

PATIENT INFORMATION SHEET AND CHILD'S ASSENT FORM (12 YEARS OLD)

STUDY TITLE:	A Phase IV, Prospective, Open Label, Multi-Centre Study of Vorasidenib in Indian Adult and Paediatric Participants 12 Years and Older with Grade 2 Astrocytoma and Oligodendroglioma with a Susceptible IDH1 or IDH2 Mutation following Surgery including Biopsy, Sub-Total Resection, or Gross Total Resection
STUDY NUMBER:	SER-VOR-001
SPONSOR:	Servier India Private Limited 1703, 17th Floor, Crescenzo Business District, 'B' Wing, Plot Nos. C-38/39, 'G' Block, BKC, Bandra (East), Mumbai 400 051, India
SUBJECT NUMBER:	
PRINCIPAL INVESTIGATOR:	DR. RIMPA BASU ACHARI
SITE NAME AND ADDRESS:	TATA MEDICAL CENTER 14, MAJOR ARTERIAL ROAD (EW) NEWTOWN, RAJARHAT KOLKATA-700160
CONTACT NUMBER OF THE PRINCIPAL INVESTIGATOR:	033-6605-8064-8065

Confidential and Proprietary to JSS Medical Research Asia Pacific Private Limited

PARTICIPANT INFORMATION SHEET

Invitation to Participate

You are being asked to take part in a research study. A research study is a way of testing medicines that have been approved but that doctors still want to learn more about, especially in patients like you. We are asking you to be in this study so that we can find out how a medicine called **Vorasidenib (VORANIGO®)** works in children and teenagers with a certain type of brain tumour.

Please read this form carefully, and talk to your mother, father, or the person taking care of you, before you decide whether you want to participate. Your parent or carer will also be asked to agree before you can join. **You cannot be in the study if your parent or carer does not agree.** Even if your parent or carer says “YES”, you can still say “NO”. If you do not want to be in the study, you are free to say so and no one will be upset with you. You will still be looked after by the doctors and nurses even if you decide not to take part.

What is a Research Study?

A research study is something like a science project at school, but more serious. When doctors and scientists want to learn more about a medicine, they must test it carefully in people. They want to see if the medicine helps people and make sure it does not harm them. The results from research studies help doctors treat patients better in the future.

Why Are You Being Asked to Be in This Study?

You are being asked to take part in this study because you are **12 years of age or older** and have been diagnosed with a type of brain tumour called a **Grade 2 glioma** (either an astrocytoma or oligodendroglioma). Tests on your tumour have shown a specific change in the tumour cells called an **IDH1 or IDH2 mutation**. You have also already had surgery for your brain tumour.

About **15 participants will take part in this study at approximately 10 hospitals** in India. Everyone in the study will receive the same study medicine, called vorasidenib. There is no placebo (dummy medicine) and no comparison group in this study.

What is the Purpose of This Research?

The brain is the control centre of the body — it helps you think, feel, and move. A brain tumour is an unusual growth of cells inside the brain. The type of tumour you have is called a Grade 2 glioma, which grows more slowly than others. Your tumour cells have a special change called an IDH1 or IDH2 mutation, which plays a role in how the tumour grows. This mutation may also make the tumour respond to a study medicine called vorasidenib.

Vorasidenib has been approved for use in India by the drugs authority (called the CDSCO). However, the drugs authority has asked the company making this medicine to collect more information about how it works in Indian patients. The purpose of this study is to find out how safe vorasidenib is and to learn whether it may help slow down or control the growth of this type of brain tumour in participants like you. Your participation will help doctors understand the medicine better and help future patients like you in India.

Confidential and Proprietary to JSS Medical Research Asia Pacific Private Limited

What Do You Have to Do?

If you decide to be in this study, you will have to answer some questions about your health and tell the doctor about any medicines that you are taking. It is very important that you are honest with the study doctor. If the doctor thinks you can join this study, you will be enrolled.

While you are in the study, you will need to:

- Take a medicine tablet called Vorasidenib once every day, at the same time each day, on an empty stomach (no food for at least 2 hours before and 1 hour after taking the tablet). Swallow the tablet whole with water — do not crush, break, or chew it.
- **If you weigh 40 kg or more:** you will take a 40 mg tablet once a day.
- **If you weigh less than 40 kg:** you will take a 20 mg tablet once a day.
- Tell the doctor about any side effects, symptoms, or health problems you notice during the study.
- Attend all the clinic visits as scheduled.
- Not take any other medicines for cancer, or any other medicines not prescribed by your study doctor, without asking first.
- Use a suitable method of contraception if you are sexually active (your doctor will explain this to you).

