Kent & Medway Cancer Collaborative

Oncological Treatment of Primary Brain and CNS Tumours

Pathway of Care

Kent & Medway Cancer Collaborative

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1.0 Introduction

- This document has been written to provide guidance on the treatment of primary brain tumours in the Kent & Medway Cancer Collaborative (KMCC).
- Radiotherapy schedules are as defined in the Kent Oncology Centre Quality System Clinical Protocols.
- See network chemotherapy prescribing proformas for details of chemotherapy / anti-cancer regimens.
- All patients will be considered for entry into a clinical trial where appropriate (see appendix A).
- All patients should be discussed within a multidisciplinary team meeting (MDM) before commencing initial treatment.
- All chemotherapy regimens listed within this document are delivered at either Maidstone and Tunbridge Wells NHS Trust or East Kent Hospitals University NHS Foundation Trust.
- Please note, some of the drugs/doses recommended within this document are outside of the U.K. licensed marketing authorisation.

1.1 Overview

Patients are referred in from the neuro-sciences MDM. Typically they will have had a biopsy or debulking surgery. Subsequent treatment intent will depend on performance status, but early input of palliative care services is recommended in all cases where appropriate.

Radiotherapy is the primary non-surgical modality of treatment however the addition of chemotherapy has been shown to improve outcome in selected patients with GBM.

In keeping with Improving Outcomes Guidance (IOG) recommendations, KMCN does not provide a cranio-spinal radiotherapy service.

2.0 Glioblastoma multiforme (GBM)

1.0 Following surgical debulking or biopsy, patients of PS 0-1 up to the age of 70 can be considered for chemoradiotherapy using the Stupp regimen; radical radiotherapy 60Gy in 30 fractions with concurrent temozolamide followed by adjuvant 6 cycles of temozolamide. Patients >70 with PS 0 will be considered on an individual basis given the increase in toxicity with the Stupp regimen.

2.0 Patients not suitable for Stupp, can be considered for concurrent chemo-radiotherapy: 40Gy in 15 fractions with 3 cycles of weekly temozolamide, followed by 12 cycles of adjuvant temozolamide or 40Gy in 15 fractions alone.

3.0 If patient is not suitable for radical radiotherapy regimes outlined above, then palliative radiotherapy can be considered if deemed appropriate; 30Gy in 6 fractions.

4.0 Patients can be considered for palliative temozolamide alone, if the patient has had a biopsy confirming GBM. Treating without a biopsy can only be considered if discussed and agreed in the respective neurosciences or local brain MDT.

5.0 Patients with PS 3-4 will not be considered for active treatment.

6.0 Radical Radiotherapy: 54Gy – 60Gy in 30 fractions; 40Gy in 15 fractions.

7.0 Palliative radiotherapy: 30Gy in 6 fractions.

At disease progression patients can be considered for further treatment if deemed appropriate. This can involve further surgery, chemotherapy or appropriate clinical trials where available.

2.1 Chemotherapy

2.1.1 Stupp regimen (Chemoradiation followed by adjuvant treatment)

This regimen involves radical radiotherapy with concurrent chemotherapy with temozolomide (daily 75mg/m^2) followed by 6 cycles of adjuvant temozolomide (usually started at 200mg/m^2/day days 1-5).

N.B. If a patient's full blood count is satisfactory at the end of treatment (Neuts $\geq$1.5 and PLT$\geq$ 75), and on day 28 post chemoradiation, start adjuvant temozolomide at 200mg/m^2.
If the full blood count does not meet these requirements, temozolomide should be started at 150mg/m^2.

NB Temozolomide causes lymphopenia and hence patients should be given prophylaxis against PCP during the concurrent phase (e.g with co-trimoxazole).

2.1.2 Palliative treatment

If patients have progressed during or immediately after primary treatment further active treatment has a very low chance of benefit which must be discussed with the patient.

At disease progression following completion of initial active treatment, patients of good PS will be considered for further active treatment, usually chemotherapy but sometimes surgery has a role to play and patients will be reviewed by the neuro-sciences MDM.

Involvement of palliative care services should be reviewed.

2.2 Gliadel® Implant in GBM

The Brain NOG do not support the use of concurrent chemoradiation for patients with GBM who have Gliadel® implants inserted into the tumour resection cavity as there is currently no data to support this. These patients will be considered for radiotherapy alone.

3.0 Glioma (excluding GBM)

Radiotherapy is usually the first non-surgical treatment outside of clinical trials; radical radiotherapy dose is 54Gy – 60Gy in 30-33 fractions.

Patients with large volume disease may be considered for primary chemotherapy outside of trials with the aim of delaying late radiotherapy toxicity; either PCV or temozolamide based on pathological and molecular features of the tumour.

Anaplastic Astrocytomas can be considered for adjuvant temozolamide for 12 cycles, following completion of radical radiotherapy.

At progression patients will be reviewed in the MDM to consider whether further surgical de-bulking is possible and then palliative chemotherapy options, as outlined in GBM above.

Adjuvant chemotherapy with 4-6 cycles PCV should be considered, following completion of radical radiotherapy, for 1p19q co-deleted anaplastic ogliodendrogliomas.

Grade 2 gliomas can be considered for radiotherapy locally in Kent, based on patient preference. Radiotherapy dose is 54Gy in 30 fractions. Consider adjuvant PCV (4-6 cycles) for oligodendroglioma subset.

Consider entry into clinical trials where appropriate.

