Subject: increased transport across bbb 1000 fold with active transport 6% of administered dose to the brain without it 0.06% with an antibody

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

Pharm Res. 2016 Dec;33(12):2930-2942.

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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.

Nounou MI[1,2,3], Adkins CE[1,4], Rubinchik E[5], Terrell-Hall TB[1,4], Afroz M[1,4], Vitalis T[5], Gabathuler R[5], Tian MM[5], Lockman PR[6].

Author information

1 School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, Texas, USA.

2 Department of Pharmaceutics, School of Pharmacy, Alexandria University, Alexandria, 21521, Egypt.

3 Department of Pharmaceutical Sciences, Appalachian College of Pharmacy, Oakwood, Virginia, 24631, USA.

4 School of Pharmacy, West Virginia University Health Sciences Center, Morgantown, West Virginia, USA.

5 biOasis Technologies Inc., Vancouver, British Columbia, Canada.

6

School of Pharmacy, West Virginia University Health Sciences Center, Morgantown, West Virginia, USA.
prlockman@hsc.wvu.edu.

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^{2+} 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^{2+} 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 HER2+ breast cancer tumors; trastuzumab (BTA)

PMID:
27528392
PMCID:
PMC5267937
[Available on 2017-12-01]
DOI:
10.1007/s11095-016-2015-0

Grant support

Grant support

- P30 GM103488/GM/NIGMS NIH HHS/United States
- R01 CA166067/CA/NCI NIH HHS/United States
- U54 GM104942/GM/NIGMS NIH HHS/United States

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