N107C

A Phase III Trial of Post-Surgical Stereotactic Radiosurgery (SRS) Compared with Whole Brain Radiotherapy (WBRT) for Resected Metastatic Brain Disease

ClinicalTrial.gov Identifier: NCT01372774

Study Background

Trial Description

RATIONALE: Stereotactic radiosurgery may be able to send x-rays directly to the tumor and cause less damage to normal tissue. Radiation therapy uses high-energy x rays to kill tumor cells. It is not yet known whether stereotactic radiosurgery is more effective than whole-brain radiation therapy in treating patients with brain metastases that have been removed by surgery. PURPOSE: This randomized phase III trial studies how well stereotactic radiosurgery works compared to whole-brain radiation therapy in treating patients with brain metastases that have been removed by surgery.

Arms:

Arm I - WBRT: (Active Comparator): Patients undergo whole brain radiotherapy (WBRT) once a day, 5 days a week, for approximately 3 weeks. Patient observation/follow up occurs at week 12 and months 6, 9, 12, 16 and 24 post registration/randomization. Event monitoring occurs every 6 months until 5 years post registration/randomization.

Arm II - SRS: (Experimental): Patients undergo stereotactic radiosurgery (SRS) using a gamma knife or a linear accelerator procedure. Patient observation/follow up occurs at week 12 and months 6, 9, 12, 16 and 24 post registration/randomization. Event monitoring occurs every 6 months until 5 years post registration/randomization.

Objectives:

- Primary Goals
    1. Overall Survival - To determine in patients with one to four brain metastases whether there is improved overall survival in patients who receive SRS to the surgical bed compared to patients who receive WBRT.
    2. Neurocognitive Progression - To determine in patients with one to four brain metastases whether there is less neurocognitive progression post-

randomization in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

- Secondary Goals
    1. Quality of Life (QOL) - To determine in patients with resected brain metastases whether there is improved QOL in patients who receive SRS to the surgical bed compared to patients who receive WBRT.
    2. Central Nervous System Failure - To determine in patients with one to four brain metastases whether there is equal or longer time to central nervous system (CNS) failure (brain) in patients who receive SRS to the surgical bed compared to patients who receive WBRT.
    3. Functional Independence - To determine in patients with one to four brain metastases whether there is longer duration of functional independence in patients who receive SRS to the surgical bed compared to patients who receive WBRT.
    4. Long-Term Neurocognitive Status - To determine in patients with one to four brain metastases whether there is better long-term neurocognitive status in patients who receive SRS to the surgical bed compared to patients who receive WBRT.
    5. Adverse Events - To tabulate and descriptively compare the post-treatment adverse events associated with the interventions.
    6. Local Tumor Bed Recurrence - To evaluate local tumor bed recurrence at 6 months with post-surgical SRS to the surgical bed in comparison to WBRT.
    7. Local Recurrence - To evaluate time to local recurrence with post-surgical SRS to the surgical bed in comparison to WBRT.
    8. CNS Failure Patterns - To evaluate if there is any difference in CNS failure patterns (local, distant, leptomeningeal) in patients who receive SRS to the surgical bed compared to patients who receive WBRT.
- OUTLINE: This is a multicenter study. Patients are stratified according to age in years (< 60 vs ≥ 60), extracranial disease controlled (≤ 3 months vs > 3 months), number of pre-operative brain metastases (1 vs 2-4), histology (lung vs radioresistant [brain metastases from a sarcoma, melanoma, or renal cell carcinoma histology] vs other), and resection cavity maximal diameter (≤ 3 cm vs > 3 cm). Patient must complete baseline QOL and neurocognitive tests prior to registration/randomization. Patients are randomized to 1 of 2 treatment arms.
    - Arm I: Patients undergo whole-brain radiotherapy (WBRT) once a day, 5 days a week, for approximately 3 weeks.
    - Arm II: Patients undergo stereotactic radiosurgery (SRS) using a gamma knife or a linear accelerator procedure.
- Event monitoring occurs up to 5 years post registration/randomization.

Study Milestones:

Start date: July 2011

Primary Completion Date: August 2016

Publication Information:

Analysis Type: Primary

Pubmed ID: 28687377

Citation: Lancet Oncol. 2017 Aug;18(8):1049-1060. doi: 10.1016/S1470-2045(17)30441-2. Epub 2017 Jul 4.

Associated Datasets: NCT01372774-D1-Dataset.csv (baseline), NCT01372774-D2-Dataset.csv (barthel), NCT01372774-D3-Dataset.csv (cogdata), NCT01372774-D4-Dataset.csv (qoldata), NCT01372774-D5-Dataset.csv (aedata)

Dataset Information:

Dataset Name: NCT01372774-D5-Dataset.csv (aedata)

Description: Dataset NCT01372774-D5-Dataset.csv (aedata) is one of 5 datasets associated with PubMed ID 28687377. This dataset includes multiple records for each patient that experienced at least one adverse event. There are 582 records for 150 patients. Included is the maximum adverse event grade experienced over the course of study treatment and active-monitoring phase.

Notes:

- This dataset contains the information presented in Table 3 in the publication, and Supplemental Tables S6a, S6b, S6c, and S6d.
- Data can be used to approximate published study findings, but exact reproduction of previous manuscripts may not be possible in some cases (e.g., when data must be modified for de-identification purposes or have undergone further data cleaning).

NCT01372774-D5-Dataset.csv (aedata) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Patient Reference	PATREF		
Arm	ARM	A = WBRT B = SRS	SRS = Stereotactic Radiosurgery WBRT = Whole Brain Radiotherapy
Adverse Event term	ae_term		Description of adverse event
Event Grade	ae_grade	1, 2, 3, 4, 5	Common Terminology Criteria for Adverse Events (CTCAE) - version 4.0
Relation to treatment	related	N=No, Y=Yes	Variable *grd5attr* in dataset NCT01372774-D1 contains grade 5 AE attribution as originally reported by treating sites. Variable *related* contains updated and corrected AE attribution after further review. Thus, the grade 5 attribution reported in this variable does not match with *grd5attr* in dataset D1.
Serious Adverse Event as reported via Expedited Reporting	aersub	1 = Yes Missing values indicate that the AE was not reported via expedited reporting	