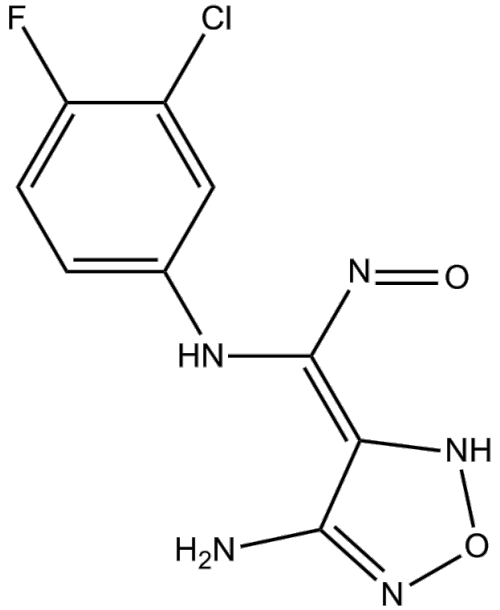
Product Data Sheet

Product Name: INCB024360 analogue
Cat. No.: GC15846

Chemical Properties

Cas. No.	914471-09-3		
Chemical Name	4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine		
SMILES	C1=CC(=C(C=C1NC(=C2C(=NON2)N)N=O)Cl)F		
Formula	$C_9H_7ClFN_5O_2$	M.Wt	271.64
Solubility	≥ 13.55mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Kinase experiment [1]:

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IDO enzyme assays	Human IDO with an N-terminal His tag was expressed in E.coli and purified to homogeneity. IDO catalyzed the oxidative cleavage of the pyrrole ring of the indole nucleus of tryptophan to yield N'-formylkynurenine. The assays were performed at room temperature using 20 nM IDO and 2 mM D-Trp in the presence of 20 mM ascorbate, 3.5 μM methylene blue and 0.2 mg/mL catalase in 50 mM potassium phosphate buffer (pH 6.5). The initial reaction rates were recorded by continuously following the absorbance increase at 321 nm due to the formation of N'-formlylkynurenine.

Cell experiment [1]:

Cell lines	Hela cells and murine B16 cells
Preparation method	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reaction Conditions	19 nM (the IC50 value for Hela cells) and 46 nM (the IC50 value for murine B16 cells)
Applications	In Hela cells, INCB024360 analogue selectively inhibited the activity of human IDO1 with an IC50 value of 19 nM. In murine B16 cells, INCB024360 analogue inhibited IDO with an IC50 value of 46 nM.

Animal experiment [1]:

Animal models	Mice bearing GM-CSF-secreting B16 tumors

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Dosage form	25, 50 and 75 mg/kg; s.c.; b.i.d, for 14 days
Applications	In mice bearing GM-CSF-secreting B16 tumors, INCB024360 analogue (75 mg/kg, b.i.d.) inhibited tumor growth in a dose-dependent manner.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Yue EW1, Douty B, Wayland B, et al. Discovery of potent competitive inhibitors of indoleamine 2,3-dioxygenase with in vivo pharmacodynamic activity and efficacy in a mouse melanoma model. J Med Chem. 2009 Dec 10;52(23):7364-7.

Background

INCB024360 analogue is a potent and selective inhibitor of IDO1 with IC50 value of 67 nM. [1]

IDO (indoleamine-pyrrole 2, 3-dioxygenase) is an enzyme which is encoded by the IDO1 gene. IDO is the rate-limiting and first enzyme of tryptophan which is one amino acid of human catabolism through kynurenine pathway. The decrease of L-tryptophan can cause halted growth of T cells as well as microbes. IDO belongs to immunomodulatory enzyme. It is produced by some activated macrophages and immunoregulatory cells. IDO is overexpressed in a wide range of cancer cells such as lung, prostatic, pancreatic, colorectal cancer. It is indentified to help cancer cells to escape the immune system by reducing the level of L-tryptophan in the microenvironment of cells.[2]

In Hela cells, INCB024360 analogue selectively inhibited the activity of human IDO1 with IC50 value of 19 nM. On the other hand, INCB024360 analogue demonstrated little inhibition activity against TDO (tryptophan 2, 3-dioxygenase). In murine B16 cells, INCB024360 analogue inhibited IDO with IC50 value of 46 nM [1].

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In naive C57BL/6 mice, 100 mg/kg INCB024360 analogue injected subcutaneously reduced kynurenine levels by >50% via inhibition of IDO activity. In C57BL/6 mice bearing GM-CSF- secreting B16 tumors, INCB024360 analogue (25, 50, and 75 mg/kg b.i.d.) injected subcutaneously for 14 days dose-dependently inhibited tumor growth [1].

References:

[1]. Yue EW1, Douty B, Wayland B, et al. Discovery of potent competitive inhibitors of indoleamine 2,3-dioxygenase with in vivo pharmacodynamic activity and efficacy in a mouse melanoma model. J Med Chem. 2009 Dec 10;52(23):7364-7.
[2]. Uyttenhove C, Pilotte L, Theate I, Stroobant V, Colau D, Parmentier N, Boon T, Van den Eynde BJ: Evidence for a tumoral immune resistance mechanism based on tryptophan degradation by indoleamine 2,3-dioxygenase. Nat Med 2003, 9(10):1269-1274.

Caution: Product has not been fully validated for medical applications. For research use only.
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