

# Carcinomatous meningitis treatment

Therapeutic options include systemic therapy (cancer-specific, CNS-penetrating chemotherapy or targeted therapies), intra-CSF administration of [chemotherapy](#) ([methotrexate](#), [cytarabine](#), [thiotepa](#)), and CNS site-specific [radiotherapy](#). Determining whom to treat remains challenging and, in part, relates to the extent of systemic disease, the neurological burden of disease, the available systemic therapies, and estimated rates of survival.

Radiation palliates local symptoms, relieves CSF flow obstruction, and treats areas such as nerve-root sleeves, Virchow-Robin spaces, and the interior of bulky lesions that chemotherapy does not reach.

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From an oncological perspective, the surgical treatment for leptomeningeal disease is limited; however, neurosurgery can be used to aid in the administration of chemotherapy and address the issue of hydrocephalus <sup>1)</sup>.

Intrathecal chemotherapy treats subclinical leptomeningeal deposits and tumor cells floating in the CSF, preventing further seeding. Cytarabine (Ara-C), [methotrexate](#) (MTX), and thiotepa are 3 agents routinely administered.

Supportive care for patients includes analgesia with opioids, anticonvulsants for seizures, antidepressants, and anxiolytics. Attention problems and somnolence from whole-brain radiation can be treated with psychostimulants or modafinil.

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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>.

## Cerebrospinal fluid shunt surgery

A combined [reservoir-on/off valve-ventriculoperitoneal shunt](#) (RO-VPS) is safe and practical to install,

results in symptomatic improvement in most patients, and allows uncomplicated and effective administration of intrathecal chemotherapy.

Cerebrospinal fluid shunt surgery should be considered in conjunction with intrathecal and systemic treatments <sup>3)</sup>.

## Intrathecal chemotherapy for carcinomatous meningitis

[Intrathecal chemotherapy for carcinomatous meningitis.](#)

<sup>1)</sup>

Volkov AA, Filis AK, Vrionis FD. Surgical Treatment for Leptomeningeal Disease. Cancer Control. 2017 Jan;24(1):47-53. PubMed PMID: 28178712.

<sup>2)</sup>

Kumthekar PU, Avram MJ, Lassman AB, Lin NU, Lee E, Grimm SA, Schwartz M, Bell Burdett KL, Lukas 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.

<sup>3)</sup>

Lin N, Dunn IF, Glantz M, Allison DL, Jensen R, Johnson MD, Friedlander RM, Kesari S. Benefit of ventriculoperitoneal cerebrospinal fluid shunting and intrathecal chemotherapy in neoplastic meningitis: a retrospective, case-controlled study. J Neurosurg. 2011 Oct;115(4):730-6. doi: 10.3171/2011.5.JNS101768. Epub 2011 Jul 1. PubMed PMID: 21721878.

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