Adenosine A2B Receptor Antagonist PBF-1129

National Cancer Institute

Source

National Cancer Institute. Adenosine A2B Receptor Antagonist PBF-1129. NCI Thesaurus. Code C148435.

An orally bioavailable antagonist of the immunomodulatory checkpoint molecule adenosine A2B receptor (A2BR; ADORA2B), with potential anti-inflammatory, immunomodulating and antineoplastic activities. Upon administration, A2BR antagonist PBF-1129 competes with adenosine for binding to A2BR expressed on various cancer cell types and numerous immune cells, such as dendritic cells (DCs), mast cells, macrophages and lymphocytes. This inhibits A2BR activity and prevents adenosine/A2BR-mediated signaling. The inhibition of A2BR in cancer cells prevents activation of downstream oncogenic pathways, which leads to an inhibition of cell proliferation and metastasis. A2BR inhibition also prevents the release of various growth factors, cytokines and chemokines, such as vascular endothelial growth factor (VEGF), interleukin-8 (IL-8) and angiopoietin-2 (Ang2) from immune cells, which may abrogate the adenosine-mediated immunosuppression in the tumor microenvironment (TME) and activate the immune system to exert anti-tumor immune responses against cancer cells leading to tumor cell killing. In addition, under non-cancerous inflammatory conditions, inhibition of A2BR leads to reduced activation and proliferation of various immune cells, which results in decreased pro-inflammatory cytokine production and may prevent inflammation. A2BR, a G protein-coupled signaling receptor, is expressed on the cell surfaces of numerous immune cells and is often overexpressed on a variety of cancer cell types; it plays a key role in their proliferation, progression and metastasis. Adenosine is overproduced under inflammatory conditions and plays a key role in pro-inflammatory actions. Adenosine is often overproduced by tumor cells and plays a key role in immunosuppression and tumor cell proliferation. The pro- and anti-inflammatory effects of adenosine and A2BR are cell type-specific and dependent on the extracellular microenvironment.