LmddA-LLO-chHER2 Fusion Protein-secreting Live-attenuated Listeria Cancer Vaccine ADXS31-164

National Cancer Institute

Source

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A cancer vaccine containing a live, highly attenuated strain of the Gram-positive bacterium Listeria monocytogenes (LmddA) encoding a fusion protein composed of a chimeric peptide comprised of three highly immunogenic epitopes of the human tumor-associated antigen (TAA) HER2/neu (chHER2) fused to a non-hemolytic fragment of the immunostimulant listeriolysin O (LLO) protein, with potential immunostimulatory and antineoplastic activities. Upon administration of the LmddA-LLO-chHER2 vaccine ADXS31-142, the LmddA is taken up by phagocytic cells; then the listeriolysin portion of the expressed LLO-chHER2 can form pores in the phagolysosomes and the fusion protein can escape into the cytosol. In turn, the LLO-chHER2 is processed and presented to the immune system by major histocompatibility complex (MHC) I on the phagocytic cells. Antigen presentation activates the immune system to exert an immune response involving the recruitment and activation of T-lymphocytes against HER2-expressing tumor cells, and inhibits tumor-infiltrating T regulatory cells (Tregs) and myeloid-derived suppressor cells (MDSCs). This eventually results in tumor cell lysis. HER2/neu, a tyrosine kinase receptor belonging to the epidermal growth factor receptor (EGFR) family, is overexpressed in various tumor cell types.