1 PROTOCOL SUMMARY

Title:

Radiation versus Observation following surgical resection of Atypical Meningioma: a randomised controlled trial (The ROAM trial).

Phase:

III

Population:

The trial will be open to all patients with newly diagnosed atypical meningioma who have undergone gross total surgical resection, and who meet the eligibility criteria.

Inclusion/exclusion criteria:
All patients who are considered for the ROAM trial must fulfil the following criteria:

Inclusion criteria

- Histologically confirmed newly diagnosed solitary atypical meningioma (WHO grade II) based on the 2016 WHO criteria [1]
- Age >/= 16 years
- All anatomical locations allowed except optic nerve sheath tumour
- Complete resection (Simpson 1, 2 or 3) as assessed by the surgeon
- Able to commence radiotherapy within 12 weeks of surgery
- WHO performance status 0, 1 or 2 (see Appendix 1)
- Women of reproductive potential must use effective contraception for the whole duration of the treatment
- Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial

Exclusion criteria

- Neurofibromatosis type II (NF-2)
- Optic nerve sheath tumours
- Multiple meningiomas
- Radiation-induced meningioma
- Clinical evidence of second malignancy, except for cervix carcinoma in situ or basal cell carcinoma, and history of invasive malignancy unless treated with curative intent and the patient has not been disease free for the last five years
- Previous intracranial tumour in the last 10 years treated with radiotherapy or chemotherapy
- Pregnant or lactating women

Study Centres and Distribution:	International multicentre European study, to be conducted in collaboration with European Organisation for Research and Treatment of Cancer (EORTC). Patients will be recruited from neurosurgical and oncology units in the UK, and throughout Europe with EORTC centres and Australia/New Zealand with the Trans Tasman Radiation Oncology Group (TROG).
Study Duration:	The trial will aim to recruit 190 patients over a period of 44 months, with approximately 118 patients to be recruited in the UK, however there will be no limit on the number of patients that either the UK sites, EORTC or TROG sites may recruit within the overall trial target. Patients will be followed up for a minimum of 5 years post surgery.
Description of Agent/ Intervention:	ROAM will be a two-arm, multi-centre, randomised controlled trial. The trial will randomise patients who have undergone gross total surgical resection of atypical (grade II) meningioma to receive either early adjuvant fractionated radiotherapy for 6 weeks (intervention) or active monitoring (comparator). This will be a 2-stage trial (both stages will run in parallel): • Stage 1 (feasibility and acceptability): this stage is designed to maximise recruitment. This is a rare condition and therefore it is important to maximise patient and clinician acceptability thereby optimising recruitment and retention. A qualitative study will be embedded within this stage of the trial (UK sites only) to achieve these goals. Patients wishing to continue will proceed to randomisation (stage 2). • Stage 2 (randomisation): patients who wish to participate in the trial will be randomised in a 1:1 ratio to either early radiotherapy or active monitoring.
Primary Objective:	To determine whether early adjuvant fractionated external beam radiotherapy reduces the risk of tumour recurrence or death due to any cause compared to active monitoring in newly diagnosed atypical meningioma
Secondary Objective/s:	• To assess the early and late effects of fractionated radiotherapy • To assess and compare quality of life in patients with atypical meningioma according to treatment arm • To assess and compare the neurocognitive function in patients with atypical meningioma according to treatment arm • To record the second line treatments (surgery, radiotherapy, radiosurgery) used at tumour recurrence according to treatment arm • To determine overall survival (OS) at 5 years • To assess the cost-effectiveness of adjuvant

radiotherapy compared to active monitoring
- To correlate proliferation rate and molecular characteristics with time to tumour recurrence (separate funding will be sought)

Schematic of study design: