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Anti-PD-L1/CD137 Bispecific Antibody MCLA-145

National Cancer Institute

Source

National Cancer Institute. *Anti-PD-L1/CD137 Bispecific Antibody MCLA-145*. NCI Thesaurus. Code C160772.

A full-length, Fc-silenced immunoglobulin G1 (IgG1) bispecific antibody targeting both the human programmed death-ligand 1 (PD-L1) and CD137 (4-1BB; tumor necrosis factor receptor superfamily member 9; TNFRSF9), with potential checkpoint inhibitory, immunostimulating and antineoplastic activities. Upon administration, anti-PD-L1/CD137 bispecific antibody MCLA-145 simultaneously targets and binds to CD137, which is expressed on a variety of leukocyte subsets including activated T-lymphocytes, and PD-L1 expressed on tumor cells, thereby crosslinking PD-L1-expressing tumor cells and T-lymphocytes. Through CD137 binding, MCLA-145 acts as a conditional CD137 agonist, resulting in T-cell co-stimulation and enhanced anti-tumor activity. At the same time, MCLA-145 prevents PD-L1 from binding to and activating its receptor, programmed cell death 1 (PD-1; PDCD1; CD279; programmed death-1). This abrogates T-cell inhibition, activates antigen-specific T-lymphocytes and enhances cytotoxic T-cell-mediated tumor cell lysis, which may lead to a reduction in tumor growth. PD-L1 binding to PD-1 on activated T-cells inhibits the expansion and survival of CD8-positive T-cells, suppresses the immune system and results in immune evasion. CD137, a surface glycoprotein of the tumor necrosis factor receptor superfamily, is an inducible costimulatory receptor that plays a key role in T-cell proliferation, survival and cytolytic activity. Crosslinking of PD-L1-expressing tumor cells and activated T-lymphocytes may enhance T-lymphocyte-mediated lysis of PD-L1-expressing tumor cells.