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Anti-HER2/Auristatin Payload Antibody-drug Conjugate XMT-1522

National Cancer Institute

Source

National Cancer Institute. *Anti-HER2/Auristatin Payload Antibody-drug Conjugate XMT-1522*. NCI Thesaurus. Code C132112.

An antibody-drug conjugate (ADC) composed of HT-19, a monoclonal antibody directed against the human epidermal growth factor receptor 2 (ERBB2; HER2), conjugated, via a proprietary biodegradable, hydrophilic polymer backbone and various linkers, to proprietary auristatin-derived payload molecules (about 15 per antibody), with potential antineoplastic activity. Upon administration of anti-HER2/auristatin payload ADC XMT-1522, the antibody moiety targets and binds to a unique epitope in the extracellular domain (ECD) of HER2. Upon internalization, cleavage and release of the cytotoxic molecules, the auristatin-derived molecules bind to tubulin and inhibit its polymerization, which results in G2/M phase arrest and induces apoptosis of HER2-expressing tumor cells. The attachment of multiple auristatin molecules to the backbone enables XMT-1522 to effectively kill tumors that express relatively low amounts of the HER2 protein; therefore, this agent shows increased therapeutic potential in tumors with low HER2 expression compared to other anti-HER2 antibody-based therapies. The polymer-based proprietary platform optimizes delivery of the cytotoxic drug payload and improves drug solubility.