

A Phase III Three-Arm Trial in Patients With 1-3 Brain Metastases Comparing Whole Brain Radiation (WBRT) and Stereotactic Radiosurgery (SRS) Alone Versus With Temozolomide or With Erlotinib

Schema

S T R A T I F Y	<u>RPA Class</u>	R A N D O M I Z E	<u>Arm 1</u>
	1. Class I: < 65 yrs old & no extra-cranial metastases		WBRT + SRS
	2. Class II: ≥ 65 yrs old or extra-cranial metastases		<u>Arm 2</u>
			WBRT + SRS + Temozolomide*
	<u>Number of Metastases</u>		<u>Arm 3</u>
	1. One		WBRT + SRS + Erlotinib*
	2. Two or Three		
	<u>Extent of Extracranial Disease</u>		
	1. None		
	2. Present		

*Temozolomide and erlotinib may be discontinued after completion of radiation therapy.

Patient Population - See Protocol Section 3.0 & 5.0 for Eligibility and Pre-Registration Requirements

- Histologically confirmed non-small cell lung cancer with 1-3 intraparenchymal brain metastases
- Well-circumscribed intraparenchymal brain lesion with maximum tumor diameter (≤ 4.0 cm per lesion). If multiple lesions are present and one lesion is at the maximum diameter, the other(s) must not exceed 3.0 cm in maximum diameter.
- Patients who have undergone subtotal resection are eligible providing residual disease is ≤ 4.0 cm in maximum diameter.
- No metastases to brain stem, midbrain, pons, medulla or within 10 mm of the optic apparatus (*optic nerves and chiasm*).
- No clinical or radiographic evidence of progression of extracranial disease in the month prior to randomization. (Patients who present with symptoms of brain metastases at the time of initial diagnosis are eligible and do not need to demonstrate one month of stable scans.)

Objectives

The main objective of the study is to determine if either temozolomide or erlotinib combined with WBRT and SRS improves survival of patients with 1- 3 brain metastases from non-small cell lung cancer compared to WBRT and SRS alone. A further objective of the study is to compare the effect of the treatment regimens on the following secondary endpoints: time to CNS progression, quality-adjusted survival, change in quality of life (FACT-Br subscale) at 3 months, change in patient performance status at 6 months, change in steroid dependence at 6 months, cause of death (neurologic vs. other), and effects of non-protocol chemotherapy.

Required Sample Size: 381

Principal Investigator: Paul W. Sperduto, MD, MAPP, psperduto@mropa.com, 952-442-6000