Explore the extended progression-free survival (PFS) analysis for VORANIGO®

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

HALT PROGRESSION WITH PRECISION

VORANIGO—Proven to significantly extend PFS[1,2]

Primary analysis: 61% reduced risk of disease progression or death vs placebo (HR=0.39; 95% CI, 0.27-0.56; *P*<0.0001).[1]

Extended analysis: 65% reduced risk of disease progression or death vs placebo (HR=0.35; 95% CI, 0.25-0.49).[2,a]

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; mIDH1/2, mutant isocitrate dehydrogenase-1 or mutant isocitrate dehydrogenase-2; 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 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

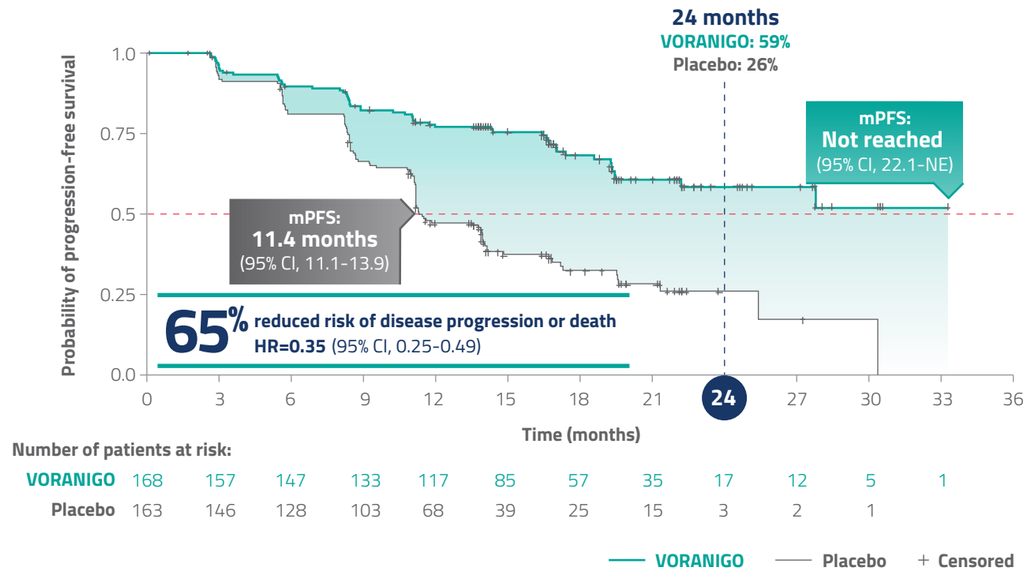
VORANIGO significantly extended PFS, giving patients with m*IDH* glioma more time without disease progression vs placebo[a,b]

Primary analysis: 61% reduced risk of disease progression or death with VORANIGO vs placebo (HR=0.39; 95% CI, 0.27-0.56; *P*<0.0001)[1]

Following the primary analysis data cutoff of September 6, 2022, the extended analysis includes 6 months of additional efficacy data.[2,c]

In the extended analysis, median PFS was not reached for VORANIGO vs 11.4 months with placebo[2]

Kaplan-Meier Curve for PFS per BIRC in the INDIGO trial: extended analysis



PFS in patients with m*IDH* glioma

Efficacy parameter	Primary analysis[1]		Extended analysis[2]	
	VORANIGO (n=168)	**Placebo** (n=163)	**VORANIGO** (n=168)	**Placebo** (n=163)
Number of events,[d] n (%)	47 (28)	88 (54)	54 (32)	104 (64)
HR (95% CI)	0.39 (0.27-0.56)		0.35 (0.25-0.49)	

The extended analysis for PFS was not controlled for multiplicity.

[a]VORANIGO was studied in the INDIGO trial—a phase 3, randomized (1:1), multicenter, double-blind, placebo-controlled trial for patients with Grade 2 m*IDH1/2* astrocytoma or oligodendroglioma (N=331).[1,3] Patients were aged ≥12 years, had prior surgery for glioma, presented with measurable, nonenhancing disease, and had not received prior anticancer treatment, including chemotherapy or radiotherapy.[1] Crossover from placebo to VORANIGO was permitted after documented radiographic disease progression. Patients were randomized to receive VORANIGO 40 mg orally once daily or placebo orally once daily until radiographic disease progression or unacceptable toxicity.

[b]The major efficacy outcome was PFS, evaluated by a BIRC per RANO-LGG criteria.[1] PFS is defined as the time from randomization to the date of the first documented disease progression or death due to any cause.[3] The RANO criteria for LGGs define progressive disease as either a radiographic disease response (a ≥25% increase in the sum of the products of perpendicular diameters of T2-weighted or T2-weighted fluid-attenuated inversion recovery hyperintense nonenhancing lesions), or the presence of a new lesion as a newly measurable or increased enhancement.

[c]The extended analysis includes an additional 6 months of data to the date of unblinding on March 7, 2023.[2]

[d]Number of events include progressive disease and death.[1]

BIRC, blinded independent review committee; mPFS, median PFS; RANO-LGG, Response Assessment in Neuro-Oncology for Low Grade Glioma.

VORANIGO is approved for patients (≥12 years) with Grade 2 m*IDH* glioma who have had prior surgery[1]

The patient criteria below illustrate types of appropriate patients for VORANIGO:

Age (years)	<12	12-39	>39	
Adult-type Diffuse Glioma Subtype	Oligodendroglioma (1p/19q-codeleted)	Astrocytoma	Glioblastoma	
IDH Status	*IDH1* mutated	*IDH2* mutated		
Surgery Status	No surgery	Biopsy only	Sub-total resection	Gross total resection
Prior Treatment	Surgery as only prior treatment	Surgery and prior treatment		
Time Since Surgery	0-11 months	>1 year		
Disease Status	Radiographically stable	Progressing		

Consistent with label

Not consistent with label

VORANIGO provides a targeted treatment option for many patient types across the Grade 2 m*IDH* glioma care continuum

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.

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.

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

Voranigo® vorasidenib tablets

Choose VORANIGO to help your patients with Grade 2 m*IDH* glioma halt progression

VORANIGO is the first FDA-approved treatment in >20 years for m*IDH* glioma

Proven to significantly extend PFS

- **Primary analysis:** 61% reduced risk of disease progression or death vs placebo (HR=0.39; 95% CI, 0.27-0.56; *P*<0.0001)[1]
- **Extended analysis:** 65% reduced risk of disease progression or death vs placebo (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 with placebo (95% CI, 11.1-13.9)[2]

Safety profile[1]

- The most common (≥15%) ARs were fatigue, COVID-19, musculoskeletal pain, diarrhea, and seizure
- 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

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Business card to be placed here

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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; 2024. **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.** 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

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