

Trastuzumab deruxtecan

Novel anti-HER2 agents, such as tucatinib, ado-trastuzumab emtansine, [trastuzumab](#) deruxtecan and neratinib, have shown intracranial efficacy. Current research efforts are ongoing not only to clarify the activity of existing treatments on the CNS, as well as to develop new drugs and innovative multi-modality approaches. This review will encompass the current treatment landscape of BMs arising from BC, with a focus on recent advancements in the field and investigational approaches ¹⁾.

Trastuzumab [deruxtecan](#) is an antibody-drug conjugate with high extracranial activity in [human epidermal growth factor receptor 2](#) (HER2)-positive metastatic breast cancer. Bartsch et al. conducted the [prospective](#), open-label, single-arm, phase 2 TUXEDO-1 trial. They enrolled patients aged ≥ 18 years with HER2-positive breast cancer and newly diagnosed untreated brain metastases or brain metastases progressing after previous local therapy, previous exposure to trastuzumab and pertuzumab, and no indication for immediate local therapy. Patients received trastuzumab deruxtecan intravenously at the standard dose of 5.4 mg per kg bodyweight once every 3 weeks. The primary endpoint was the intracranial response rate measured according to the response assessment in neuro-oncology brain metastases criteria. A Simon two-stage design was used to compare a null hypothesis of $<26\%$ response rate against an alternative of 61%. Fifteen patients were enrolled in the intention-to-treat population of patients who received at least one dose of study drug. Two patients (13.3%) had a complete intracranial response, nine (60%) had a partial intracranial response and three (20%) had stable disease as the best intracranial response, with a best overall intracranial response rate of 73.3% (95% confidential interval 48.1-89.1%), thus meeting the predefined primary outcome. No new safety signals were observed and global [quality of life](#) and cognitive functioning was maintained over the treatment duration. In the TUXEDO-1 trial (NCT04752059, EudraCT 2020-000981-41), trastuzumab deruxtecan showed a high intracranial response rate in patients with active [brain metastases](#) from HER2-positive breast cancer and should be considered as a treatment option in this setting ²⁾.

1)

Corti C, Antonarelli G, Criscitiello C, Lin NU, Carey LA, Cortés J, Poortmans P, Curigliano G. Targeting brain metastases in breast cancer. *Cancer Treat Rev.* 2022 Feb;103:102324. doi: 10.1016/j.ctrv.2021.102324. Epub 2021 Dec 16. PMID: 34953200.

2)

Bartsch R, Berghoff AS, Furtner J, Marhold M, Bergen ES, Roider-Schur S, Starzer AM, Forstner H, Rottenmanner B, Dieckmann K, Bago-Horvath Z, Haslacher H, Widhalm G, Ilhan-Mutlu A, Minichsdorfer C, Fuereder T, Szekeres T, Oehler L, Gruenberger B, Singer CF, Weltermann A, Pühr R, Preusser M. Trastuzumab deruxtecan in HER2-positive breast cancer with brain metastases: a single-arm, phase 2 trial. *Nat Med.* 2022 Aug 8. doi: 10.1038/s41591-022-01935-8. Epub ahead of print. PMID: 35941372.

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