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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-D4-Dataset.csv (qoldata)

Description: Dataset NCT01372774-D4-Dataset.csv (qoldata) is one of 5 datasets associated with PubMed ID 28687377. This dataset includes one record per patient for QOL Scores at different time points.

Notes:

- FACT-Br subscores and scores were generated using the standard scoring algorithm for this instrument. The scoring algorithm does not produce a subscore if more than 50% of the items in the subsection are missing. This dataset reflects these instances as missing (blank) data.
- For the other QOL items included, blanks represent unanswered items.
- For analysis, QOL scores were transformed to a 0-100 scale (as included in this dataset), with higher scores being higher quality of life. A 10-point change on this scale was considered clinically significant.
- Supplemental tables S4a, S4b, S5a, and S5b can be reproduced using this data.
- 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-D4-Dataset.csv (qoldata) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Patient Reference	PATREF		
Arm	ARM	A = WBRT B = SRS	SRS = Stereotactic Radiosurgery WBRT = Whole Brain Radiotherapy
Time Point	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 an evaluation was completed
Physical well-being subscore	pwb_sc	0-100	For all scores, higher scores indicate better quality of life. Missing = indicates data is unavailable per scoring algorithm
Social/Family well-being subscore	sfwb_sc	0-100	
Emotional well-being subscore	ewb_sc	0-100	

Functional well-being	fwb_sc	0-100	
subscore			
General section Score	factg_sc	0-100	
Additional concerns section Score	br_sc	0-100	
Total score FactBr	factbr_sc	0-100	
Overall Quality of Life	BL_UNISC	0-100	For all scores, higher scores indicate better quality of life. Missing = indicates data is unavailable (i.e., patient did not complete questions)
Level of Fatigue	BL_FATIG	0-100	
Overall QOL	LASA01	0-100	
Overall Mental Well Being	LASA02	0-100	
Overall Physical Well Being	LASA03	0-100	
Overall Emotional Well Being	LASA04	0-100	