TIGIT-targeting Agent MK-7684

National Cancer Institute

Source

National Cancer Institute. TIGIT-targeting Agent MK-7684. NCI Thesaurus. Code C140041.

An antagonistic agent targeting the co-inhibitory molecule and immune checkpoint inhibitor T-cell immunoglobulin (Ig) and immunoreceptor tyrosine-based inhibitory motif (ITIM) domains (TIGIT; T-cell immunoreceptor with Ig and ITIM domains; T-cell immunoglobulin and ITIM domain), with potential immune checkpoint inhibitory and antineoplastic activities. Upon administration, MK-7684 targets and binds to TIGIT expressed on various immune cells, particularly on tumor-infiltrating T-lymphocytes (TILs) and natural killer (NK) cells, thereby preventing the interaction of TIGIT with its ligands CD112 (nectin-2; poliovirus receptor related-2; PVRL2) and CD155 (poliovirus receptor; PVR; nectin-like protein 5; NECL-5), which are expressed on T-cells, NK cells and certain cancer cells. This enhances the interaction of CD112 and CD155 with the costimulatory receptor CD226 (DNAX Accessory molecule-1; DNAM-1), which is expressed on immune cells, such as NK cells and CD8+ T-cells, and activates CD226-mediated signaling. This activates the immune system to exert a T-cell-mediated immune response against cancer cells. TIGIT, a member of the Ig super family and an immune inhibitory receptor, is overexpressed on tumor antigen-specific CD8+ T-cells and CD8+ TILs and plays a key role in the suppression of T-cell proliferation and activation; it is involved in tumor cell immune evasion, and the inhibition of antiviral immune responses.