IDO1 Inhibitor PF-06840003

National Cancer Institute

Source

National Cancer Institute. IDO1 Inhibitor PF-06840003. NCI Thesaurus. Code C129375.

An orally available hydroxyamidine and inhibitor of indoleamine 2,3-dioxygenase 1 (IDO1), with potential immunomodulating and antineoplastic activities. Upon administration, IDO1 inhibitor PF-06840003 targets and binds to IDO1, an enzyme responsible for the oxidation of tryptophan into kynurenine. By inhibiting IDO1 and decreasing kynurenine in tumor cells, PF-06840003 increases and restores the proliferation and activation of various immune cells, including dendritic cells (DCs), natural killer (NK) cells, and T-lymphocytes; PF-06840003 also induces increased interferon (IFN) production, and causes a reduction in tumor-associated regulatory T cells (Tregs). Activation of the immune system, which is suppressed in many cancers, may inhibit the growth of IDO1-expressing tumor cells. IDO1, a cytosolic enzyme responsible for tryptophan catabolism and the conversion of tryptophan into kynurenine, is overexpressed by a variety of tumor cell types and antigen presenting cells (APCs); it plays an important role in immunosuppression. Tryptophan depletion inhibits T-lymphocyte proliferation and activation, and subsequently suppresses the immune system.