

**Phase II Trial of Observation for Low-Risk Meningiomas and  
of Radiotherapy for Intermediate- and High-Risk Meningiomas**

**Schema**

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**Step 1**

Central pathology review/  
histology confirmation

**Step 2**

Treat/follow according to  
risk group

**Group I (Low Risk)**

Observation

**Group II (Intermediate Risk)**

Radiotherapy (54 Gy in 30 fractions)  
May be 3D-CRT or IMRT

**Group III (High Risk)**

Radiotherapy (60 Gy in 30 fractions)  
Must be IMRT

**Patient Population** - See Protocol Sections 3.0 & 5.0 for Eligibility and Pre-Registration Requirements

- Histopathologically confirmed meningioma **confirmed by central pathology review prior to Step 2 registration.**
- Risk categories are defined as follows:
  - Low (Group I): Patients with a newly diagnosed gross totally resected (Simpson's grade I, II, or III resections with no residual nodular enhancement on postoperative imaging) or subtotally resected (residual nodular enhancement or Simpson grade IV or V excision) World Health Organization (WHO) grade I meningioma. The extent of resection will be based upon the neurosurgeon's assessment and postoperative MR imaging.
  - Intermediate (Group II): Patients with a newly diagnosed gross totally resected WHO grade II meningioma or a recurrent WHO grade I meningioma irrespective of the resection extent. Resection extent will be assessed according to Simpson's grade on the same basis described above for the low-risk group.
  - High (Group III): Patients with high-risk features including a newly diagnosed or recurrent WHO grade III meningioma of any resection extent; a recurrent WHO grade II meningioma of any resection extent; or a newly diagnosed subtotally resected WHO grade II meningioma. Resection extent will be recorded on the same basis described above for the low-risk group.

**Objectives**

The **primary objective** of the study is to estimate the rates of progression-free survival (PFS) at 3 years in each of the patient risk groups. **Secondary objectives** are: to study the concordance, or lack thereof, between central and parent institution histopathologic diagnosis, grading, and subtyping; to estimate the incidence rates of grade 2+ acute and late adverse events for Group II (intermediate-risk) and Group III (high-risk) patients; to appraise histopathologic correlates of PFS including light microscopy, immunohistochemical analysis and microarray analysis; to evaluate, via central neuroradiology review, imaging (MRI) predictors at diagnosis, at any failure, and at 3 years; to conduct molecular correlative studies; to evaluate adherence to protocol-specific target and normal tissue radiation therapy parameters; and to estimate the rates of overall survival at 3 years in each of the patient risk groups.

**Required Sample Size**    **165 (55 Group I, 55 Group II, 55 Group III)**

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