"Phase III Trial of Post-Surgical Single Fraction Stereotactic Radiosurgery (SRS) Compared with Fractionated SRS for Resected Metastatic Brain Disease"

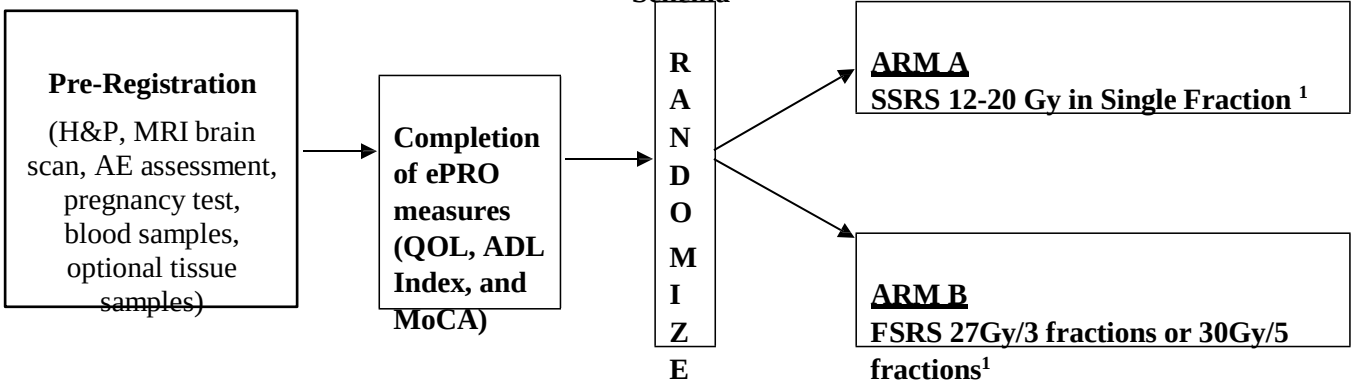
Pre-Registration Eligibility Criteria (see Section 3.2)

- Resected brain metastasis must be non-CNS primary site
- ≤3 unresected brain metastases at the time of screening
- Unresected lesions must measure <4.0cm in size
- One brain metastasis must be completely resected ≤30 days prior to registration
- Resected brain metastasis must measure ≥2 cm
- Resection cavity must measure <5.0 cm
- Age ≥18 years
- Karnofsky Performance Status of ≥60
- Women of childbearing potential must have negative urine or serum pregnancy test done ≤7 days prior to pre-registration
- Ability to complete an MRI of the head with contrast
- No evidence of leptomeningeal metastasis
- No prior whole brain radiation therapy
- Past radiosurgery to other lesions is allowed (i.e. however, cannot be the same location/lesion as the resected brain metastasis. Repeat SRS to the same lesion/location is NOT allowed.)
- May not have primary germ cell tumor, small cell carcinoma, or lymphoma
- Brain metastasis must be located ≥5 mm of the optic chiasm and outside the brainstem
- May not have had resection of more than one brain metastasis
- Must be fluent in English, Spanish, or French.

Registration Eligibility Criteria (see Section 3.3)

- Completion of the ePRO measures (or QOL booklet) and MoCA

Schema



[1] Unresected brain metastases will be treated with SRS; details as outlined in the treatment section.

Patients will be followed for 5 years or until death, whichever comes first.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.

3.0 PATIENT SELECTION

For questions regarding eligibility criteria, see the Study Resources page. Please note that the Study Chair cannot grant waivers to eligibility requirements.

3.1 On-Study Guidelines

This clinical trial can fulfill its objectives only if patients appropriate for this trial are enrolled. All relevant medical and other considerations should be taken into account when deciding whether this protocol is appropriate for a particular patient. Physicians should consider the risks and benefits of any therapy, and therefore only enroll patients for whom this treatment is appropriate.

Physicians should consider whether any of the following may render the patient inappropriate for this protocol:

- Psychiatric illness which would prevent the patient from giving informed consent.
- Medical conditions such as uncontrolled infection (including HIV), uncontrolled diabetes mellitus or a cardiac disease which, in the opinion of the treating physician, would make this protocol unreasonably hazardous for the patient.

