

# Intrathecal trastuzumab

Intrathecal chemotherapy (methotrexate, cytarabine, thiotepa), intrathecal trastuzumab, whole-brain radiotherapy, and systemic therapy are commonly used treatment options in [HER2-Positive Breast Cancer With Leptomeningeal Disease](#)<sup>1)</sup>.

A [multicenter study](#) enrolled 34 LMD patients in a combined Phase I/II study in treating patients with intrathecal [trastuzumab](#). Any [HER2](#)-positive histology was allowed in Phase I; Phase II was limited to [HER2-positive breast cancer](#).

Intrathecal trastuzumab was well tolerated, with one dose-limiting toxicity of grade 4 ([arachnoiditis](#)) occurring at 80 mg twice the weekly dose. The recommended Phase II dose was 80 mg intrathecally twice weekly. Twenty-six patients at dose level 80mg were included in the evaluation for efficacy: the [partial response](#) was seen in 5 (19.2%) patients, stable disease was observed in 13 (50.0%), and 8 (30.8%) of the patients had progressive disease. The median [overall survival](#) (OS) for Phase 2 dose-treated patients was 8.3 months (95% CI 5.2 to 19.6). The Phase II [HER2-positive breast cancer](#) patients' median OS was 10.5 months (95% CI 5.2 to 20.9). Pharmacokinetic (PK) studies were limited in the setting of concurrent systemic trastuzumab administration, however, did show stable CSF concentrations with repeated dosing suggesting that trastuzumab does not accumulate in the CSF in toxic concentrations.

This study suggests promise for potentially improved outcomes for HER-positive LMD patients when treated with intrathecal trastuzumab while remaining safe and well-tolerated for patients<sup>2)</sup>.

Among 19 enrolled patients, 16 (84%) had concomitant brain metastases, and 15 of them had received prior radiotherapy to the brain. All patients had received at least one line of systemic anti-HER2 therapy. After 8 weeks, 14 patients (74%) were free of neurological progression. The median LM-related-PFS was 5.9 months and the median OS was 7.9 months. According to the QLQ-C30 and BN20 scales, the global health-related QoL status seemed preserved, and no toxicity above grade 3 was observed.

Conducting studies on patients with LM poses significant challenges and ethical dilemmas inherent to this population. Despite some limits, this phase II study's findings in terms of clinical neurologic response and quality of life control confirm weekly administration of 150 mg of IT trastuzumab as a valuable option for HER+BC patients with LM and support the interest for further investigations<sup>3)</sup>.

## Intrathecal trastuzumab for carcinomatous meningitis

1)

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2)

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RV, Dixit K, Perron I, Zhang H, Gradishar WJ, Pentsova EI, Jeyapalan S, Groves MD, Melisko M, Raizer JJ. A Phase I/II Study of Intrathecal [Trastuzumab](#) in HER-2 Positive Cancer with Leptomeningeal Metastases: Safety, Efficacy, and Cerebrospinal Fluid Pharmacokinetics. *Neuro Oncol*. 2022 Aug 10;noac195. doi: 10.1093/neuonc/noac195. Epub ahead of print. PMID: 35948282.

3)

Oberkamp F, Gutierrez M, Trabelsi Grati O, Le Rhun É, Trédan O, Turbiez I, Kadi A, Dubot C, Taillibert S, Vacher S, Bonneau C. Phase II study of intrathecal administration of trastuzumab in patients with HER2-positive breast cancer with leptomeningeal metastasis. *Neuro Oncol*. 2022 Jul 22;noac180. doi: 10.1093/neuonc/noac180. Epub ahead of print. PMID: 35868630.

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