VOR (doses < 100 mg once daily [QD]) was associated with a favorable safety profile, with no serious treatment-related deaths. INDIGO is a global, multicenter, double-blind, randomized, placebo-controlled, phase 3 study evaluating Vorasidenib (VOR; AG-881) in patients with residual or recurrent grade II glioma with an isocitrate dehydrogenase 1/2 (IDH1/2) mutation.

Further information is available at www.indigostudy.com

INDIGO STUDY DESIGN

OBJECTIVES OF THE PHASE 3 INDIGO STUDY

Primary objective:
- To demonstrate the efficacy of VOR compared with placebo, based on radiographic PFS in patients with residual or recurrent grade 2 glioblastoma and astrocytoma with an IDH1/2 mutation, and with those undergoing surgery on their only treatment

Secondary objectives:
- To compare the efficacy of VOR with placebo, based on ORR and tumor growth rate as assessed by MRI
- To evaluate the time to next intervention and health-related quality of life (HRQoL) by Functional Assessment of Cancer Therapy (FACT)-Br and FACT-Br [23,24]

INDIGO STUDY DESIGN

Phase III: multicenter, parallel-group, double-blind, randomized, placebo-controlled, phase 3 study in patients with residual or recurrent grade 2 glioma with an IDH1/2 mutation (ClinicalTrials.gov NCT03493157)

Study design and schedule of study assessments are shown in Figure 2

Figure 2. MRI of a patient with grade 2 meningioma with a partial response following VOR treatment in a phase 1 study

Figure 3. INDIGO study design and schema for assessments

Eligible patients with IDH1/2 oligodendroglia or astrocytoma with IDH1/2 mutation (ClinicalTrials.gov NCT03493157) and baseline tumor size (≥ 2 cm vs < 2 cm)

VOR: 140 mg once daily in two or three divided doses (28-day cycle) Placebo: matching 45 mg QD coated tablet orally in continuous 28-day cycle

Crossover to VOR: Persistent progressive, confirmed radiographic PD

Study endpoints

Primary
- Radiographic PFS per blinded independent central review committee

Secondary
- Safety and tolerability
- Tumor extension
- Time to next intervention

Exploratory
- Neurocognitive function
- PFS-C

Statistics
- Assuming a median PFS of 18 months in the control arm, a study has 80% power to detect a hazard ratio of 0.687 with 4.1-sided alpha of 0.025

SUMMARY AND CURRENT STATUS

The favorable safety profiles and encouraging preliminary efficacy data of VOR from phase 1 studies in patients with nonconverting glioma support the development of VOR in the phase 3 INDIGO study.

The global phase 3 INDIGO study in patients with grade 2 IDH1/2 gliomas who have had surgery as their only treatment is currently enrolling in the US.

The study will also be activated at centers outside the US, including throughout Canada, Europe, and Asia.

Further information is available at www.indigostudy.com

REFERENCES