Pertuzumab

- Stereotactic radiosurgery for brain metastases from human epidermal receptor 2 positive breast Cancer: an international, multi-center study
- Multidisciplinary management of HER2-positive breast cancer with brain metastases: An evidence-based pragmatic approach moving from pathophysiology to clinical data
- Trastuzumab deruxtecan in HER2-positive breast cancer with brain metastases: a single-arm, phase 2 trial
- Prognostic factors of brain metastasis and survival among HER2-positive metastatic breast cancer patients: a systematic literature review
- Favourable outcome of patients with breast cancer brain metastases treated with dual HER2 blockade of trastuzumab and pertuzumab
- Circular HER2 RNA positive triple negative breast cancer is sensitive to Pertuzumab
- Intrathecal administration of anti-HER2 treatment for the treatment of meningeal carcinomatosis in breast cancer: A metanalysis with meta-regression
- Impressive Long-term Response with Pertuzumab and Trastuzumab in HER2-positive Breast Cancer with Brain Metastasis

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HER2-positive breast cancer patients have an elevated risk of developing brain metastases (BM), despite adjuvant HER2-targeted therapy. The mechanisms underpinning this reduced intracranial efficacy are unclear. Lim et al. optimized the in situ proximity ligation assay (PLA) for the detection of the high-affinity neuregulin-1 receptor, HER2-HER3 (a key target of pertuzumab), in archival tissue samples and developed a pipeline for high throughput extraction of PLA data from fluorescent microscope image files. Applying this to a large BM sample cohort (n = 159) showed that BM from breast, ovarian, lung, and kidney cancers have higher HER2-HER3 levels than other primary tumor types (melanoma, colorectal and prostate cancers). HER2 status, and tumor cell membrane expression of pHER2(Y1221/1222) and pHER3(Y1222) were positively, but not exclusively, associated with HER2-HER3 frequency. In an independent cohort (n = 78), BM had significantly higher HER2-HER3 levels than matching primary tumors (p = 0.0002). For patients who had two craniotomy procedures, HER2-HER3 dimer levels were lower in the consecutive lesion (n = 7; p = 0.006). We also investigated the effects of trastuzumab and pertuzumab on five different heterodimers in vitro: HER2-EGFR, HER2-HER4, HER2-HER3, HER3-HER4, and HER3-EGFR. Treatment significantly altered the absolute frequencies of individual complexes in SKBr3 and/or MDA-MB-361 cells, but in the presence of neuregulin-1, the overall distribution was not markedly altered, with HER2-HER3 and HER2-HER4 remaining predominant. Together, these findings suggest that markers of HER2 and HER3 expression are not always indicative of dimerization and that pertuzumab may be less effective at reducing HER2-HER3 dimerization in the context of excess neuregulin [1)]

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Lim M, Nguyen TH, Niland C, Reid LE, Jat PS, Saunus JM, Lakhani SR. Landscape of Epidermal Growth Factor Receptor Heterodimers in Brain Metastases. Cancers (Basel). 2022 Jan 21;14(3):533. doi: 10.3390/cancers14030533. PMID: 35158800; PMCID: PMC8833370.