NRG-BN012
SCHEMA

Radiographic confirmation of surgical/stereotactic radiosurgery (SRS) candidates with 1-4 brain metastases, one of which requires resection

STRATIFY

- lesion number (1 versus 2-4)
- breast cancer histology (yes versus no)
- posterior fossa resection (yes versus no)
- targeted or immunotherapy within 4 weeks prior to registration or planned for within 8 weeks after surgery (yes versus no)

RANDOMIZE*

↓

Arm 1: Post-resection SRS

Surgery
↓
Post-resection SRS to the resection cavity (12 to 20 Gy in a single fraction) within 10-30 days after resection

↓

Arm 2: Pre-resection SRS

Pre-resection SRS (12 to 20 Gy in a single fraction) within 7 days prior to surgical resection
↓
Surgery

* Randomization is 1:1

3. ELIGIBILITY AND INELIGIBILITY CRITERIA

Notes: Per NCI guidelines, exceptions to inclusion and exclusion criteria are not permitted. For questions concerning eligibility see protocol cover page. For radiation therapy-related eligibility questions, please contact RTQA (see protocol cover page).

3.1 Eligibility Criteria

A patient cannot be considered eligible for this study unless ALL of the following conditions are met.

NOTE: For calculations, the date of a test result is considered Day 0.

3.1.1 Radiographic confirmation of 1-4 brain metastases, one of which requires resection, as defined by MRI with contrast obtained within 14 days prior to registration

- The maximum diameter of the lesion to be resected on the post-contrast MRI, as measured on any orthogonal plane (axial, sagittal, coronal), must measure ≥ 2.0 cm and ≤ 5.0 cm.
- The maximum diameter of any lesion which will not be resected must be ≤ 4.0 cm in maximum diameter.

3.1.2 Known active or history of invasive non-CNS primary cancer based on documented pathologic diagnosis within the past 3 years.

3.1.3 All brain metastases must be located ≥ 5 mm from the optic chiasm and outside the brainstem.

3.1.4 Patient is able to medically tolerate surgery and SRS.

3.1.5 Lesions chosen for surgical therapy must be deemed appropriate targets for safe, gross total resection by the treating surgeon.

3.1.6 History/physical examination within 14 days prior to registration;

3.1.7 Age ≥ 18;

3.1.8 Karnofsky Performance Status (KPS) ≥ 60 within 14 days prior to registration;

3.1.9 A negative urine or serum pregnancy test (in persons of childbearing potential) within ≤ 14 days prior to registration. Childbearing potential is defined as any person who has experienced menarche and who has not undergone surgical sterilization (hysterectomy or bilateral oophorectomy) or who is not postmenopausal.

3.1.10 Participants who are sexually active must agree to use medically acceptable forms of contraception during treatment on this study to prevent pregnancy.

3.1.11 The patient or a legally authorized representative must provide study-specific informed consent prior to study entry and, for patients treated in the U.S., authorization permitting release of personal health information.

3.2 Ineligibility Criteria

Patients with any of the following conditions are NOT eligible for this study.

3.2.1 Prior cranial radiotherapy, including whole brain radiotherapy, or SRS to the resection site. Note: The index lesion to be resected cannot have been previously treated with SRS (i.e. repeat radiosurgery to the same location/lesion is not allowed on this protocol). Previous SRS to other lesions is allowed.

3.2.2 Evidence of leptomeningeal disease (LMD).
Note: For the purposes of exclusion, LMD is a clinical diagnosis, defined as positive CSF cytology and/or unequivocal 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. 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.

3.2.3 Any medical conditions which would make this protocol unreasonably hazardous, including, but not limited to: contraindications to general endotracheal anesthesia; intracranial surgery; and stereotactic radiosurgery.

3.2.4 Primary histology of germ cell tumor, small cell carcinoma or lymphoma.

3.2.5 More than one brain metastasis planned for resection.

3.2.6 Inability to undergo MRI with contrast.

3.2.7 Planned administration of cytotoxic chemotherapy or tyrosine/multi-kinase inhibitors within the 3 days prior to, the day of, or within 3 days after the completion of SRS. Note: chemotherapy and immunotherapy outside of this window are allowed.