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# Anti-cancer Antibody Trastuzumab-Melanotransferrin Conjugate (BT2111) for the Treatment of Metastatic HER2+ Breast Cancer Tumors in the Brain: an In-Vivo Study.

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## Abstract

### PURPOSE:

The ability of human melanotransferrin (hMTf) to carry a therapeutic concentration of trastuzumab (BTA) in the brain after conjugation (in the form of trastuzumab-melanotransferrin conjugate, BT2111 conjugate) was investigated by measuring the reduction of the number and size of metastatic human HER<sup>2+</sup> breast cancer tumors in a preclinical model of brain metastases of breast cancer.

### METHODS:

Human metastatic brain seeking breast cancer cells were injected in NuNu mice (n=6-12 per group) which then developed experimental brain metastases. Drug uptake was analyzed in relation to metastasis size and blood-tumor barrier permeability. To investigate in-vivo activity against brain metastases, equimolar doses of the conjugate, and relevant controls (hMTf and BTA) in separate groups were administered biweekly after intracardiac injection of the metastatic cancer cells.

### RESULTS:

The trastuzumab-melanotransferrin conjugate (BT2111) reduced the number of preclinical human HER<sup>2+</sup> breast cancer metastases in the brain by 68% compared to control groups. Tumors which remained after treatment were 46% smaller than the control groups. In contrast, BTA alone had no effect on reducing number of metastases, and was associated with only a minimal reduction in metastasis size.

### CONCLUSIONS:

The results suggest the novel trastuzumab-melanotransferrin conjugate (BT2111) may have utility in treating brain metastasis and validate hMTf as a potential vector for antibody transport across the Blood Brain Barrier (BBB).

### KEYWORDS:

antibody trastuzumab-melanotransferrin conjugate (BT2111); blood brain barrier (BBB); brain metastases; human melanotransferrin (hMTf); metastatic HER<sup>2+</sup> breast cancer tumors; trastuzumab (BTA)

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