HER-2-positive B-cell Peptide Antigen P467-DT-CRM197/Montanide Vaccine IMU-131

National Cancer Institute

Source

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A cancer vaccine consisting of a fusion peptide, composed of three peptides derived from the extracellular domain (ECD) of the HER2 peptide antigen found on B-cells (P4, P6 and P7; P467), conjugated to the carrier protein DT-CRM197, a non-toxic, mutated form of diphtheria toxin (DT), and combined with the immunoadjuvant montanide ISA 51, with potential immunostimulatory and antineoplastic activities. Upon administration, IMU-131 vaccine induces the production of polyclonal antibodies against the HER2 protein. In turn, the antibodies bind to three separate binding sites on HER2 expressed on tumor cells and inhibit HER2 dimerization and activity, which leads to the inhibition of HER2-mediated signal transduction pathways. This induces apoptosis in and reduces cellular proliferation of HER2-overexpressing tumor cells. In addition, IMU-131 induces a cytotoxic T-lymphocyte (CTL) response against the HER2-expressing tumor cells. The tumor-associated antigen (TAA) HER2, also called Neu or ErbB2, is a tyrosine kinase receptor for epidermal growth factor (EGF) and is often overexpressed by a variety of tumor cell types. Montanide ISA 51, also known as incomplete Freund's adjuvant or IFA, is a stabilized water-in-oil (w/o) emulsion adjuvant containing mineral oil with mannide oleate added as a surfactant that non-specifically stimulates cell-mediated immune responses to antigens. DT-CRM197 is used to increase the immunogenicity of the HER2/neu peptide antigen. In P467, the three B-cell epitopes were combined in a specific order into a single 49 amino acid peptide antigen.