Study Design

This study is:

- **Phase IV:** This means the medicine is already approved, and this study is being done to collect more safety and effectiveness information in Indian patients.
- **Prospective:** Your health will be followed forward from when you join the study.
- **Open-label:** Both you and your doctor will know which medicine you are receiving.
- **Single treatment group:** All participants receive Vorasidenib. There is no placebo or comparison group.

Each treatment period lasts **28 days** (called a “cycle”). You will take vorasidenib every day during each cycle, with no breaks between cycles. You will receive up to **6 cycles** (about 6 months of treatment), unless the doctor recommends stopping earlier.

Your total time in this study will be about **8-9 months**, including:

- **Screening:** Up to 28 days (to check if you are eligible)
- **Treatment:** 6 cycles of 28 days each (about 6 months)
- **Safety Follow-up:** 1 visit within 7 weeks after your last dose

After the main study ends, you may be invited to take part in an optional **Extension Phase** (may be up to 18 months). This is entirely your choice, and you will be asked to sign a separate agreement before entering this phase.

What Are the Study Procedures?

Once you agree to join the study, your doctor will check whether you qualify by doing some tests. This is called the **Screening Period** (up to 28 days). The following will be done during screening and during the study:

Screening Period (before the study starts):

- Questions about your health, medical history, and current medicines
- A physical examination (including your height, weight, blood pressure, and pulse)
- An ECG (electrocardiogram) — a simple, painless test to check your heart's electrical activity using sticky pads placed on your chest
- Confirmation of your IDH1/IDH2 mutation using a tissue sample from your earlier surgery (no new biopsy is needed)
- A brain MRI scan to check the size and characteristics of your tumour (if a recent MRI was done within 28 days before joining, it may be used)
- Blood tests to check your blood counts, kidney function, liver function, and other safety measurements
- A pregnancy blood test (for girls/young women who could become pregnant)

During the Treatment Phase (Cycle 1 to Cycle 6, every 28 days):

- Vital signs: blood pressure, heart rate, and temperature
- Physical examination
- ECG
- Blood tests: blood counts, liver function tests, and other safety tests
- Brain MRI scan at Screening, Cycle 3 Day 1, and Cycle 6 Day 1 (End of Treatment)
- Urine pregnancy test at each cycle visit (for girls/young women who could become pregnant)
- Review of side effects and other medicines you may be taking
- Collection and review of your study diary

Important — Liver monitoring:

Vorasidenib can sometimes affect how the liver works. So, the study doctor will check your liver with special blood tests very regularly:

- Every 2 weeks during the first 2 months of treatment
- At some mid-cycle visits in months 3 and 4
- Once a month in months 5 and 6

If your liver tests show changes, the doctor may pause your dose, lower your dose, or stop treatment.

End of Treatment and Safety Follow-up Visits:

When you finish your 6 cycles (or if you stop treatment earlier), you will have one more clinic visit within 3 days. About 7 weeks later, there will be a brief safety follow-up visit (this may be by phone). The doctor will check that you are well and note any remaining side effects.

Blood Collection:

Confidential and Proprietary to JSS Medical Research Asia Pacific Private Limited

Blood will be collected during several visits using needle pricks. The total amount of blood collected across all study visits will be approximately 125 mL (about 8.5 tablespoons). For comparison, a standard blood donation is about 480 mL (about 32 tablespoons). Additional blood samples may be taken if your doctor needs to check your health between visits.

What If You Do Not Want to Be in This Study?

If you do not want to take part, or if you change your mind at any time during the study, just tell your parent/carer or the study doctor. You may be advised about how to stop the treatment safely. If you leave the study, you may be asked to come in for a few more tests to make sure you are fine, but you do not have to agree to those if you do not want to.

Your decision not to participate, or to leave the study at any time, **will not affect your medical care** or your relationship with your doctor or hospital. Your doctor will still look after you, and you will not lose any benefits to which you are entitled.

Will You Get Anything for Being in the Study?

You or your parents will not be paid for taking part in this study. However, Servier India Private Limited (the company running this study, also called the Sponsor) will pay for any reasonable travel costs for coming to the study visits. You will receive up to INR ___1500___/— per visit.

Your safety is our highest priority. If you think you have been injured or harmed because of being in this study, you and/or your parent/carer must tell the study doctor right away. The study doctor will provide **free medical care** for any study-related injury, for as long as needed. These costs will be paid by the Sponsor.

In the unlikely event that you have a study-related injury or death, **Servier India Private Limited** will provide financial compensation in addition to medical care costs, as required under **Rule 39 and Rule 40 of the New Drugs and Clinical Trials Rules, 2019**. Compensation applies when the injury or death is related to the study medicine, a study procedure, or other reasons defined in the Rules.

In the event of study-related injury or death, you and/or your parent/carer may also contact **JSS Medical Research Asia Pacific Private Limited** to make a claim for financial compensation over and above medical expenses. Contact details are given in the section below.

