

Phase I Study of Stereotactic Radiation and Sacituzumab Govitecan with Zimberelimab in the Management of Metastatic Triple Negative Breast Cancer with Brain Metastases (NCT06238921)

Kamran A. Ahmed MD[1], Youngchul Kim PhD[2], Robin Dowell BS[1], Daniel E. Oliver MD[1], Matthew N. Mills MD[1], Rajesh Nair PhD[3], Avan Armaghani MD[4], Ricardo L. Costa MD[4], Tracey O'Connor MD[4], Geethapriya Rajasekaran Rathnakumar MD[4], Hatem Soliman MD[4], Aixa E. Soyano MD[4], Elizabeth Tan-Chiu MD[4], Peter A. Forsyth MD[5], John A. Arrington MD[6], H. Michael Yu MD[1], Hyo S. Han MD[4]

[1]Departments of Radiation Oncology, [2]Biostatistics, [3]Pharmacy, [4]Breast Oncology, [5]Neuro-Oncology, and [6]Radiology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL 33612, USA

H. LEE MOFFITT CANCER CENTER & RESEARCH INSTITUTE,
AN NCI COMPREHENSIVE CANCER CENTER – Tampa, FL
1-888-MOFFITT (1-888-663-3488) www.MOFFITT.org

© 2010 H. Lee Moffitt Cancer Center and Research Institute, Inc.

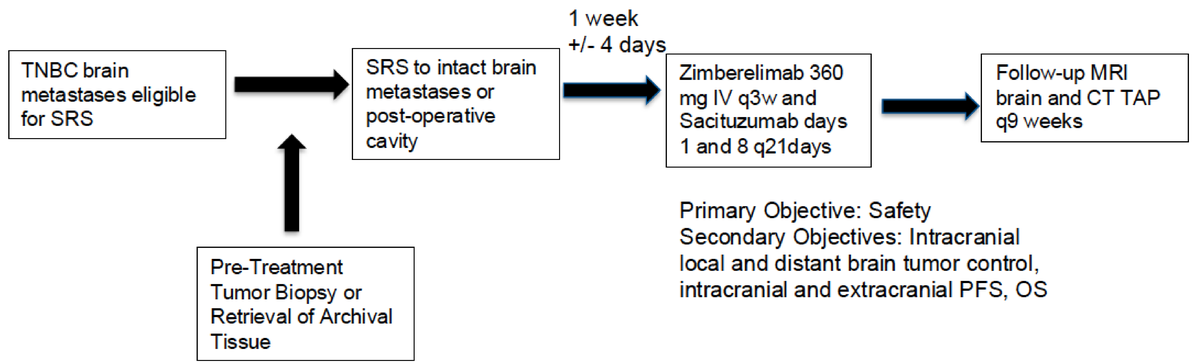
Introduction

- Patients with triple negative breast cancers (TNBC) are at high risk to develop breast cancer brain metastases.
- The prognosis and quality of life for triple negative brain-metastatic breast cancer remains very poor.
- Sacituzumab govitecan (SG) has shown blood brain barrier (BBB) penetration in preclinical studies. Stable brain metastases were treated on the phase III ASCENT Trial (NCT02574455)(1).
- Radiotherapy can open the BBB and has been shown to be safe in combination with anti-PD-1 therapy in our previous IIT (NCT03807765)(2). Therefore, combining radiation with the anti-PD-1 monoclonal antibody, zimberelimab, and SG may provide a synergistic anti-tumor approach.
- We hypothesize the use of stereotactic radiosurgery (SRS) sequentially with SG and zimberelimab among patients with metastatic TNBC with brain metastases will be safe and improve progression free survival compared to treatment with SG alone.

Methods

- The study is designed as a single-arm, nonrandomized, open-label, phase I/II trial of SG and zimberelimab with SRS among patients with metastatic TNBC with brain metastases.
- The primary endpoint is neurologic toxicity defined by CTCAE v5 criteria (phase I).
- Key inclusion criteria: Age ≥ 18, TNBC brain metastases ≥ 0.5 cm per RANO-BM criteria will be enrolled, ≤ 15 brain metastases eligible for SRS to brain metastases or to the post-operative bed. Key exclusion criteria: Presence of LMD, previous receipt of topoisomerase 1 inhibitors in the setting of brain metastases.

Trial Schematic



Results

Table 1: Patient Characteristics

Variable	n	%
No. of Patients	3	
Age, Median (Range)	56 (49-57)	
KPS		
90	2	67%
70	1	33%
Ethnicity		
Black or African American	2	67%
White	1	33%
Number of Previous Systemic Therapy Regimens		
0	1	33%
1	1	33%
2	1	33%
Previous CNS Therapy		
None	2	67%
Stereotactic Radiation Therapy	1	33%

Table 2: Adverse Events

	Grade 1	Grade 2	Grade 4
TSH Increased	1 (33%)		
Fatigue		1 (33%)	
Headache	1 (33%)		
Hyperglycemia	1 (33%)		
Neutrophil Count Decreased		2 (67%)	1 (33%)
Blood LDH Increased	1 (33%)		

- The best RANO-BM intracranial response has been a partial response (PR) in 3 patients (100%).
- The best irRECIST systemic response has been a PR (n=1), stable disease (n=1), and progressive disease (n=1).
- Two patients continue study therapy currently. One patient discontinued due to disease progression. No DLTs were noted.
- No deaths have occurred.

Phase II Objectives

- Phase II Primary endpoint- Intracranial PFS
- The single-arm two-stage phase 2 trial is designed using a Restricted-Kwak-and-Jung's method (3) to test the null hypothesis that the median time-to progression of 2.8 months.
- The alternative hypothesis is a median PFS of 3.6 months. A total of up to 31 patients will be enrolled.
- An interim analysis will be conducted when 21 patients have been enrolled.

Conclusions

- **Results from the phase I portion reveals safety of a combined approach with SRS and SG with zimberelimab.**
- **Accrual is ongoing to the phase II portion and efficacy continues to be assessed (NCT06238921)**

References

1. Hurvitz S, et al. Subgroup analysis from the phase 3 ASCENT study of Sacituzumab govitecan in metastatic triple-negative breast cancer. *NPJ Breast Cancer*, 2024;10.

2. Ahmed KA, et al. Nivolumab and stereotactic radiosurgery for patients with breast cancer brain metastases: long term results and biomarker analysis from a nonrandomized, open label phase Ib study. *Journal for Immunotherapy of Cancer*, 2025.

3. Belin L, et al. A two-stage design for phase II trials with time-to-event endpoint using restricted follow-up. *Contemporary Clinical Trials Communications* 2017; 8.

Contact

PI: Kamran Ahmed MD, kamran.ahmed@moffitt.org

Trial Coordinator: Robin Dowell, robin.dowell@moffitt.org