

Radiation Therapy Followed by Intrathecal (IT) Trastuzumab/Pertuzumab in the Management of HER2+ Breast Leptomeningeal Disease: Interim Results from a Phase II Multi-Institutional Study (NCT04588545)

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Introduction

- HER2+ breast cancer patients with leptomeningeal disease (LMD) represent a poor prognosis population with a high unmet clinical need (1).
- IT trastuzumab has been shown to be safe and efficacious in the management of HER2+ LMD (2).
- Given the role of radiotherapy in the management of LMD along with the role of pertuzumab in the management of HER2+ breast cancer, there is a strong clinical rationale to combine radiotherapy with IT trastuzumab/pertuzumab in the management of HER2+ breast LMD.
- We previously reported results from the phase I portion of the study which revealed safety of the combined approach with a RP2D of 80 mg IT pertuzumab with 80 mg IT trastuzumab (3).
- We now report interim results from the phase II portion of the study.

Methods

- The study is designed as a single-arm, nonrandomized, open-label, phase II trial
- **Key Inclusion Criteria:** HER2+ breast cancer patients with LMD identified by MRI or CSF, life expectancy > 8 weeks, left ventricular ejection fraction >50%, KPS ≥ 60
- **Key Exclusion Criteria:** History of allergy or hypersensitivity to any of the study drugs or study drug components
- Phase II primary objective: Overall survival

Results

Table 1: Patient Characteristics

Variable	n	%
No. of Patients	20	
Follow-Up, median (months)	20.7	
Age, median (range)	48 (33-63)	
Karnofsky Performance Status		
90	6	30%
80	6	30%
</= 70	8	40%
Receptor Status		
HR-/HER2+	11	55%
HR+/HER2+	9	45%
Race		
White	14	70%
Black or African American	2	10%
Unknown	4	20%
Ethnicity		
Hispanic or Latino	1	5%
Non-Hispanic	15	75%
Unknown	4	20%

Table 2: Adverse Events

	Grade 1	Grade 2	Grade 3
Vomiting	1 (5%)	1 (5%)	
Photophobia	1 (5%)		
Paresthesia	2 (10%)		
Pain in Extremity	3 (15%)	1 (5%)	
Nausea	3 (15%)	1 (5%)	1 (5%)
Memory Impairment	1 (5%)		
Headache	1 (5%)		
Fatigue	5 (25%)	2 (10%)	
Diarrhea	1 (5%)		
Back Pain	1 (5%)		
Arthralgia	1 (5%)		
Abdominal Pain	1 (5%)		

Figure 1: Kaplan-Meier LMD PFS

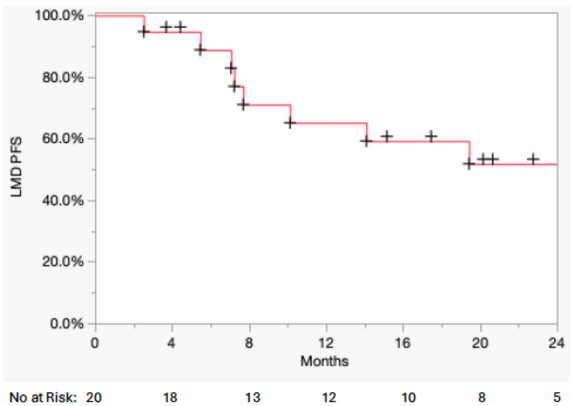
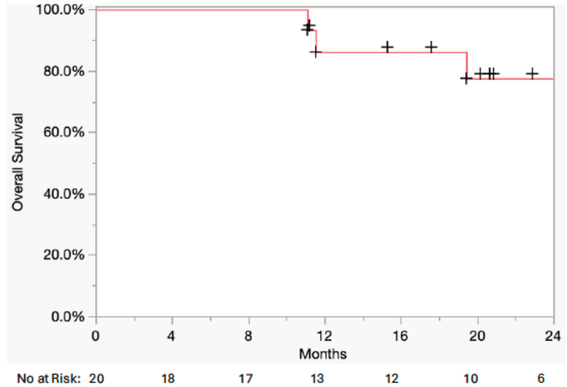


Figure 2: Kaplan-Meier Overall Survival



Median survival has not been reached (95% CI: 19.4 – Not reached (NR)) with a 12-month OS of 86%.

Median LMD progression free survival (LMD-PFS) has not been reached (95% CI 7.2 – NR) with a 12-month LMD-PFS of 65%.

Results

Table 3: Best LMD Response

Best LMD Response	N	%
Complete Response (CR)	4	20%
Partial Response (PR)	5	25%
Stable Disease (SD)	11	55%

Currently, twelve patients (60%) continue study therapy with 28.1 months as the longest treatment duration.

Conclusions

- The study met its predetermined endpoint for OS to warrant continuing enrollment in the second stage of the phase II trial.
- Initial trial results are encouraging with study therapy that is well tolerated.

References

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