Could You Be Hurt by Being in the Study?

Like all medicines, Vorasidenib can cause side effects. Here are the things that could happen:

Common side effects (may affect many people):

- **Liver changes detected by blood tests:** The most common side effects are rises in liver enzymes (called ALT, AST, and GGT). These are detected through blood tests. In most cases, the levels return to normal when the dose is adjusted or stopped. Your doctor will check your liver regularly. Please tell the doctor right away if you feel: yellowing of your skin or eyes, dark urine, pain on the right side of your tummy, unusual tiredness, or loss of appetite.
- **Tiredness or weakness:** This was seen in about 1 in 3 patients in the main study.
- **Diarrhoea:** Loose or watery stools, seen in about 1 in 4 patients.
- **Tummy pain:** Pain in the abdomen (upper or lower).

Confidential and Proprietary to JSS Medical Research Asia Pacific Private Limited

- **Other blood test changes:** Lower platelet counts, raised blood sugar, low phosphate, or other findings seen through blood tests.

Rare but serious side effects (seen in very few patients):

- Serious liver injury (including liver failure, liver tissue damage, or autoimmune hepatitis) — very rare but possible.

Effects related to pregnancy and fertility:

- Vorasidenib is not recommended during pregnancy. Based on animal studies, it could harm an unborn baby. Breastfeeding is not recommended during the study and for 2 months after the last dose.
- Vorasidenib may also affect fertility in both girls/women and boys/men. These effects were not fully reversible in some animal studies. If you are thinking about having children in the future, please talk to your study doctor before starting treatment.
- **Important:** Vorasidenib can make some birth-control medicines less effective. If this applies to you, the study doctor will talk with you and your parent/guardian about using a reliable, non-hormonal method to prevent pregnancy during the study and for 3 months after the last dose.

Risks from study procedures:

- **Blood draws:** Needle pricks may cause pain, bruising, redness, swelling, or rarely infection at the needle site. If you feel faint, tell the study staff right away.
- **Brain MRI:** MRI does not use radiation and is safe. If a dye (contrast) is used, there is a small chance of an allergic reaction. Tell the doctor if you have metal implants or feel anxious inside the MRI machine.
- **ECG:** The sticky pads used may be cold or cause mild skin irritation. This is not harmful.

There may be other rare or unknown side effects not listed here. Please tell the study doctor about **any** changes in how you feel during the study. If you feel sick or scared that something is wrong, tell an adult at once.

Whom Should You Contact During the Study?

For further questions or concerns, you and/or your parent/carer can contact any of the following people:

For Queries Related to the Study		
Role in the Study	Name	Contact Details
Principal Investigator	Dr. Rimpa Basu Achari Dept. of Radiation Oncology [TATA MEDICAL CENTER 14, MAJOR ARTERIAL ROAD (EW) NEWTOWN,	Ph:033-6605-8064/8065 Fax:

Confidential and Proprietary to JSS Medical Research Asia Pacific Private Limited

	RAJARHAT KOLKATA-700160]	
For Queries Related to Your Rights as a Participant in a Clinical Study		
Chairperson, Ethics Committee	Institutional Review Board [TATA MEDICAL CENTER 14, MAJOR ARTERIAL ROAD (EW) NEWTOWN, RAJARHAT KOLKATA-700160]	Ph:033-6605 7579 Fax:
Member Secretary, Ethics Committee	Institutional Review Board [TATA MEDICAL CENTER 14, MAJOR ARTERIAL ROAD (EW) NEWTOWN, RAJARHAT KOLKATA-700160]	Ph: 033-6605 7579 Fax:

☐ NO, I do not want to participate in the study

☐ YES, I will participate in the study

Participant (Child / Adolescent)		
Complete Name (In CAPITAL LETTERS)	Signature / Thumb Impression	Date & Time (DD/MMM/YYYY)

Statement of Person Obtaining Assent

I, the undersigned, certify that to the best of my knowledge, the individual signing this Participant Assent Form was carefully informed of the study in accordance with applicable law. The participant's questions were reviewed and answered to the best of my knowledge. The individual understands the nature, risks, and benefits of participation in this research study. A copy of this signed and dated assent form will be provided to the participant and/or his/her parent/Legally Acceptable Representative.

Investigator / Designee Obtaining Assent (as per Delegation Log)

Confidential and Proprietary to JSS Medical Research Asia Pacific Private Limited

Complete Name (In CAPITAL LETTERS)	Signature	Date & Time (DD/MMM/YYYY)

Impartial Witness ☐ Tick if not applicable (<i>Applicable only if participant is unable to read and write</i>)		
Complete Name (first name, middle name, last name)	Signature	Date (DD/MMM/YYYY)