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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-D3-Dataset.csv (cogdata)

Description: Dataset NCT01372774-D3-Dataset.csv (cogdata) is one of 5 datasets associated with PubMed ID 28687377. This dataset includes one record per patient for Cognitive Scores per timepoint available. 191 randomized patients have at least one evaluation. There are 605 records in this data set.

Notes:

- Instead of providing the tests raw scores, this dataset includes the standardized scores (z-scores) for each test. Published normative data was used for this standardization.
- The change in z-score from baseline was calculated to determine deterioration for each test at 6-month. In the publication listed above, cognitive deterioration was defined as a drop of greater than 1 SD from baseline in at least one of the six cognitive tests (see Table 2).
- The following tables in the supplementary appendix were created using the change from baseline in the z-scores and different thresholds to define cognitive deterioration:
    - Tables S1a: Cognitive Deterioration at 6 months (cognitive deterioration defined as 1.5 SD drop in at least 2 test scores)
    - Table S1b: Cognitive Deterioration at 6 months (cognitive deterioration defined as 2.0 SD drop in at least 1 test score)
    - Table S1c: Cognitive Deterioration at 6 months (cognitive deterioration defined as 3.0 SD drop in at least 1 test score)
    - Table S2: Cognitive Deterioration at 3 months (cognitive deterioration defined as 1SD drop in at least 1 test score)
- A missing Z-score represents data unavailable, due to the patient not attempting that section of the evaluation. This dataset does not include data for patients who did not attempt any portion of the cognitive evaluation at that time point.
- This dataset contains information presented in Tables 1 and 2 in the publication and Supplemental Tables S1a, S1b, S1c and S2.
- 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-D3-Dataset.csv (cogdata) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Patient Reference	PATREF		
Arm	ARM	A = WBRT B = SRS	SRS = Stereotactic Radiosurgery WBRT = Whole Brain Radiotherapy

	timepoint	0 = Baseline 1 = 3-month 2 = 6-month 3 = 9-month 4 = 12-month 5 = 16-month 6 = 24-month	Time point at which the evaluation was completed
Z Score: HVLT Total Recall	ztotrec		Hopkins Verbal Learning Test-Revised (HVLT-R): Immediate Recall Sum of Trial 1, Trial 2, Trial 3
Z Score: HVLT Delayed Recall	zdelrec		Hopkins Verbal Learning Test-Revised (HVLT-R): Delayed recall total
Z Score: HVLT Delayed Recognition	zdrecog		Hopkins Verbal Learning Test-Revised (HVLT-R): Delayed Recognition
Z Score: TMA time to complete	ztma_sec		Trail Making Test Part A Time to complete (seconds) Discontinued after 3 minutes
Z Score: TMB time to complete	ztmb_sec		Trail Making Test Part B Time to complete (seconds) Discontinued after 5 minutes
Z Score: COWAT Total	zcowatot		Controlled Oral Word Association Test: Total Adjusted score (total words + correction)