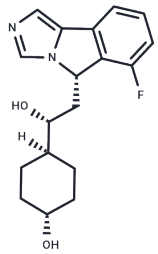
Data Sheet (Cat.No.TQ0071)

TargetMol

Navoximod

Chemical Properties



CAS No. : 1402837-78-8

Formula: C18H21FN2O2

Molecular Weight: 316.37

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Navoximod (GDC-0919) (NLG- 919, GDC-0919) is a potent indoleamine-(2,3)-dioxygenase (IDO) pathway inhibitor (Ki/EC50: 7 nM/75 nM).
Targets(IC50)	IDO,Indoleamine 2,3-Dioxygenase (IDO)
In vitro	Navoximod potently blocks IDO-induced T cell suppression and restores robust T cell responses (ED50: 80 nM) using IDO-expressing human and mouse dendritic cells (DCs) in allogeneic mixed lymphocyte reaction (MLR) and in vitro models from tumor-draining lymph nodes (ED50: 120 nM) [1]. It inhibits IDO activity in a concentration-dependent manner (EC50: 0.95 μM). PEG2k-Fmoc-NLG(L) is less active (EC50: 3.4 μM) compared to Navoximod, while PEG2k-Fmoc-NLG(S) is the least active (EC50>10 μM). Coculture of IDO+ tumor cells with BALB/c mouse splenocytes shows significant inhibition of T-cell proliferation, which is attenuated by Navoximod. PEG2k-Fmoc-NLG(L) also reverses the inhibitory effect of tumor cells, albeit slightly less potently than Navoximod [3].
In vivo	In mice, a single oral administration of Navoximod reduces the concentration of plasma and tissue Kyn by ~50%. In vivo, in mice bearing large established B16F10 tumors, administration of Navoximod markedly enhances the anti-tumor responses of na?ve, resting pmel-1 cells to vaccination with cognate hgp100 peptide plus CpG-1826 in IFA. In this stringent established-tumor model, Navoximod plus pmel-1/vaccine produces a dramatic collapse of tumor size within 4 days of vaccination (~95% reduction in tumor volume compared to control animals receiving pmel-1/vaccine alone without Navoximod) [1]. When combined with Temozolomide (TMZ)+radiation therapy (RT), both Navoximod and 1-methyl-D-tryptophan (D-1MT, indoximod) enhance survival relative to mice treated with TMZ+RT alone [2].
Cell Research	Briefly, HeLa cells are seeded in a 96-well plate at a cell density of 5000 cells per well and allowed to grow overnight. Recombinant human IFN-γ is then added to each well with a final concentration of 50?ng/mL. At the same time, various concentrations of PEG2k-Fmoc-NLG(L), PEG2k-Fmoc-NLG(S) or Navoximod (NLG919) (50?nM-20?μM) are added to the cells. After 48?h of incubation, 150?μL of the supernatants per well is transferred to a new 96-well plate. Seventy-five μL of 30% trichloroacetic acid is added into each well and the mixture is incubated at 50°C for 30?min to hydrolyse N-formylkynurenine to kynurenine. For the colorimetric assay, supernatants are transferred to a new 96-well plate, mixed with an equal volume of Ehrlich reagent (2% p-dimethylamino-benzaldehyde w/v in glacial acetic acid), and incubated for 10?min at

Cell Research	RT. The reaction product is measured at 490?nm by a plate reader [3].
Animal Research	Mice are anesthetized with 4% isoflurane, and the surgical plane of anesthesia is maintained with 2% isoflurane in oxygen. Mice are immobilized in a stereotactic frame for tumor implantation. Briefly, the skull is shaved and exposed with a 0.5 cm skin incision. With the antiseptic technique, 10^5 GL261 cells (suspended in 3 μL RPMI-1640) are injected at the following coordinates with respect to the bregma on the right side (antero-posterior, -2 mm; medio-lateral, 2 mm; dorsoventral, 3 mm). This placement reproducibly yielded tumor growth in a paracortical area of the posterolateral right frontal lobe. Tumor-bearing mice are treated with combinations of oral DL-1MT (2 mg/mL D-1MT mixed with 2 mg/mL L-1MT) in drinking water, D-1MT (4 mg/mL) in drinking water, Navoximod (6 mg/mL) in drinking water, intraperitoneal cyclophosphamide, intraperitoneal temozolomide, and/or total-body radiation (500 cGy from a 137Cs source), as detailed in figure legends. Mice are observed daily and sacrificed when they became ill or moribund [2].

Solubility Information

Solubility	DMSO: 100 mg/mL (316.09 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4 mg/mL (12.64 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.1609 mL	15.8043 mL	31.6086 mL
5 mM	0.6322 mL	3.1609 mL	6.3217 mL
10 mM	0.3161 mL	1.5804 mL	3.1609 mL
50 mM	0.0632 mL	0.3161 mL	0.6322 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Mario R. Mautino, et al. Abstract 491: NLG919, a novel indoleamine-2,3-dioxygenase (IDO)-pathway inhibitor drug candidate for cancer therapy. AACR 104th Annual Meeting 2013; Apr 6-10, 2013.
Li M, et al. The indoleamine 2,3-dioxygenase pathway controls complement-dependent enhancement of chemo-radiation therapy against murine glioblastoma. J Immunother Cancer. 2014 Jul 7;2:21.
Chen Y, et al. An immunostimulatory dual-functional nanocarrier that improves cancer immunochemotherapy. Nat Commun. 2016 Nov 7;7:13443.

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481