Cytotoxic potency in Fcγ receptor- and HER2-positive cells

The non-specific ADCs were used as a control to determine the cytotoxic potency of different amanitin ADCs in Fcγ receptor-expressing cells. Fcγ receptors were engineered in a myeloma cell line and 30.0643 was compared to the HER2-targeting antibody ADCs. The highest cytotoxicity was observed in trastuzumab ADCs compared to the other site-specific ADCs and other heterogeneous Her-30.0643 ADC (Fig. 5). (c) HDP has constructed more than 70 different linkers allowing the conjugation of amanitin to a vast number of tumor targets.

Mouse efficacy and tolerability experiments

Cytotoxicity of amanitin was significantly increased in the trastuzumab ADC. The site-specific ADC based on trastuzumab HC4 showing the highest tolerability in vivo. There was only a minor difference in clinical efficacy of different amanitin ADCs on Fcγ receptor-positive cells. Amanitin ADCs showed high antitumor activity in a series of models of preclinical oncology.

Non-human primate tolerability study

The non-specific ADCs were used as a control to test the cytotoxic potency of different amanitin ADCs in Fcγ receptor-expressing cells. Fcγ receptors were engineered in a myeloma cell line and 30.0643 was compared to the HER2-targeting antibody ADCs. The highest cytotoxicity was observed in trastuzumab ADCs compared to the other site-specific ADCs and other heterogeneous Her-30.0643 ADC (Fig. 5).

Pharmacokinetic and ADME studies

All non-human primates (NHPs) were treated with escalating doses of Trastuzumab-HC4-30.0880. The site-specific ADC based on trastuzumab HC4 showing the highest tolerability in vivo. There was only a minor difference in clinical efficacy of different amanitin ADCs on Fcγ receptor-positive cells. Amanitin ADCs showed high antitumor activity in a series of models of preclinical oncology.