

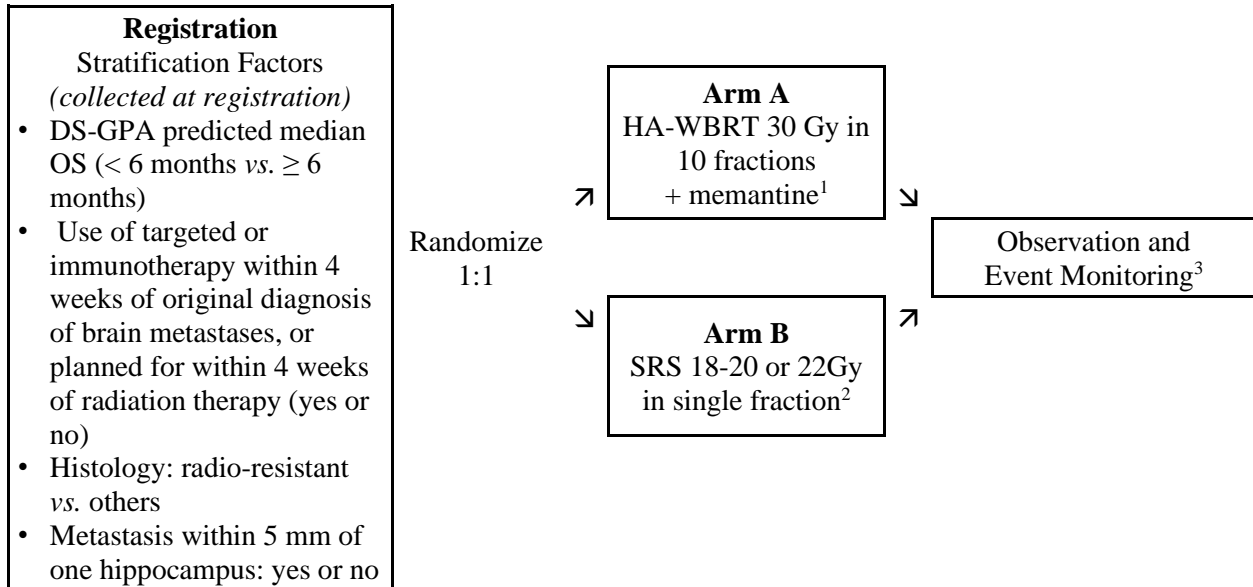
TREATMENT SCHEMA

This is an international multi-centre, open-label, randomized phase III trial comparing stereotactic radiosurgery (SRS) to hippocampal-avoidant whole brain radiotherapy (HA-WBRT) plus memantine in patients with 5 or more brain metastases.

Stratification

- DS-GPA predicted median overall survival [*Sperduto 2012; Sperduto 2017*] (< 6 months vs. \geq 6 months)
- Use of targeted or immunotherapy within 4 weeks of original diagnosis of brain metastases, or planned for within 4 weeks of radiation therapy (yes or no)
- Histology (radio-resistant* vs. other)
- Metastasis within 5 mm of one hippocampus (yes or no)

* Radio-resistant is defined as brain metastases from a sarcoma, melanoma, or renal cell carcinoma histology.



1. Memantine will start the same day as HA-WBRT and must start no later than before the fourth HA-WBRT treatment. The target dose for memantine is 20 mg (10 mg divided twice daily). Dose will be escalated by 5 mg per week.
2. Lesions < 4 cc in volume will receive 22Gy while lesions 4-10 cc in volume will receive 18-20; details as outlined in the treatment section.
3. In the event of progressive brain metastases or systemic progression the patient remains under observation

N = 206