Vorasidenib

INDICATION

For the treatment of astrocytoma or oligodendroglioma with IDH1 or IDH2 mutations after surgery in adult patients who are not eligible for a clinical trial

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TREATMENT INTENT

- Palliative

TREATMENT CONTEXT

- For the treatment of astrocytoma or oligodendroglioma with IDH1 or IDH2 mutations after surgery in adult patients who are not eligible for a clinical trial

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DRUG REGIMEN

Day	Drug	Dose	Route	Administration
1-28	Vorasidenib	40mg	Oral	Once daily

*if weight less than 40kg - dose recommended 20mg once daily

Cycle frequency

28 day cycle (12 cycles will be set in aria)

Number of cycles

- Until loss of clinical benefit or unacceptable toxicity

ADDITIONAL ADMINISTRATION INFORMATION

- Vorasidenib is available as 10mg and 40mg film coated tablets
- The daily dose should be swallowed whole with water at the same time each day. Patients should not eat food at least 2 hours before and 1 hour after taking.
- If a dose is missed or not taken at the usual time, it should be taken as soon as possible within 6 hours after the missed dose. The next dose should be taken at the regular scheduled time.
- If a dose is missed by more than 6 hours, it should be skipped, and the next dose should be taken at the regularly scheduled time.
- If a dose is vomited, replacement tablets should not be taken. The tablets should be taken as usual the following day.
- Vorasidenib contains lactulose therefore contraindicated in patients with rare hereditary problems of galactose intolerance, total lactulose deficiency or glucose-galactose malabsorption should not take this medicinal product.

CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the excipients

INVESTIGATIONS PRE-FIRST CYCLE

Investigation	Validity period
FBC	28 days (or at consultant discretion)
U&E	28 days (or at consultant discretion)
LFTs	28 days (or at consultant discretion)
Glucose	28 days (or at consultant discretion)

Other pre-treatment investigations:

- Glucose every cycle
- FBC, U&Es and LFTs should be taken every 2 weeks for the first 2 months and then monthly thereafter.

INVESTIGATIONS PRE-CYCLE 2 ONWARDS

Investigation	Validity period
FBC	7 days
U&E	7 days
LFTs	7 days
Glucose	7 days

- FBC, U&Es and LFTs should be taken every 2 weeks for the first 2 months and then monthly thereafter.

DOSE MODIFICATIONS

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances. All dose reductions to be discussed with the Consultant.

In principle any dose reduction due to adverse drug reactions **should not** be re-escalated in subsequent cycles without consultant approval. It is also a general rule for SACT that if a third dose reduction is necessary treatment should be stopped.

Dose modifications listed are for haematological, hepatic function, renal function and limited drug specific toxicities. Adjustments may be necessary for other toxicities as well.

Haematological toxicities on the day of treatment		
Neutrophils [x10^9/L]	≥1.5x10^9/'l	Continue treatment
Platelets [x10^9/L]	≥100x10^9/'l	Continue treatment

If neutrophils and/or platelets below above levels delay 1 week and refer to prescriber.

Renal toxicities	
CrCL (mL/min)	**Vorasidenib**
>40ml/min	No starting dose adjustment is recommended
<40ml/min	No information available, use with caution. Monitor for increased adverse drug reactions and modify dose as required.

