Protocol for Planning and Treatment

The process to be followed when a course of chemotherapy is required to treat:

Primary Oligodendroglioma, Astrocytoma and Oligoastrocytoma Grade II

Patient information given at each stage following agreed information pathway

1. DIAGNOSIS

These rare tumours may present with a variety of low grade neurological symptoms and signs, depending on the anatomical location of the tumour, or as an incidental finding CNS imaging performed for other reasons.

Patients will be discussed at the CNS MDT. A decision will be made to either perform serial imaging as part of an observation policy, or to proceed with a biopsy.

Biopsy will usually be recommended if the lesion is greater than 6cm in size, crosses the midline, if the patient is greater than 40 years old, and if the patient has unresolved symptoms, as this may suggest a higher grade tumour.

Tissue samples are sent to Edinburgh for review, where an expert neuropathology diagnosis is provided by Professor Ironside and Dr C Smith and Dr A Tongersen.

Definitive diagnosis of a Grade II oligodendrolglioma or astrocytoma is therefore occasionally based on the results of a biopsy, but frequently a radiological diagnosis of low grade glioma is accepted.

2. STAGING

Since these are localised tumours the staging investigations are based upon T1, T2 and T-gadolinium-enhanced MRI scan of the brain.

3. HISTOPATHOLOGY

Oligodendrogliomas are distinctive, consisting of homogeneous, compact, rounded cells with distinct borders and clear cytoplasm surrounding a dense central nucleus, giving them a "fried egg" appearance. There may also be areas of calcification. Classically they tend to have a vasculature of finely branching capillaries that may take on a “chicken wire” appearance.

They may be associated with co deletion of chromosomal arms 1p 19q (loss of heterozygosity: LOH) which may predict for better outcomes and improved response to both chemotherapy and radiotherapy [1-4]. As such this should be assessed for, and treatment discussed in light of this result.

4. RADIOTHERAPY / SURGERY

Surgery

A biopsy only may be appropriate to obtain pathological diagnosis. Debulking may be performed depending on individual circumstances.

Radiotherapy

Early XRT should only be considered if multiple poor prognostic features – age >40, lesion >6cm, crosses midline, pre op neurological deficit.

54Gy in 30# over 6 weeks – see XRT protocol.

5. CHEMOTHERAPY

Historically no role for chemotherapy. RTOG 9802 published abstract ASCO 2008 [(5)] has shown that 6 cycles of adjuvant PCV leads to a significant PFS and OS advantage following XRT in Grade II glioma, irrespective of subtype and 1p19q status, after 2 years. 84% vs 72% risk of being alive at 5 years (HR 0.52 p=0.02)

PCV

Lomustine 100 mg/m² po Day 1
Procarbazine 100 mg/m² po Days 1 -10
Vincristine 1.5 mg/m² iv Day 1 (Max 2mg)

Repeated every 6 weeks for a maximum of 6 cycles.

6. SUPPORTIVE THERAPY

All patients with brain tumours should be referred to the Macmillan Nurse. Patients may wish to have support from the Macmillan Nurse in the community and they should be told of the opportunity of visiting the Macmillan Centres at Roxburghe House, Macmillan House, Perth or Macmillan Centre at Stracathro.

Dexamethasone to reduce cerebral oedema is rarely needed by these patients, and the minimum dose required to control symptoms should be used. Gastric protection in the form of a proton pump inhibitor should be prescribed. All patients should carry a steroid card at all times.

7. TREATMENT DEFINITIONS

PCV

Lomustine 100 mg/m² po Day 1
Procarbazine 100 mg/m² po Days 1 -10
Vincristine 1.5 mg/m² iv Day 1 (Max 2mg)

8. REVIEW

Patients treated with XRT

Weekly review by radiotherapy support team.

To be seen in clinic 4 weeks after completion of XRT to assess toxicities and to discuss commencing PCV chemotherapy.

Patients treated with chemotherapy

To be reviewed in clinic after cycle 3 and 6 to assess toxicities and with MRI / CT to assess response to treatment.

9. REFERENCES

1. C. Walker et al "Clinical use of genotype to predict chemosensitivity in oligodendroglial tumors" Neurology 2006;66:166 http://www.neurology.org/cgi/content/abstract/66/11/1661

2. Stege EM et al "Successful treatment of low-grade oligodendroglial tumors with a chemotherapy regimen of procarbazine, lomustine, and vincristine." Cancer 2005 Feb 15; 103 (4):802-9.http://www.ncbi.nlm.nih.gov/pubmed/15637687

3. Cairncross JG et al "Specific genetic predictors of chemotherapeutic response and survival in patients with anaplastic oligodendrogliomas."
http://www.ncbi.nlm.nih.gov/pubmed/9776413

4. Labussiere M et al "*IDH1* Gene Mutations: A New Paradigm in Glioma Prognosis and Therapy? The Oncologist February 2010 vol. 15 no. 2 196-199
http://theoncologist.alphamedpress.org/content/15/2/196.long

5. van den bent M et al "Adjuvant Procarbazine, Lomustine,and Vincritine improves PFS but not OS in newly diagniosed anaplastic oligodendrogliomas and oligoastrocytomas: A randomised EORTC Phase III trial. JCO Vol 24 No 18 June 20 2006 and updated ASCO 2008 abstract.