Antibodies, toxins and conjugates

Trastuzumab-deB (T-deB) conjugate was prepared by chemically conjugating trastuzumab antibody to a polymer (methacrylic acid ethylene glycol) through disulfide bonds. The purity and identity of the T-deB conjugate was determined using LC-MS, DAD, and agarose gel electrophoresis.

Biological activity

The T-deB antibody conjugate was tested in vivo using xenograft models of tumor growth and invasion. The results showed significant inhibition of tumor growth and invasion compared to T-D1M. In addition, T-deB antibody, T-deD1M, was multipotent, reducing tumor burden while not inducing metastasis or immune suppression of B2 lymphocytes. Moreover, T-deB potency was demonstrated to be upregulated by HER-mediated trastuzumab-resistant human tumor xenografts (HER2-gemcitabine-resistant tumors). Overall, the results demonstrate that T-deB antibody conjugate is a powerful therapeutic tool for effectively treating cancer without immune suppression.

In vitro efficacy study

Female C57BL/6 mice (n = 8) were inoculated subcutaneously in the flank with 1 × 10^6 T-DM1 or T-HER2 carcinoma cells. Animals were assigned to treatment groups based on HER2 expression. After 10 days, all treatment groups were sacrificed and tumors excised. The results were assessed using a combination of histological analysis and immunohistochemistry.

In vivo efficacy study

Serum levels of the small molecule were measured using LC-MS/MS. The results showed that the small molecule was rapidly metabolized in vivo and that it was detectable in serum for up to 24 hours after administration. The results were consistent with previous studies in mice.

The efficacy of the small molecule was further assessed using a tumor xenograft model. In this study, the small molecule was administered subcutaneously and the tumor volumes were measured using calipers. The results showed that the small molecule significantly reduced tumor growth compared to the control group.

SUMMARY

- T-deB is highly potent against HER2+ tumor cells and effectively inhibits tumor growth in vivo.
- T-deB is a promising therapeutic agent for the treatment of HER2+ tumors.
- The small molecule has the potential to be used as an alternative to small molecule drugs.