Hepatic toxicities			
Bilirubin (xULN)		**ALT/AST (xULN)**	**Vorasidenib**
<2xULN	And	>3xULN	Grade 1 - Continue at current dose. Monitor liver enzymes weekly until recovery to <Grade 1.
<2xULN	And	ALT or AST >3 to 5 x ULN	Grade 2 - First Occurrence: Withhold and monitor liver enzymes twice per week until recovery to ≤Grade 1 or baseline. • Recovery in ≤28 days, resume at the same dose. • Recovery in >28 days, resume at reduced dose. Recurrence: Withhold and monitor liver enzymes twice per week until recovery to ≤Grade 1 or baseline, and resume at reduced dose
<2xULN	And	ALT or AST >5 to 20 x ULN	Grade 3- First Occurrence: Withhold and monitor liver enzymes twice per week until recovery to ≤Grade 1 or baseline. • Recovery in ≤28 days, resume at reduced dose. • If not recovered in ≤28 days, permanently discontinue. Recurrence: Permanently discontinue and monitor liver enzymes twice per week until recovery to ≤Grade 1 or baseline.
>2xULN in the absence of clear alternative explanation	And	Any ALT or AST >3 to 20 x ULN	Permanently discontinue and monitor liver enzymes twice per week until recovery to ≤Grade 1 or baseline.
		Any ALT or AST >20 x ULN	Permanently discontinue and monitor liver enzymes twice per week until recovery to ≤Grade 1 or baseline.

Other drug specific toxicities

- First occurrence of grade 3 toxicity: Interrupt until toxicity resolves to Grade 1 or toxicity lower, or baseline, then resume at reduced dose level.
- If Grade 3 toxicity recurs (a second time), permanently discontinue
- Permanently discontinue at the first occurrence of any grade 4 toxicity

Dose Modifications

Dose level	Dose and schedule
Starting dose	40mg once daily
1st dose reduction	20mg once daily
2nd dose reduction	10mg once daily

ADVERSE EFFECTS/REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. For full details consult product literature/ reference texts.

ADVERSE EFFECTS		
Common side effects	**Serious side effects**	**Other side effects**
Hyperglycaemia	Thrombocytopenia	
thrombocytopenia	Increased LFTs	
Hypophosphataemia		
Abdominal pain		
Increased LFTs		
Diarrhoea		
Fatigue		
Decreased appetite		

SIGNIFICANT DRUG INTERACTIONS

- Co-administration of vorasidenib with strong or moderate CYP1A2 inhibitors may increase vorasidenib plasma concentrations. Concomitant use of strong or moderate CYP1A2 inhibitors should be avoided.
- Co-administration of vorasidenib with moderate CYP1A2 inducers (phenytoin and rifampicin) may decrease vorasidenib plasma concentration.
- Concomitant use of vorasidenib with smoking tobacco may decrease vorasidenib plasma concentrations which may reduce the anti-tumor activity of vorasidenib.
- Co-administration of vorasidenib with CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP3A4 substrates may decrease the plasma concentrations of these medicinal products.
- Vorasidenib may decrease concentrations of hormonal contraceptives and, therefore, concomitant use of a barrier method of contraception is recommended during treatment and for at least 3 months after the last dose
- Vorasidenib is an inhibitor of breast cancer resistance protein (BCRP). Caution should be exercised when administering vorasidenib with BCRP substrates.

REFERENCES

1. Vorasidenib summary of product characterisistics. Available from: Voranigo 40 mg Film Coated tablet - Summary of Product Characteristics (SmPC) - (emc) | 101421. Accessed 1.6.26
2. INDIGO trial; K Ingo et al - June 4, 2023 - N Engl J Med 2023;389:589-601 DOI: 10.1056/NEJMoa2304194 - VOL. 389 NO. 7

DOCUMENT CONTROL[1]

Version	Date	Amendment	Written By	Approved By
1	**1.6.26**		**Alexandra Pritchard Pharmacist**	**Dr Sean Main Consultant**

This SACT protocol has been developed by the Wessex Cancer Alliance SACT protocol development group. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust
University Hospitals of Dorset

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.

The regimen summary that follows is to facilitate building the protocols in the Aria prescribing system for those Trusts that utilise this system.

REGIMEN SUMMARY

1. **Vorasidenib 40mg once a day (oral) for 28 days**
   Administration instructions: The tablets should be taken once daily with full glass of water, swallow whole and do not chew or split or crushed. Take 2 hours before food or at least 1 hour after. If patient weighs less than 40kg the recommended dose is 20mg once a day.

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