

Immunotherapeutic Combination Product CMB305

National Cancer Institute

Source

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An immunotherapeutic combination product composed of LV305, an engineered lentiviral vector that both targets dendritic cells (DCs) and contains nucleic acids encoding the human tumor-associated cancer-testis antigen NY-ESO-1 (CTAG1), and G305, a cancer vaccine comprised of an NY-ESO-1 recombinant protein and glucopyranosyl lipid adjuvant (GLA)-stable emulsion (GLA-SE), with potential synergistic immunostimulatory and antineoplastic activities. Upon intradermal administration of LV305, the DC-targeting lentiviral vector targets and binds to dermal DCs via the DC-specific intercellular adhesion molecule-3-grabbing non-integrin (DC-SIGN) receptor. Upon internalization of the vector, the NY-ESO-1 protein is expressed, which stimulates DC maturation, and activates the immune system to mount a cytotoxic T-lymphocyte (CTL) response against NY-ESO-1-expressing cells; this may result in tumor cell lysis. Upon the sequential intramuscular injection of G305, the adjuvant portion of G305 binds to toll-like receptor 4 (TLR-4) expressed on various immune cells, including DCs, monocytes, macrophages and B-cells. The activated DCs present the NY-ESO-1 antigen to CD4-positive Th1 T-lymphocytes. The induction of antigen-specific CD4-positive T-lymphocytes further induces a CTL response against NY-ESO-1-expressing tumor cells. In addition, G305 induces an NY-ESO-1-specific antibody response. NY-ESO-1, expressed in normal testes and on the surfaces of various tumor cells, plays a key role in tumor cell proliferation and survival.