ICOS Anti-HER2 V-mAbs: Localizing Engineered ICOSL Costimulatory Agonists to HER2+ tumors through trastuzumab

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Abstract

The Immunoglobulin Superfamily (IgSF) includes a large, diverse family of immunoreceptors that operate as immune checkpoints. Abs containing ICOSL, Fc-KR, and/or vIgD domains have been evaluated in clinical trials. Immune synapse signaling has also been enabled through engineered bispecific antibodies (bAbs, vIgD) targeting ICOSC and/or CD28. These two domains can be designed to achieve high-affinity binding (KD, low nM) and bi- or tri-specific activity.

Methods

ICOSL and potential therapeutic applications. The ICOSL domain from an engineered ICOSL domain was attached to the A allele of the mouse A/C terminus of the HER2 oncogene and transduced to a nonsynthetic, HER2-expressing cell line (NCI-N87). The resulting HER2 ICOSL V-mAbs were titrated against NCI-N87 cells and analyzed by flow cytometry in the presence or absence of soluble ICOSL or ICOSL-HER2 bAbs.

Results

10"4 ICOSL Anti-HER2 V-mAbs: Localizing Engineered ICOSL Costimulatory Agonists to HER2+ tumors

Conclusions and Summary

The V-mAb approach has broad potential to enable tumor-localized immune modulation via the diverse array of ICOSL and potential therapeutic applications. The ICOSL domain from an engineered ICOSL domain was attached to the A allele of the mouse A/C terminus of the HER2 oncogene and transduced to a nonsynthetic, HER2-expressing cell line (NCI-N87). The resulting HER2 ICOSL V-mAbs were titrated against NCI-N87 cells and analyzed by flow cytometry in the presence or absence of soluble ICOSL or ICOSL-HER2 bAbs.