NRG CC009

Phase III Trial of Stereotactic Radiosurgery versus Hippocampal Avoidant WBRT for Small Cell Lung Cancer Brain Metastases

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Background

• Whole-brain radiotherapy is standard of care for small-cell lung cancer brain metastases
  – Prior brain metastasis trials of SRS vs WBRT or HA-WBRT did not include small-cell lung cancer

• Cognitive toxicity from WBRT
  – Mitigated with SRS, memantine, hippocampal avoidance
  – Historic objections to SRS in small-cell related to concern for short interval CNS progression impacting OS
Background

- Emerging evidence re: SRS for SCLC brain mets
  - Serizawa et al\textsuperscript{2}: SRS SCLC n=34 vs. NSCLC n=211
    Comparable OS, CNS control, neurologic death
  - Yomo, Hayashi\textsuperscript{3}: SRS SCLC n=70 (46 without prior PCI/WBRT)
    Med OS 7.8 mos
  - NCDB\textsuperscript{4}: N=200 SRS vs. WBRT for SCLC brain mets
    Favorable OS with SRS overall and in matched data
  - Cifarelli et al\textsuperscript{5}: N=293 SRS (61 without prior PCI/WBRT)
    Median OS 7.5 mo with upfront SRS, necrosis rate 5%
First-line Radiosurgery vs Whole-Brain Radiotherapy for Small Cell Lung Cancer Brain Metastases: The FIRE-SCLC Cohort Study
Rusthoven et al., *JAMA Oncology.* 2020 Jun 4

Stereotactic radiosurgery versus whole brain radiotherapy in patients with intracranial metastatic disease and small-cell lung cancer: a systematic review and meta-analysis
Karolina Gaebe, Alyssa Y Li, Amy Park, Ambica Parmar, Benjamin H Lok, Arjun Sahgal, Kelvin K W Chan, Anders W Erickson, Sunit Das

**Summary**

**Background** Patients with small-cell lung cancer (SCLC) are at high risk for intracranial metastatic disease (IMD). Although stereotactic radiosurgery (SRS) has supplanted whole brain radiotherapy (WBRT) as first-line treatment for IMD in most solid cancers, WBRT remains first-line treatment for IMD in patients with SCLC. We aimed to evaluate the efficacy of SRS in comparison with WBRT and assess treatment outcomes following SRS.

- After SRS, 34% underwent salvage SRS vs 16% salvage WBRT
- Leptomeningeal progression (10.8%), neurological mortality (12.4%)
Reinventing the Wheel: Safer Delivery of WBRT

- Practice-changing evidence re: WBRT

RTOG 0614\textsuperscript{1}:

Hazard ratio of memantine = 0.78

NRG CC001\textsuperscript{2}:

Hazard ratio of hippocampal avoidance added to memantine = 0.74

\textsuperscript{1}Brown et al. Neuro-Onc 2013 \textsuperscript{2}Brown, Gondi et al. JCO
NRG CC009: Phase III Trial Stereotactic Radiosurgery versus Hippocampal-Avoidant Whole-Brain Radiotherapy for 10 or Fewer Brain Metastases from Small Cell Lung Cancer

PIs: Chad Rusthoven (Univ of Colorado) + Vinai Gondi (Northwestern)

Sample Size: 200 patients

**Basic Eligibility:** Small cell lung cancer; ≤10 brain mets≤3cm; total vol 30cc; KPS≥70

**Primary endpt:** Time to cognitive failure--HVLT-R, COWA, and TMT A and B

**Basic Statistical Design:**
Cognitive fxn failure 58.8% at 6 mos with HA-WBRT+mem vs. 41.8% at 6 mos with SRS.
150 analyzable pts

*Pts enrolled on SWOG trial will have been exposed to NCF Testing*
Logistics and Trial Accrual

• Collaboration:
  – Support from SWOG, Alliance
  – SWOG MRI surveillance +/- PCI trial: brain met failures on observation arm can dual-enroll

February 2021: Protocol Activated
As of 7/1/22, N=28 enrolled
N=15 in past 6 months (surpassed accrual in 2021)

March 2022 (13 months after activation):
Trial activated at 77 sites, pending activation at 209 sites
NRG CC003: Trial activated 140 sites one year into activation