Study: Phase II trial of Hippocampal-Avoiding Whole Brain Irradiation with Simultaneous Integrated Boost for Treatment of Brain Metastases

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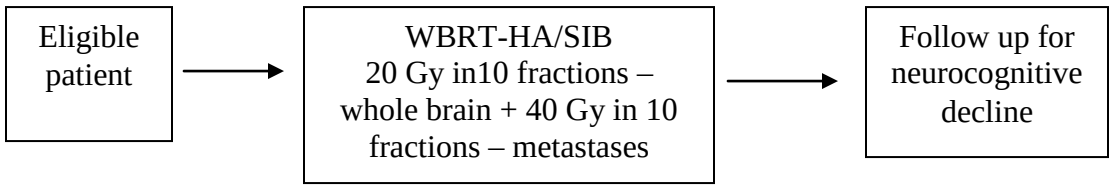
1.0 SCHEMA



Patient Population: (See Section 3.0 for Eligibility)

1. Pathologically proven diagnosis of a non-hematopoietic malignancy other than small cell lung cancer and germ cell malignancy.
2. Patients with less than 9 discrete metastases on MRI.
3. Measurable brain metastasis outside a 5-mm margin around either hippocampus
4. Have not been treated with SRS or surgical resection.
5. RTOG RPA class I or II
6. Life expectancy of at least 6 months
7. Age ≥ 18 years
8. Karnofsky performance status ≥ 70

Required sample size: 102

2.0 OBJECTIVES

2.1 Primary Objective

Evaluate delayed recall as assessed by the Hopkins Verbal Learning Test-Revised (HVTL-R) 6 months after whole-brain radiotherapy modified as outlined (WBRT-HA/SIB) for brain metastases.

2.2 Secondary Objectives

2.2.1 Evaluate time to neurocognitive failure as measured by cognitive decline on a battery of tests: the HVLT-R for free recall, delayed recall, and delayed recognition; the Controlled Word Association Test (COWAT); the Trail Making Test Parts A and B (TMT); the Medical Outcomes Scale-Cognitive Functioning Subscale (MOS); and the Mini-Mental Status Examination (MMSE) after WBRT-HA/SIB for brain metastases

2.2.2 Evaluate fatigue, as assessed by the Multidimensional Fatigue Inventory (MFI-20) after WBRT-HA/SIB for brain metastases.

2.2.3 Evaluate local control within the brain

2.2.3.1 Evaluate local control of brain metastases treated with integrated boost

2.2.3.2 Evaluate local control within the region of brain within the CTV receiving 20 Gy.

2.2.3.3 Evaluate local control within the hippocampal regions.

2.2.4 Evaluate time to radiographic progression after WBRT-HA/SIB for brain metastasis.
2.2.5 Evaluate overall survival after WBRT-HA/SIB for brain metastasis.
2.2.6 Evaluate adverse events according to CTCAE criteria.

3.0 PATIENT SELECTION

3.1 Conditions for Patient Eligibility

3.1.1 Pathologically (histologically or cytologically) proven diagnosis of a non-hematopoietic malignancy other than small cell lung cancer and germ cell malignancy.. Direct biopsy of CNS lesions is not necessarily required although could constitute an allowed site of tissue confirmation as medically prudent. Patients who have been disease free for more than 5 years prior to the appearance of CNS metastases should undergo repeat biopsy of either a systemic metastasis or the CNS metastases to confirm the recurrent malignancy.
3.1.2 Patients with measurable brain metastasis outside a 5-mm margin around either hippocampus
3.1.3 Patients with measurable brain metastasis who have not been or will not be treated with SRS or surgical resection (Note: These treatment options are only permitted at relapse)
3.1.4 History/physical examination within 28 days prior to registration
3.1.5 Patients must fall into RTOG recursive partitioning analysis (RPA) class I or II
3.1.6 Patients must have a life expectancy of at least 6 months.
3.1.7 Age $\geq$ 18 years
3.1.8 Karnofsky performance status $\geq$ 70
3.1.9 Patients must provide study-specific informed consent prior to study entry
3.1.10 Women of childbearing potential and male participants must practice adequate contraception
3.1.11 Women of childbearing potential must have a negative, qualitative serum pregnancy test $\leq$2 weeks prior to study entry

3.2 Conditions for Patient Ineligibility

3.2.1 Patients with greater than 9 discrete metastases on MRI.
3.2.2 Patients with leptomeningeal metastases
3.2.3 Patients with measurable brain metastasis not resulting from small cell lung cancer and germ cell malignancy
3.2.4 Plan for chemotherapy or targeted therapies during WBRT or over the subsequent 7 days
3.2.5 Contraindication to MR imaging such as implanted metal devices or foreign bodies, severe claustrophobia AND patients unable to receive gadolinium contrast agents
3.2.6 Serum creatinine > 1.4 mg/dl $\leq$ 28 days prior to study entry
3.2.7 Prior radiation therapy to the brain
3.2.8 Patients planning to undergo radiosurgery to any CNS lesion OR patients planning to have surgical resection of ALL of their CNS lesions