Explore updated outcomes from the INDIGO extended analysis published in *The Lancet Oncology*

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

Extended INDIGO data for VORANIGO®: PFS, tumor growth rate, and best percentage change in tumor volume

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]



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

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

The extended analysis[a] for PFS was not controlled for multiplicity.

See more VORANIGO results from the INDIGO trial

[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.

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

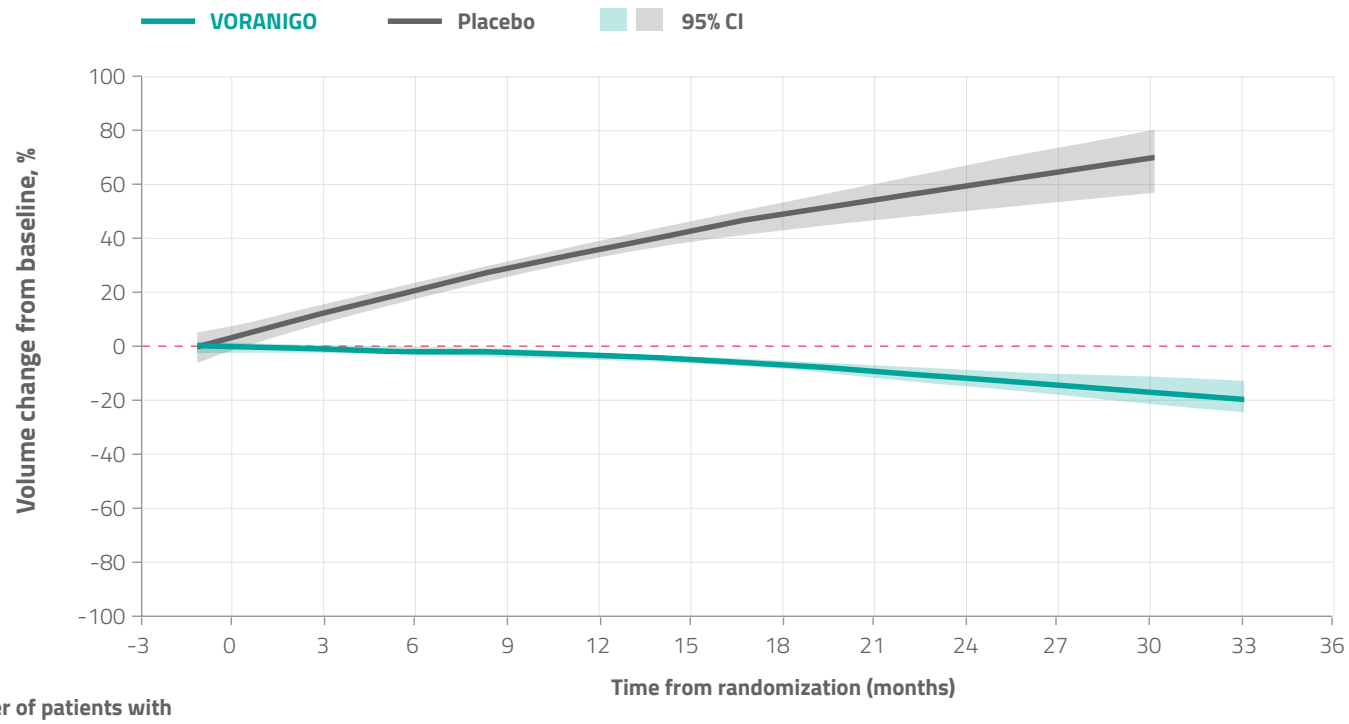
Secondary outcome: Tumor growth rate (TGR)[2]

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 (95% CI)	**-1.3%** (-3.2 to 0.7)	**14.4%** (12.0 to 16.8)
Difference between slopes	**15.9%** (95% CI, 12.6 to 19.3)	

Tumor volume change from baseline with VORANIGO vs placebo[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.

