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Anti-HER2 Antibody-drug Conjugate MEDI4276

National Cancer Institute

Source

National Cancer Institute. *Anti-HER2 Antibody-drug Conjugate MEDI4276*. NCI Thesaurus. Code C126355.

An antibody-drug conjugate (ADC) composed of a bispecific antibody against the extracellular domain of human epidermal growth factor receptor 2 (HER2; ERBB2) comprised of the single-chain variable fragment (scFv) of the anti-HER2 monoclonal antibody trastuzumab, which binds to domain IV of HER2, fused to the heavy chains of the anti-HER2 monoclonal antibody 39S, which binds to domain II of HER2, and conjugated, via a cleavable linker, to the cytotoxic anti-microtubule agent tubulysin, with potential antineoplastic activity. Upon administration of ADC MEDI4276, the anti-HER2 bispecific antibody specifically targets and binds to HER2 on the surface of certain cancer cells. Upon binding, crosslinking and internalization of antibody-HER2 complexes occurs and MEDI4276 is transported to the lysosome where the linker is cleaved, thereby delivering tubulysin inside HER2-expressing cancer cells. Tubulysin binds to tubulin and inhibits microtubule polymerization, which blocks cell division. This results in G2/M phase arrest, tumor cell apoptosis, and decreased proliferation of HER2-expressing tumor cells. HER2, a tyrosine kinase receptor, is overexpressed by many cancer cell types.