Alliance for Clinical Trials in Oncology N0574:

Phase III Randomized Trial of the Role of Whole Brain Radiation Therapy in Addition to Radiosurgery in the Management of Patients with One to Three Cerebral Metastases

ClinicalTrials.gov Identifier: NCT00377156

Study Background

Trial Design: A randomized phase III trial, using a 1:1 randomization, patients go on to

- Arm A: Radiosurgery (SRS)
- Arm B: Radiosurgery (SRS) + Whole Brain Radiation (WBRT)

This study was designed to include 70 patients who were accrued by Z0300, as N0574 is meant to be a continuation of ACOSOG Z0300.

Objectives: Primary

To ascertain in patients with one to three brain metastases whether there is less neurocognitive progression at 3 months post-radiosurgery in patients who receive SRS alone (Arm A) compared to patients who receive SRS combined with WBRT (Arm B).

Secondary

- To ascertain in patients with one to three brain metastases whether there is equal (or greater) time to central nervous system (CNS) failure (brain) in patients who receive SRS alone (Arm A) compared to patients who receive SRS combined with WBRT (Arm B).
- To ascertain in patients with one to three brain metastases whether there is improved QOL in patients who receive SRS alone (Arm A) compared to patients who receive SRS combined with WBRT (Arm B).
- To ascertain in patients with one to three brain metastases whether there is longer duration of functional independence in patients who receive SRS alone (Arm A) compared to patients who receive SRS combined with WBRT (Arm B).
- To ascertain in patients with one to three brain metastases whether there is better long-term neurocognitive status in patients who receive SRS alone (Arm A) compared to patients who receive SRS combined with WBRT (Arm B).
- To tabulate and descriptively compare the post-treatment adverse events associated with the interventions.

- To compare in patient with one to three brain metastases the overall survival in patients who receive SRS alone (Arm A) compared to patients who receive SRS combined with WBRT (Arm B).

Stratification Factors:

1. Age (years)
   - 18 to 59
   - ≥ 60
2. Extracranial disease controlled (months)
   - ≤ 3
   - > 3
3. Number of brain metastases
   - 1
   - 2
   - 3

Study History:

07/28/2006 Study was activated. This trial is a continuation of the ACOSOG trial Z0300, which was closed by ACOSOG leadership in 2004.

10/24/2008 Amendment 3, updated the objectives of the study to make neurocognitive progression the primary endpoint.

12/19/2013 Study permanently closed to accrual.

Publication Information

Analysis Type: Primary Endpoint Analysis

PubMed ID: 27458945

Citation: Brown PD, Jaeckel K, Ballman KV, Farace E, Cerhan JH, Anderson SK, Carrero XW, Barker FG, Deming R, Burri SH, Ménard C, Chung C, Stieber VW, Pollock BE, Galanis E, Buckner JC, Asher, AL. Effect of Radiosurgery Alone vs Radiosurgery With Whole Brain Radiation Therapy on Cognitive Function in Patients With 1 to 3 Brain Metastases: A Randomized Clinical Trial. *JAMA.* 2016;316(4):401-409. doi:10.1001/jama.2016.9839

Associated Datasets:
NCT00377156-D1 (BASE)
NCT00377156-D2 (NCOG3MO)
NCT00377156-D3 (QOLDATA)
NCT00377156-D4 (LTSURV)
NCT00377156-D5 (AE3PLUS)

Dataset Information

Dataset Name: NCT00377156-D2 (NCOG3MO)

Description: The NCT00377156-D2 (NCOG3MO) dataset is one of 5 datasets associated with PubMed ID 27458945. This dataset includes one record per patient for Cognitive Scores 3-month only. Includes only patients evaluable for primary endpoint (N = 111).

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).

NCT00377156-D2 (NCOG3MO) Data Dictionary

Variable Name	Variable Description	Codes	Notes
STUDY_ID	Study Identifier	N0574	
SUBJECT	Subject	Character values	De-identified patient ID
ARM	Randomized Treatment Arm	A = SRS B = SRS + WBRT	SRS = Radiosurgery WBRT = Whole Brain Radiotherapy
Cognitive Test Scores – at 3-month evaluation Z-scores are computed using published normative data for each score included in testing. A missing Z-score represents data unavailable, due to patient not completing that sections of the cognitive evaluation. From the z-scores provided in this dataset, different definitions of deterioration and cognitive progression can be used. In the manuscript reporting the primary endpoint: For each score *deterioration* was defined as a drop ≥ 1.0 from baseline; and *cognitive progression* was defined as a drop of at least one standard deviation from baseline in at least one cognitive test scores. Deterioration: if score $_{3\ month}$ – score $_{baseline}$ ≤ -1.0 Cognitive progression: at least one of the scores met the condition for deterioration Supplemental tables report deterioration and cognitive progression using different definitions.			
ztotrec	Hopkins Verbal Learning Test-Revised (HVLT-R): Immediate Recall		Sum of Trial 1, Trial 2, Trial 3
zdelrec	Hopkins Verbal Learning Test-Revised (HVLT-R): Delayed recall total		
zdindex	Hopkins Verbal Learning Test-Revised (HVLT-R): Recognition		

Variable Name	Variable Description	Codes	Notes
ztmatime	Trail Making Test Part A		Time to complete (seconds) Discontinued after 3 minutes
ztmbtime	Trail Making Test Part B		Time to complete (seconds) Discontinued after 5 minutes
zcowatot	Controlled Oral Word Association Test: Total		Adjusted score (total words + correction)
zgpstime	Grooved Pegboard Test		Time to complete in seconds (for dominant hand)