Anti-CD47 Monoclonal Antibody AO-176

National Cancer Institute

Source

National Cancer Institute. Anti-CD47 Monoclonal Antibody AO-176. NCI Thesaurus. Code C159600.

A humanized immunoglobulin G2 (IgG2) monoclonal antibody targeting the human cell surface antigen CD47, with potential phagocytosis-inducing and antineoplastic activities. Upon administration, anti-CD47 monoclonal antibody AO-176 preferentially binds to CD47 on tumor cells because it exhibits enhanced binding at the acidic pH found in the tumor microenvironment (TME). This blocks the interaction of CD47 with signal regulatory protein alpha (SIRPalpha), an inhibitory protein expressed on macrophages and dendritic cells (DCs), which prevents CD47/SIRPalpha-mediated signaling and abrogates the CD47/SIRPalpha-mediated inhibition of phagocytosis. This induces pro-phagocytic signaling mediated by the binding of calreticulin (CRT), which is specifically expressed on the surface of tumor cells, to low-density lipoprotein (LDL) receptor-related protein (LRP), expressed on macrophages, which results in macrophage activation and the specific phagocytosis of tumor cells. Additionally, blocking CD47 signaling activates both an anti-tumor T-lymphocyte immune response and T-cell-mediated killing of CD47-expressing tumor cells. In addition, AO-176 induces immunogenic cell death (ICD) and releases damage-associated molecular patterns (DAMPs) from tumor cells, thereby further stimulating immune responses. AO-176 is also able to induce direct cytotoxic cell death by a cell autonomous mechanism. CD47, also called integrin-associated protein (IAP), is a tumor-associated antigen (TAA) expressed on normal, healthy hematopoietic stem cells (HSCs) and overexpressed on the surface of a variety of cancer cells. Expression of CD47, and its interaction with SIRPalpha, leads to the inhibition of macrophage activation and protects cancer cells from phagocytosis, which allows cancer cells to proliferate.