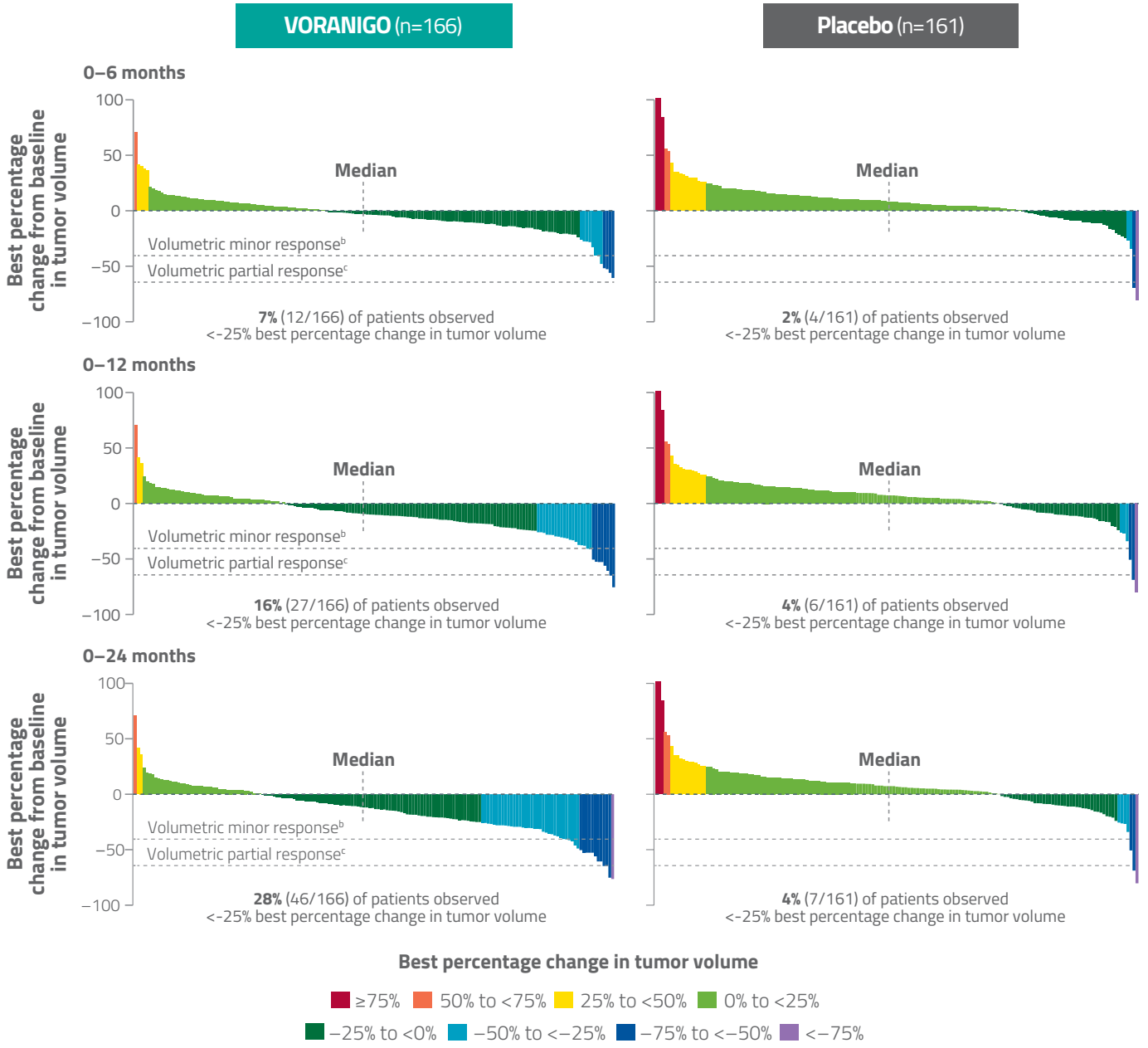
RANO-LGG, Response Assessment in Neuro-Oncology for Low Grade Glioma.

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: Best percentage change in tumor volume in individual patients at 6, 12, and 24 months[2a]



A rigorous statistical conclusion cannot be made because best percentage change in tumor volume was an exploratory outcome, and the results should be interpreted with caution.

[a]The figure shows the best percentage change from baseline tumor volume in individual patients between 0 and 24 months until study unblinding. Data cutoff was March 7, 2023.
[b]Volumetric minor response criteria: ≥40% to <65% decrease in tumor volume vs baseline[3]
[c]Volumetric partial response criteria: ≥65% decrease in tumor volume vs baseline[3]

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.

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

VORANIGO® is the first and only FDA-approved targeted therapy[1,4-5]

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]

Safety profile[1]:

- The most common (≥15%) ARs 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 neutrophils decreased (2.4%)
- Permanent discontinuation due to ARs occurred in 3.6% of patients treated with VORANIGO

Access the abstract from *The Lancet Oncology* publication on PubMed

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

Exploratory outcome: Best percentage change in tumor volume

With up to 24 months of follow-up, a reduction in tumor volume was observed in

73% (122/166) of patients taking VORANIGO

vs. 29% (46/161) of patients taking placebo[2]

A rigorous statistical conclusion cannot be made because best percentage change in tumor volume was an exploratory outcome, and the results should be interpreted with caution.

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; 2025. **2.** Cloughesy TF, van den Bent MJ, Touat M, et al. Vorasidenib in IDH1-mutant or IDH2-mutant low-grade glioma (INDIGO): secondary and exploratory endpoints from a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol.* 2025;26(12):1665-1675. doi:10.1016/S1470-2045(25)00472-3 **3.** Ellingson BM, Sanvito F, Cloughesy TF, et al. A neuroradiologist's guide to operationalizing the Response Assessment in Neuro-Oncology (RANO) criteria version 2.0 for gliomas in adults. *AJNR Am J Neuroradiol.* 2024;45(12):1846-1856. doi:10.3174/ajnr.A8396 **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

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US-03885 02/2026

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