3.1 Palliative treatment

Patients must be PS 0-2 to be considered suitable for palliative chemotherapy. Palliative care input should be reviewed on a regular basis.

Elderly patients (>70) having PS 0-1 can be considered for palliative temozolomide (funding approval required), if they have either gliomatosis that has been radiologically diagnosed **or** histologically proven high grade glioma and have significant small vessel disease where radiotherapy would be contraindicated.

Patients not suitable for any radical radiotherapy options can be considered for single agent temozolamide.

Treatment for this patient cohort should be discussed within the local MDT.

Palliative chemotherapy options include: PCV; Temozolamide; Single agent lomustine; carboplatin and etoposide.

4.0 Meningioma

Surgery is the primary treatment modality for meningioma. Elderly patients considered unfit for surgery are very unlikely to be suitable for radiotherapy as hypofractionated courses are not of benefit in meningioma.

4.1 Radiotherapy

- Radiotherapy can be considered for patients with:
    - Recurrent grade 1 following debulking surgery
    - Inoperable grade 1
    - Incomplete excision of atypical meningioma (grade 2)
    - Malignant meningioma (grade 3)
    - G1 meningiomas: 50Gy in 30 fractions or 54Gy in 30 fractions.
    - Anaplastic meningiomas: 54Gy in 30 or 60Gy in 30 fractions

4.2 Systemic therapy

Chemotherapy and endocrine therapies have a small role to play but may be considered in individual cases. The use of endocrine therapy will be guided by progesterone receptor (PR) status.

5.0 Pituitary / craniopharyngioma

Patients will be referred by the King's Pituitary MDT in the post-operative period.

5.1 Postoperative primary treatment

- Radiotherapy
- Benign non functioning pituitary: 45Gy in 25 fractions
- Benign functioning pituitary or bulky residual disease: 50Gy in 30 fractions
- Craniopharyngioma: 54Gy in 30 fractions

6.0 Primary brain lymphoma / ALL

CNS lymphoma is predominantly treated at Guys/Kings by haemato-oncology teams with systemic therapies. Radical radiotherapy for CNS lymphoma should be led and delivered at Guys Cancer Centre lymphoma team.
If any patient is to be treated in Kent, case-by-case discussion with the Guys lymphoma team is required and treatment may be supervised by the lymphoma clinical oncology team with local neuro-oncology input as appropriate.

7.0 Appendix A: Clinical Trials

Refer to the local research team who will provide on request an orientation handbook, list of current trials and associated trial protocols and summaries.

Contact numbers

MTW – Clinical Trials Office	01622 225 033
East Kent Hospitals – Clinical Trials Office:	
Solid Tumours	01227 866 393

8.0 Personnel and Contact Information

A comprehensive, up to date list of MDM contact details can be found on the KMCN website via the following link: http://www.kentmedwaycancernetwork.nhs.uk/home-page/for-professionals/

9.0 Glossary

Acronyms in common usage throughout KMCN documentation

CNB	Cancer Network Board
CYP	Children & Young People (in relation to the IOG)
DCCAG	Diagnostic Cross Cutting Advisory Group
DOG	Disease Orientated Group (NSSG/TSSG/TWG)
DVH	Darent Valley Hospital
EK	East Kent
EKHUFT	East Kent Hospitals University Foundation Trust
HoP	High Level Operational Policy
IOSC	Improving Outcomes: A Strategy for Cancer
K&C	Kent & Canterbury Hospital, Canterbury, (EKHUFT)
KMCN	Kent & Medway Cancer Network
KMCRN	Kent & Medway Cancer Research Network
LSESN	London & South East Sarcoma Network
MFT	Medway Foundation Trust
MTW	Maidstone & Tunbridge Wells NHS Trust
NOG	Non Surgical Oncology Group *(Permanent oncologist sub group of the DOGs with a specific responsibility for chemo/rad pathways and advice to the DOG, Network and GEOGRAPHICAL LOCATIONs on new drugs)*
PoC	Pathway of Care *(Network agreed disease site specific clinical guidelines)*
QEQM	Queen Elizabeth the Queen Mother Hospital, Margate (EKHUFT)
QoL	Quality of life
RAT	Research and Trial Group *(Permanent sub-group of the DOGs with a specific responsibility for taking forward the clinical trials agenda)*
RMH	Royal Marsden Hospital
RNOH	Royal National Orthopaedic Hospital
QVH	Queen Victoria Foundation Trust Hospital East Grinstead
UCLH	University College Hospital London
WHH	William Harvey Hospital, Ashford (EKHUFT)
WK	West Kent

10.0 Document Administration

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Revision History			
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Feb 2012	1.1	Draft	Revision of document and change of title to capture treatment of benign tumours
Feb 2012	2	Final	Published
Mar – July 2013	2.1	Addition of bevacizumab as palliative treatment option for glioma Addition of temozolomide for palliative treatment of glioma for elderly patients. (section 3)	
August 2013	3	Final	K Nathan
June 2014	4	Final – removal of bevacizumab as 3rd line palliative treatment option for glioma Minor amendments to section 3 for Glioma	K Nathan
April 2015	4.1	Addition of: PCV as possible for adjuvant therapy for glioma. Single agent Lomustine as a palliative treatment option for glioma	K Nathan
June 2015	5	Final - Published	

January 2017	6	Updated guidelines with new practise recommendations and discussed NOG Dec 16	K Nathan
June 17	6	Published	
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