

| Trial | Compound | Phase and Status | Description | Results |
|--------------------------------|-----------------------------------|------------------|--|--|
| NCT04420598 (DEBBRAH Study) | Trastuzumab Deruxtecan (DS-8201a) | Phase II | A Multicenter, Open-Label, Single-Arm, Multicohort Phase II Clinical Trial of Trastuzumab Deruxtecan (DS-8201a) in pretreated, unresectable locally advanced or metastatic Human Epidermal Growth Factor Receptor 2 (HER2)-positive or HER2-low expressing breast cancer (BC) with untreated or treated brain metastases (BMs) or leptomeningeal carcinomatosis (LMC). | Awaited in late 2020 |
| NCT01713699 | Collection of Cerebrospinal fluid | Not applicable | The purpose of this study is to determine whether the quantitative detection of circulating tumor cells (CTCs) in patients with Epcam expressing tumors can be used compared to standard qualitative method - cytology both in the cerebrospinal fluid of patients, clinically suspected for leptomeningeal metastases. | Awaited in late 2020 Associated publications: Milojkovic Kerklaan B et al.. EpCAM-based flow cytometry in cerebrospinal fluid greatly improves diagnostic accuracy of leptomeningeal metastases from epithelial tumors. Neuro Oncol. 2016 Jun;18(6):855-62. doi: 10.1093/neuonc/nov273. Epub 2015 Nov 12. |
| NCT00424242 | Pemetrexed dissodium | Phase 1 | This clinical trial is studying the side effects and how well pemetrexed disodium works in | Awaited in late 2020/ beginning 2021 |

| | | | | |
|-------------|--|-----------------------------------|---|---------------------------|
| | | | treating patients with leptomeningeal metastases. | |
| NCT02422641 | High-dose Methotrexate (HD-MTX) | Phase 2 Recruiting | This prospective study will evaluate systemic, intravenous HD-MTX in breast cancer patients with LMD with or without brain parenchymal metastasis. | Awaited in beginning 2021 |
| NCT03719768 | Avelumab + Whole Brain Radiotherapy (WBRT) | Phase 1B Recruiting | This study is to find a safe dose of the combination of Avelumab and WBRT in patients with LMD | Awaited in 2021 |
| NCT02939300 | Nivolumab + Ipilimumab | Phase 2 Active, not recruiting | Researchers hope to study the effects of the combination of Nivolumab and Ipilimumab in LMD from any solid tumor. | Awaited in 2021 |
| NCT03696030 | Chimeric Antigen Receptor T-Cell Therapy – HER2-CAR T Cells | Phase 1 Recruiting | This phase I trial studies the side effects and best dose of HER2-CAR T cells in treating patients with cancer that has spread to the brain or leptomeninges and has come back (recurrent). HER2-CAR T cells delivered into the ventricles of the brain may recognize and kill tumor cells. | Awaited in 2021 |
| NCT03661424 | HER2 BATs HER2 BATs are bi-specific antibody (HER2Bi) armed activated T-cells | Phase 1 Recruiting | This study uses HER2 BATs to target breast cancer cells that have metastasized to the membranes surrounding the brain and spinal cord. Two doses will be evaluated in order to | Awaited in 2021 |

| | | | | |
|-------------|---|------------------------------------|---|-----------------|
| | | | determine a safe dose. Before, during and after study treatment, participants will be monitored objectively by brain MRIs and clinically through physical and neurological exams, and blood and cerebrospinal fluid will be collected to evaluate immune responses. | |
| NCT03520504 | Proton Craniospinal Irradiation (CSI) | Phase 1B Active, not recruiting | The purpose of this study is to find the safest and most effective dose for delivering proton beam to the space containing CSF, brain, and spinal cord, in treating LMD. The researchers think that using proton beam radiation to treat the space containing CSF, brain, and spinal cord, instead of treating only the areas where the metastasized tumor cells are causing symptoms, would improve the treatment of this disease. | Awaited in 2021 |
| NCT00445965 | Iodine 131 monoclonal antibody 3F8 Iodine I 131 monoclonal antibody 3F8, is a radiolabeled monoclonal antibody | Phase 2 Active, not recruiting | This phase II trial is studying the side effects and how well iodine I 131 monoclonal antibody 3F8 works in treating patients with central nervous system cancer or leptomeningeal cancer. | Awaited in 2021 |

