Trastuzumab Duocarmazine

National Cancer Institute

Source

National Cancer Institute. Trastuzumab Duocarmazine. NCI Thesaurus. Code C118674.

An antibody-drug conjugate (ADC) composed of the recombinant humanized anti-epidermal growth factor receptor 2 (HER2) monoclonal antibody trastuzumab linked, via a cleavable linker, to the duocarmycin prodrug, seco-duocarmycin-hydroxybenzamide-azaindole (seco-DUBA), with potential antineoplastic activity. Upon administration of trastuzumab duocarmazine, the trastuzumab moiety binds to HER2 on the tumor cell surface, which triggers the endocytosis of this agent. The linker is then cleaved inside the tumor cell by proteases at the dipeptide valine-citrulline (vc), and releases the active moiety, duocarmycin. Duocarmycin binds to the minor groove of DNA, alkylates adenine at the N3 position, and induces cell death. In addition, trastuzumab induces antibody-dependent cell-mediated cytotoxicity (ADCC) against tumor cells that overexpress HER2. HER2 is overexpressed by many carcinomas and is associated with a poor prognosis.