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Radiation therapy followed by intrathecal (IT) trastuzumab/pertuzumab in the management of HER2+ breast leptomeningeal metastasis: Results from a phase II multi-institutional study, (INSPIRE-LM)

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Background

Treatment options for HER2$^+$ leptomeningeal metastasis (LM) remain limited. We previously reported 80 mg as the recommended phase II dose of IT pertuzumab alongside 80 mg IT trastuzumab and now report preliminary results from the phase II study.

Methods

The study is a multi-institutional, phase II trial of radiation therapy (RT) followed by IT trastuzumab/pertuzumab in the management of HER2$^+$ breast LM. HER2$^+$ LM patients with a life expectancy > 8 weeks, and KPS ≥ 60 were eligible. RT was completed prior to the delivery of IT therapy but was not required in patients that received prior intracranial RT. Patients could continue treatment with systemic agents if controlling disease and LM developed while on these therapies. The primary objective was to evaluate overall survival (OS) following study treatment. Secondary objectives included LM progression free survival (LM-PFS) and LM response.

Results

A total of 30 patients were enrolled between November 2022 and May 2026. Median age was 48 (range: 33-65) and 15 patients (50%) had a baseline KPS </= 70. The median number of prior systemic therapies was 34 (range: 1-9). Most patients received whole brain radiation therapy or proton cranial spinal irradiation (n=29; 97%) either prior to IT therapy or before study entry. Median follow-up is 26 months. The study met its predetermined endpoint for OS. Median survival is 36.2 months (95% CI: 19.4 – Not reached (NR)) with a 12-month OS of 79%. Median LM progression free survival (LM-PFS) is 19.3 months (95% CI 7.2 – NR) with a 12-month LM-PFS of 61%. The best LM response was a complete response in 5 (17%), partial response in 5 (17%), and stable disease in 17 (57%). The most common grade ≥ 2 adverse events attributed to IT trastuzumab/pertuzumab included nausea/vomiting (n=3; 10%), fatigue (n=2; 7%), and headache (n=2; 7%). Currently, twelve patients (40%) continue study therapy with 38.7 months as the longest treatment duration.

Conclusions

The study met its predetermined endpoint for OS with the longest median OS reported to date in HER2+ LM. Complete responses were noted in a subset of patients. IT trastuzumab/pertuzumab should be considered in the management of HER2+ LM.

Clinical trial identification

NCT04588545.

Legal entity responsible for the study

Moffitt Cancer Center.

Funding

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Disclosure

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