Indoximod Prodrug NLG802

National Cancer Institute

Source

National Cancer Institute. Indoximod Prodrug NLG802. NCI Thesaurus. Code C150393.

An orally bioavailable prodrug of indoximod, a methylated tryptophan, with immune checkpoint inhibitory and antineoplastic activities. Upon oral administration, the indoximod prodrug NLG802 is converted to indoximod. Indoximod targets, binds to and inhibits the enzyme indoleamine 2,3-dioxygenase (IDO; IDO1), which converts the essential amino acid tryptophan into the immunosuppressive metabolite kynurenine. By increasing tryptophan levels and decreasing kynurenine levels, indoximod 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 IDO1-expressing tumor cells, thereby inhibiting their growth. 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. NLG802 elicits increased plasma concentrations of indoximod and improves its efficacy, compared to the direct administration of indoximod.