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:

- Age (years)
  - 18 to 59
  - ≥ 60
- Extracranial disease controlled (months)
  - ≤ 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-D1 (BASE)

Description: The NCT00377156-D1 (BASE) dataset is one of 5 datasets associated with PubMed ID 27458945. This dataset provides information on patient evaluability, baseline demographics, stratification factors, baseline QOL measures, baseline cognitive scores, and intracranial (brain) tumor progression and survival status and time. There is one observation per patient accrued to this study (N=213).

Note: There may be some discrepancies between the data and supplemental eTable 12, but the data are correct.

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-D1 (BASE) 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
EVALUABL	Evaluable for primary analysis	Y = Yes N = No	111 were included in the primary end point analysisas defined in the study protocol.
ptflow	Subject Flow	A = Baseline Cognitive Evaluation not done B = Follow-up < 90 days C = Died prior to 90 days D = Clinical Evaluation at 3-months, but Cognitive Evaluation not done E = Evaluable	Refer to Figure 1 of the manuscript for Participant Flow in the trial.
ptflowrsn	Reason patient was not included in the primary endpoint analysis	Missing = Evaluable for primary analysis	Refer to Figure 1 of the manuscript for Participant Flow in the trial.
LTSURV	Long-term Survivor	Y = Yes N = No	34 evaluable patients who survived for 12 months after

Variable Name	Variable Description	Codes	Notes
			randomization and had at least one neurocognitive evaluation after 3 months.
Stratification Factors			
AGE_G	Age Group	1 = 18 to 59 years 2 = ≥ 60 years	
DZ_CNTRL	Extra cranial disease controlled	1 = ≤ 3 months 2 = > 3 months	
N_BRMET	Number of brain metastases	1 2 3	
SEX	Gender	m = Male f = Female	
AGE	Age at randomization		Years
RACEW	Race	1 = White 2 = Non-White 9 = Not reported	Category "Non-White" includes: • Black or African American • Asian • American Indian or Alaska Native
PS	ECOG Performance Score	0 = Asymptomatic and fully active. 1 = Symptomatic; fully ambulatory; restricted in physical strenuous activity. 2 = Symptomatic; ambulatory; capable of all self-care; more than 50% of waking hours are spent out of bed. Missing = patient evaluated, data not recorded.	
TUMSITE	Primary Tumor Site	1 = Breast 2 = Colorectal 3 = Lung 4 = Skin/Melanoma 5 = Prostate 6 = Bladder 7 = Kidney 8 = Sarcoma	

Variable Name	Variable Description	Codes	Notes
		9 = Gynecologic 10 = Other Missing = unknown primary	
CRANIAL	Neurologic Examination	1 = Normal 2 = Abnormal Missing = patient not evaluated.	
SENSATN	Neurologic Examination	1 = Normal 2 = Abnormal Missing = patient not evaluated.	
MOTOR	Neurologic Examination	1 = Normal 2 = Abnormal Missing = patient not evaluated.	
CEREBELR	Neurologic Examination	1 = Normal 2 = Abnormal Missing = patient not evaluated.	
pwb	Physical Well-Being Subscore	0-28	Raw scores (generated by scoring algorithm) Missing = score unavailable
sfwb	Social/Family Well-Being Subscore	0-28	
ewb	Emotional Subscore	0-24	
fwb	Functional Subscore	0-28	
factg	FACT-Br General Score	0-108	
br	Additional Concerns	0-92	
factbr	FACT-Br Total Score	0-200	
barthel	Barthel ADL index (Functional Independence)	0 to 100 in 5-point increments Missing = patient not evaluated.	
ztotrec	Hopkins Verbal Learning Test-Revised (HVLT-R): Immediate Recall	Missing = score unavailable	Sum of Trial 1, Trial 2, Trial 3
zdelrec	Hopkins Verbal Learning Test-Revised (HVLT-R): Delayed recall total	Missing = score unavailable	
zdindex	Hopkins Verbal Learning Test-Revised (HVLT-R):	Missing = score unavailable	

Variable Name	Variable Description	Codes	Notes
	Recognition		
ztmatime	Trail Making Test Part A	Missing = score unavailable	Time to complete (seconds) Discontinued after 3 minutes
ztmbtime	Trail Making Test Part B	Missing = score unavailable	Time to complete (seconds) Discontinued after 5 minutes
zcowatot	Controlled Oral Word Association Test: Total	Missing = score unavailable	Adjusted score (total words + correction)
zgpstime	Grooved Pegboard Test	Missing = score unavailable	Time to complete in seconds (for dominant hand)
lpgstat	Local Brain Progression Status	0 = censor (no death and no progression) 1 = competing risk (death or other progression) 2 = brain progression	
dpgstat	Distant Brain Progression Status	0 = censor (no death and no progression) 1 = competing risk (death or other progression) 2 = brain progression	
pgtime	Time to Brain Progression		Time (days) to first brain progression or last evaluation/known alive
fustat	Vital status	0 = alive 1 = death	
futime	Vital status time		Time (days) to last known alive or death date
SUBTX	Subsequent treatment	Character field Missing = No subsequent treatment reported	Treatment received after protocol treatment ended.
CNS_NECR	Safety and Toxicity	0 = Did not experience 1 = Experienced at least once	Patient experienced CNS Necrosis (any grade)
AE3PLUS	Safety and Toxicity	0 = Did not experience 1 = Experienced at least once	Patient experienced at least one grade 3 or higher adverse event