3.2 Pre-Registration Eligibility Criteria

Use the spaces provided to confirm a patient's eligibility by indicating Yes or No as appropriate. It is not required to complete or submit the following page(s).

When calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test was performed on a Monday, the Monday one week later would be considered Day 7.

___ **3.2.1 Non-CNS Primary Site**

Pathology from the resected brain metastasis must be consistent with a non-central nervous system primary site. Patients with or without active disease outside the nervous system are eligible (including patients with unknown primaries), as long as the pathology from the brain is consistent with a non-central nervous system primary site.

___ **3.2.2 Number of Unresected Brain Metastases**

Three or fewer (i.e. 0 to 3) unresected brain metastases (as defined on the post-operative MRI) at the time of screening.

Note: Dural based metastases (e.g. commonly seen in breast cancer) are eligible.

___ **3.2.3 Size of Unresected Metastases**

Unresected lesions must measure <4.0 cm in maximal extent on the contrasted post-operative treatment MRI brain scan. The unresected lesions will be treated with SRS as outlined in the treatment section of the concept.

Note: The metastases size restriction does not apply to the resected brain metastasis.

___ **3.2.4 Number of Resected Brain Metastasis**

One brain metastasis must be completely (gross total resection) resected ≤30 days prior to pre-registration. For reference, please find Residual Disease Exclusion Cases under Supplemental Documents on the A071801 landing page on the CTSU website.

NOTE: May not have had resection of more than one brain metastasis

___ **3.2.5 Size of Resected Brain Metastasis**

The resected brain metastasis must measure 2 cm or larger on the pre-operative MRI.

___ **3.2.6 Size of Resection Cavity and Extent of Resection**

Resection cavity must measure <5.0 cm in maximal extent and the resection must be complete (gross total resection) on the post-operative MRI obtained ≤30 days prior to pre-registration.

___ **3.2.7 Age ≥ 18 years**

___ **3.2.8 Karnofsky Performance Status of ≥60**

___ **3.2.9 For women of childbearing potential only, a negative urine or serum pregnancy test done ≤ 7 days prior to pre-registration is required**

- Men and women of childbearing potential must be willing to employ adequate contraception throughout the study and for men for up to 3 months after completing treatment.
- A female of childbearing potential is a sexually mature female who: 1) has not undergone a hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal for at least 12 consecutive months (i.e., has had menses at any time in the preceding 12 consecutive months).

___ **3.2.10 Ability to complete an MRI of the head with contrast**

___ **3.2.11 The brain metastasis must be located >5mm of the optic chiasm and outside the brainstem**

___ **3.2.12 Must not have any prior whole brain radiation therapy.**

___ **3.2.13 Past radiosurgery to other lesions is allowed**

NOTE: The surgically resected lesion cannot be the same location treated in the past with radiosurgery (i.e. repeat radiosurgery to the same location/lesion is not allowed on this protocol)

___ **3.2.14 May not have primary germ cell tumor, small cell carcinoma, or lymphoma.**

___ **3.2.15 No evidence of leptomeningeal metastasis (LMD).**

NOTE: For the purposes of exclusion, LMD is a clinical diagnosis, defined as positive CSF cytology and/or equivocal radiologic or clinical evidence of leptomeningeal involvement. Patients with leptomeningeal symptoms in the setting of leptomeningeal enhancement by imaging (MRI) would be considered to have LMD even in the absence of positive CSF cytology, unless a parenchymal lesion can adequately explain the neurologic symptoms and/or signs. In contrast, an asymptomatic or minimally symptomatic patient with mild or nonspecific leptomeningeal enhancement (MRI) would not be considered to have LMD. In that patient, CSF sampling is not required to formally exclude LMD, but can be performed at the investigator's discretion based on level of clinical suspicion [47].

___ **3.2.16 Must be fluent in English, Spanish, or French.**

3.3 Registration Eligibility Criteria

___ **3.3.1 Completion of all baseline ePRO (or booklet quality of life measures) and MoCA.**