BC Cancer Protocol Summary of Therapy for Grade 2 Astrocytoma or Oligodendroglioma with IDH-1 or IDH-2 Mutation using Vorasidenib

Protocol Code: *UCNVORA*

Tumour Group: *Neuro-oncology*

Contact Physician: *CN Systemic Therapy*

ELIGIBILITY:
Patients must have:
- Grade 2 astrocytoma or oligodendroglioma,
- Confirmed IDH1 or IDH2 mutation,
- Had surgery for glioma within the previous 5 years,
- Presence of residual disease on MRI at the time of therapy initiation,
- No immediate need for radiation therapy or chemotherapy
- BC Cancer “Compassionate Access Program” request approval prior to treatment

Patients should have:
- Good performance status

Note: It is recommended that all patients are presented at the CNS multidisciplinary conference prior to treatment initiation.

EXCLUSIONS:
Patient must not:
- Have Grade 3 tumours or tumours with high-risk features
- Have prior anticancer therapy for glioma other than surgery
- Be receiving therapeutic doses of steroids for glioma (patients using steroids for symptom management are eligible)

TESTS:
- Baseline: CBC & Diff, total bilirubin, ALT, alkaline phosphatase, GGT
- Baseline, if clinically indicated: creatinine, random glucose
- Every 2 weeks during Cycles 1 and 2: CBC & Diff, total bilirubin, ALT, alkaline phosphatase, GGT
- Cycles 2 to 24 prior to each cycle, then every third cycle: CBC & Diff, total bilirubin, ALT, alkaline phosphatase, GGT
- If clinically indicated: creatinine, random glucose

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
vorasidenib	40 mg* once daily	PO

*For patients weighing less than 40 kg, dose is 20 mg once daily

Cycle = 28 days.

Treat until disease progression or unacceptable toxicity.

DOSE MODIFICATIONS:

Starting Dose	Dose Level -1	Dose Level -2
40 mg	20 mg	10 mg

1. Hepatic Dysfunction:

Total bilirubin		ALT	Dose
Less than 2 x ULN	and	Greater than ULN to 3 x ULN	• Continue at current dose • Monitor liver function tests weekly until recovery to less than ULN

	and	Greater than 3 x ULN to 5 x ULN	• **If first occurrence**: withhold vorasidenib until recovery of ALT to less than or equal to 3 x ULN or baseline
			  • If recovery occurs in 28 days or less, resume treatment with same dose
			  • If recovery takes longer than 28 days, resume treatment at next lower dose level
			• **If second or subsequent occurrence:** withhold vorasidenib until recovery of ALT to less than or equal to 3 x ULN or baseline, then resume at next lower dose level

	and	Greater than 5 x ULN to 20 x ULN	• **If first occurrence:** withhold vorasidenib until recovery of ALT to less than or equal to 3 x ULN or baseline
			  • If recovery occurs in 28 days or less, resume treatment at next lower dose level
			  • If no recovery within 28 days or less, permanently discontinue vorasidenib
			• **If toxicity recurs:** permanently discontinue vorasidenib

Greater than or equal to 2 x ULN	and	Greater than 3 x ULN to 20 x ULN	• **If first occurrence:** withhold vorasidenib until recovery to less than or equal of ALT to less than or equal to 3 x ULN or baseline, then resume at next lower dose level • **If toxicity recurs:** permanently discontinue vorasidenib
Any	and	Greater than 20 x ULN	Permanently discontinue vorasidenib

ULN = upper limit of normal

2. Other Adverse Reactions:

Severity	Management
Grade 3	• **If first occurrence:** withhold vorasidenib until recovery to less than or equal to Grade 1 or baseline, then resume at next lower dose level • **If toxicity recurs:** permanently discontinue vorasidenib
Grade 4	Permanently discontinue vorasidenib

PRECAUTIONS:

1. **Hepatotoxicity** has been reported in patients treated with vorasidenib. Serious events such as hepatic failure, hepatic necrosis, and autoimmune hepatitis have been reported. Baseline and regular monitoring of liver function tests is recommended. Patients with pre-existing severe hepatic impairment may be treated with vorasidenib only after careful risk/benefit assessment and with close monitoring. Based on the severity and persistence of hepatotoxicity, vorasidenib dose interruption, dose reduction, and/or permanent discontinuation may be required.
2. **Renal Impairment:** Pharmacokinetics and safety of vorasidenib have not been evaluated in patients with creatinine clearance less than or equal to 40 mL/min or in renal impairment requiring dialysis. Use caution in this patient population, and only after careful risk/benefit assessment, with close monitoring.
3. **Drug Interactions:** vorasidenib is a substrate of CYP 1A2. Avoid concurrent use with moderate or strong CYP 1A2 inhibitors and inducers. If coadministration with CYP 1A2 inhibitors cannot be avoided, monitor for increased vorasidenib toxicity and consider dose reduction as indicated. Avoid concomitant use of vorasidenib with CYP2C19 and CYP3A4 substrates with a narrow therapeutic index, as vorasidenib is a strong inducer of CYP 3A and weak to moderate inducer of CYP 2C19.

Contact the CN Systemic Therapy physician at your regional cancer centre or the CN Systemic Therapy Chair with any problems or questions regarding this treatment program.

REFERENCES:

1. Mellinghoff IK, van den Bent MJ, Blumenthal DT et al. Vorasidenib in IDH1- or IDH2-Mutant Low-Grade Glioma. N Engl J Med. 2023 Aug 17;389(7):589-601.
2. Vorasidenib (VORANIGO) Canada's Drug Agency (CDA-AMC) Reimbursement Recommendation. Canadian Journal of Health Technologies Dec 2025; 5(12): 1-15.