| | | | | |
|-------------|---|-----------------------|--|----------------------|
| NCT03423628 | <p>AZD1390 + Radiation Therapy</p> <p>AZD1390 is a highly potent brain penetrant ATM (Ataxia telangiectasia mutant) kinase inhibitor that blocks ATM-dependent signaling and repair of DNA double strand breaks (DSBs) in the genome.</p> | Phase 1 Recruiting | This study will test an investigational drug called AZD1390 in combination with radiation therapy for the treatment of brain tumors. This is the first time AZD1390 is being given to patients. This study will test safety, tolerability and PK (how the drug is absorbed, distributed and eliminated) of ascending doses of AZD1390 in combination with distinct regimens of radiation therapy | Awaited in 2022 |
| NCT03501979 | Tucatinib, Trastuzumab, and Capecitabine | Phase 2 Recruiting | Assess the safety and efficacy of the combination of tucatinib and trastuzumab with capecitabine for the treatment of LMD in HER2-neu positive breast cancer. | Awaited in late 2022 |
| NCT04192981 | <p>GDC-0084 + Whole Brain radiation therapy (WBRT)</p> <p>GDC-0084 (Paxalisib) is a brain penetrant inhibitor of PI3K and mTOR</p> | Phase 1 Recruiting | This study will test the safety of the study drug, GDC-0084, in combination with radiation therapy in people who have solid tumor brain metastases or leptomeningeal metastases. All participants will have cancer with a PIK3CA mutation. The researchers will test increasing doses of GDC-0084 to find the highest dose that causes few or mild side effects in participants. | Awaited in late 2022 |

| | | | | |
|-------------------------------|--|-------------------------------|--|---|
| | | | The study will also try to find out if the combination of the study drug with radiation is effective against participants' cancer. | |
| NCT03974204 | Collection of Cerebrospinal fluid and blood sample at the initial diagnostic assessment; at 1 and 3 months if conclusions of initial diagnostic assessment are "confirmed", "probable" or "possible", leading to LMD specific treatment; and at least 3 months after initial diagnostic assessment if conclusions are "Lack of evidence" according to EANO-ESMO classification | Not applicable | This is a multicenter, interventional, prospective study among breast cancer patients with a suspicion of metastatic meningitis. The current study aims to assess the use of proteomic profile issued from cerebrospinal fluid microvesicles for diagnosis of leptomeningeal metastases. | Awaited in late 2022 |
| NCT03613181 (ANGLed Study) | ANG1005 (paclitaxel trevatide) ANG1005 is a novel peptide–drug conjugate consisting of 3 paclitaxel molecules covalently linked to Angiopep-2 (proprietary 19-amino acid peptide designed to cross the CNS barriers via low-density lipoprotein receptor-related protein 1 (LRP1) mediated transcytosis. | Phase 3 Not yet recruiting | A randomized open-label multi-center pivotal study of ANG1005 compared with Physician`s Best Choice (one of three pre-determined choices of therapies: capecitabine or eribulin or HD-MTX) in HER2-negative breast cancer patients with newly diagnosed LMD and previously treated brain metastases. | Preclinical and clinical evidence of efficacy with ANG1005 has been previously shown in Phase I and Phase II trials. Awaited in 2023 |
| NCT04343573 | Proton Craniospinal Radiation Therapy (proton CSI) vs. Partial Photon Radiation Therapy for Leptomeningeal Metastasis from Solid Tumors | Phase 2 Recruiting | This is a randomized (2:1) phase II single institution trial in patients with leptomeningeal metastases from NSCLC and breast cancer. | Awaited in 2023 |

| | | | | |
|-------------|--|--|--|------------------------|
| | <p>The proton CSI targets the entire space containing the CSF, brain, and spinal fluid.</p> <p>The partial photon radiation therapy treats only areas where the patient is having symptoms, such as the entire brain or part of the spine.</p> | | <p>The aim of this study is to find out whether proton craniospinal radiation therapy (proton CSI) or partial photon radiation therapy is more effective at preventing leptomeningeal metastasis from worsening. The investigators also want to find out if proton CSI improves the symptoms patients may be experiencing because of the leptomeningeal metastasis. In addition, the investigators will compare the side effects of proton CSI and partial photon therapy.</p> | |
| NCT04315246 | <p>177Lu-DTPA-omburtamab</p> <p>177Lu-DTPA-omburtamab is a radioactive labelling of a murine monoclonal antibody targeting B7-H3.</p> | <p>Phase 1/2</p> <p>Not yet recruiting</p> | <p>A Phase I/II Trial of Intracerebroventricular 177Lu-DTPA-Omburtamab Radioimmunotherapy for Leptomeningeal Metastasis From Solid Tumors</p> | <p>Awaited in 2024</p> |