Linrodostat

National Cancer Institute

Source

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An orally available inhibitor of indoleamine 2,3-dioxygenase 1 (IDO1), with potential immunomodulating and antineoplastic activities. Upon administration, linrodostat specifically targets and binds to IDO1, a cytosolic enzyme responsible for the oxidation of the amino acid tryptophan into the immunosuppressive metabolite kynurenine. By inhibiting IDO1 and decreasing kynurenine in tumor cells, BMS-986205 restores and promotes the proliferation and activation of various immune cells, including dendritic cells (DCs), natural killer (NK) cells, and T-lymphocytes, and causes a reduction in tumor-associated regulatory T-cells (Tregs). Activation of the immune system, which is suppressed in many cancers, may induce a cytotoxic T-lymphocyte (CTL) response against the IDO1-expressing tumor cells, thereby inhibiting the growth of IDO1-expressing tumor cells. IDO1, overexpressed by multiple tumor cell types, plays an important role in immunosuppression. Tryptophan depletion inhibits T-lymphocyte proliferation and activation, and subsequently suppresses the immune system.