after the last dose, since VORANIGO can render some hormonal contraceptives ineffective. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with VORANIGO and for 3 months after the last dose.

# Exploratory outcome: Seizure activity—subgroup analysis in patients who reported ≥1 on-treatment seizure[2,d,e]

**In the INDIGO trial, investigators reported seizure as an adverse event (AE) for all grades in 16% of patients treated with VORANIGO and 15% of patients treated with placebo[1]**

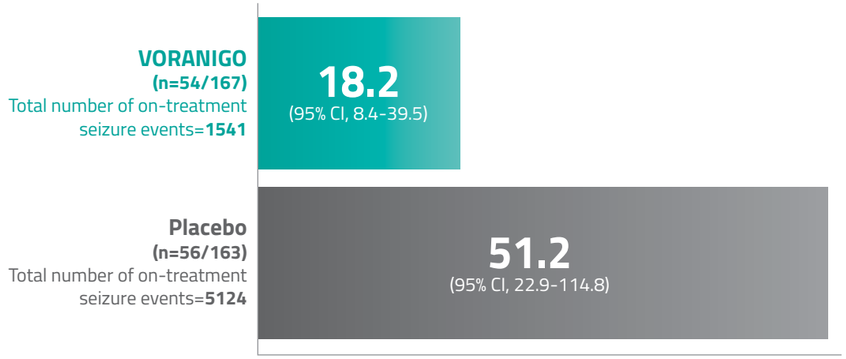
Seizure AEs were assessed and reported in the Prescribing Information if qualified as an AE.[3]

## Seizure activity was also assessed as an exploratory outcome[3]

**Data based on patient self-reported diary that captured the number and severity of seizures during each cycle[2]**

- Only patients with controlled seizures were included in the INDIGO trial[2,f]
- Antiseizure medication was prescribed at the investigator's discretion[2]

**Subgroup analysis in patients who reported at least 1 seizure while on treatment[2]**




**The seizure rate for VORANIGO was 64% lower compared to placebo[g]**

A rigorous statistical conclusion cannot be made because seizure activity was an exploratory outcome, and the results should be interpreted with caution. This outcome was not controlled for multiplicity.

[d]Grouped term includes partial seizures, generalized tonic-clonic seizure, epilepsy, clonic convulsion, and simple partial seizures.[1]
[e]On-treatment seizure activity was calculated using a negative binomial model, a commonly used statistical model in epilepsy evaluations. The model was adjusted by baseline seizure number and stratification factors (chromosome 1p/19q-codeletion status and tumor size at baseline).[2]
[f]Uncontrolled seizures were defined as persistent seizures interfering with activities of daily life and failed 3 lines of antiepileptic drug regimens including at least 1 combination regimen.[4]
[g]Ratio of rates for VORANIGO vs placebo was 0.36 (95% CI, 0.14-0.89).[2]

## IMPORTANT SAFETY INFORMATION (cont'd)

### ADVERSE REACTIONS

The most common (≥15%) adverse reactions included fatigue, headache, COVID-19, musculoskeletal pain, diarrhea, nausea, and seizure. Grade 3 or 4 (≥2%) laboratory abnormalities were ALT increased, AST increased, GGT increased, and neutrophils decreased.

### DRUG INTERACTIONS

Avoid concomitant use of VORANIGO with strong and moderate CYP1A2 inhibitors. Avoid concomitant use with moderate CYP1A2 inducers and smoking tobacco. Avoid concomitant use with CYP3A substrates, where a minimal concentration change can reduce efficacy. If concomitant use of hormonal contraception cannot be avoided, use nonhormonal contraception methods.

**Please see additional Important Safety Information throughout and accompanying Full Prescribing Information.**

Voranigo® vorasidenib tablets

For patients with Grade 2 m*IDH1/2* astrocytoma or oligodendroglioma

# Choose VORANIGO®, the only FDA-approved targeted therapy[1,5]

In the INDIGO pivotal trial, VORANIGO reduced the risk of disease progression or death by 61% compared to placebo (HR=0.39; 95% CI, 0.27-0.56; *P*<0.0001).[1]

**Look inside to see the VORANIGO extended analysis data including tumor growth rate and seizure activity results[2]**

**Safety profile[1]:**

- The most common (≥15%) adverse reactions in patients treated with VORANIGO were fatigue (37%), COVID-19 (33%), musculoskeletal pain (26%), diarrhea (25%), and seizure (16%)
- Grade 3 or 4 (≥2%) laboratory abnormalities were ALT increased (10%), AST increased (4.8%), GGT increased (3%), and neutrophil decreased (2.4%)
- Permanent discontinuation due to ARs occurred in 3.6% of patients treated with VORANIGO

Scan to visit **VoranigoHCP.com** to explore additional data, dosing and administration considerations, and patient support offerings.

ALT, alanine aminotransferase; AR, adverse reaction; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase.

## IMPORTANT SAFETY INFORMATION (cont'd)

### LACTATION

Advise women not to breastfeed during VORANIGO treatment and for 2 months after the last dose.

### IMPAIRED FERTILITY

VORANIGO may impair fertility of females and males of reproductive potential.

**References: 1.** Voranigo. Package insert. Servier Pharmaceuticals LLC; 2025. **2.** Mellinghoff IK, van den Bent MJ, Touat M, et al. A global, randomized, double-blinded, Phase 3 study of vorasidenib versus placebo in patients with adult-type diffuse glioma with an IDH1/2 mutation (INDIGO): UPDATED RESULTS. Presented at: Society for Neuro-Oncology Annual Meeting; November 21-24, 2024; Houston, TX. **3.** Data on file. Servier Pharmaceuticals LLC. **4.** Mellinghoff IK, van den Bent MJ, Blumenthal DT, et al. Vorasidenib in IDH1- or IDH2-mutant low-grade glioma. *N Engl J Med.* 2023;389(7):589-601. doi:10.1056/NEJMoa2304194 **5.** Ninatti G, Moresco RM, Sollini M. Molecular imaging of IDH-mutant gliomas in the new era of IDH inhibitors: preparing for future challenges. *Eur J Nucl Med Mol Imaging.* 2024;51(5):1421-1422. doi:10.1007/s00259-024-06591-3

**Please see additional Important Safety Information throughout and accompanying Full Prescribing Information.**

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