Systemic Anti Cancer Therapy Protocol

Procarbazine

PROTOCOL REF: MPHAPROCNS
(Version No: 2.1)

The protocol has been temporarily amended – please see the Oral SACT Operational Changes during Covid-19. Amendments may include less frequent blood monitoring, telephone SACT assessments and longer durations of treatment being dispensed.

Approved for use in:

Third line treatment for recurrent glioma following treatment with temozolomide and lomustine

ECOG Performance Status 0 - 2

Dosage:

Drug	Dosage	Route	Frequency
Procarbazine	50mg twice daily	Oral	Days 1 – 14* every 28 days until disease progression

May be given for 10 days initially if caution is needed due to toxicities from prior treatments (can then increase to 14 days for subsequent cycles if well tolerated).

Supportive treatments:

- Ondansetron PO 4mg twice a day for 14 days
- Domperidone PO 10mg three times daily when required

  Or
- Cyclizine PO 50mg three time daily when required

Extravasation risk:

Not applicable

Administration:

Procarbazine is available as a 50mg capsule and can be taken with or without food.

Please refer to "*Interactions*" section for information about high tyramine-containing foods which should be avoided whilst on procarbazine (a diet patient information sheet should be provided to patients at pre-assessment).

Drug interactions:

Anti-depressants, opioids and anti-emetics - Procarbazine is a weak monoamine-oxidase inhibitor (MAOI) so concurrent use may increase the risk of Serotonin Syndrome

Anti-epileptics – increased risk of hypersensitivity reaction when phenobarbital, phenytoin or carbamazepine are given with procarbazine

Alcohol - consumption of alcohol whilst taking procarbazine may cause a disulfiram-like reaction (nausea, vomiting, flushing, dizziness, and headache)

High tyramine-containing foods – tyramine is released as proteins age and breakdown therefore is usually found in aged, fermented, pickled or smoked foods or in food that has not been stored correctly and has started to spoil.

The reaction to eating these foods whilst on procarbazine can be relatively mild (facial flushing and rash) but can also be quite severe (sudden onset headache, neck stiffness, nausea and vomiting, sensitivity to light, sweating, chills, pounding heart). Symptoms of any reaction usually resolve within a few hours.

Food that should be completely avoided includes mature or aged cheese, concentrated yeast or meat extracts (marmite, gravy or stock cubes) and broad-bean pods.
Food that may be eaten but in moderation include over-ripe fruit, beer, wine, sour cream, yoghurt, cured meats, banana and soy sauce.

Main Toxicities:

- Nausea and vomiting
- Loss of appetite
- Lethargy
- Allergic skin reactions
- Pneumonitis
- Abnormal LFT results
- Anaemia
- Thrombocytopenia
- Neutropenia

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Clinical Assessment	X	X	X	X	Every cycle
SACT Assessment		X	X	X	Every cycle
FBC	X	X	X	X	Every cycle
U&E & LFTs	X	X	X	X	Every cycle
MRI scan	X				Every 3 cycles
Informed Consent	X				
PS recorded	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	Every cycle
Height recorded	X				

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:-

ANC ≥ 1.5 x 10^9/L	Platelets ≥ 100 x 10^9/L

Delay 1 week on day 1 if:-

ANC ≤ 1.4 x 10^9/L	Platelets ≤ 99 x 10^9/L

Consider reducing course length to 10 days in event of haematological toxicity.

Non-haematological toxicities

In the event of non-haematological toxicities, consider reducing course length to 10 days.

Renal impairment

Procarbazine is eliminated primarily via the kidneys. Caution is advised for patients with renal dysfunction. Patients with a serum creatinine > 177µmol/l should be considered for a dose reduction.

Hepatic impairment

Procarbazine is metabolized by the liver therefore should be used with caution in patients with hepatic impairment. Consider a dose reduction if bilirubin > 50 µmol/L. Procarbazine is contra-indicated if bilirubin is > 85µmol/L or AST > 180 IU/L.

References:

1. The British National Formulary (BNF). Available at https://bnf.nice.org.uk
2. Procarbazine 50mg Capsules Summary of Product Characteristics (November 2014)
3. Available at: https://www.medicines.org.uk/emc/product/3732
4. The North London Cancer Network “Dose Adjustments for Cytotoxics in Hepatic Impairment” (January 2009)
5. The North London Cancer Network “Dose Adjustments for Cytotoxics in Renal Impairment” (January 2009)