Product Data Sheet

Product Name: INCB 3284 dimesylate
Cat. No.: GC14821

Chemical Properties

Cas. No.	887401-93-6		
Chemical Name	N-(2-((1-(4-hydroxy-4-(6-methoxypyridin-3-yl)cyclohexyl)pyrrolidin-3-yl)amino)-2-oxoethyl)-3-(trifluoromethyl)benzamide dimethanesulfonate		
SMILES	COC1=NC=C(C2(O)CCC(N3CCC(NC(CNC(C4=CC(C(F)(F)F)=CC=C4)=O)=O)C3)CC2)C=C1.CS(=O)(O)=O.CS(=O)(O)=O		
Formula	$C_{28}H_{39}F_3N_4O_{10}S_2$	M.Wt	712.76
Solubility	DMF: 11 mg/ml,DMSO: 12 mg/ml,PBS (pH 7.2): 5 mg/ml	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	INCB 3284 dimesylate		

Protocol

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Animal experiment:

Mice[2]Male C57Bl/6 mice (20 to 25 g) are given free access to water and rodent chow and are housed in constant temperature, humidity, and 12 h light-dark cycling. Acute liver failure is induced via a single intraperitoneal (ip) injection of 100 mg/kg of azoxymethane (AOM). In parallel, systemic inhibition of CCR2 and CCR4 activity is accomplished via pretreatment with INCB 3284 (1 mg/kg/day ip) or C021 (1 mg/kg/day ip) for 3 days prior to injection of AOM. Following injection, mice are placed on heating pads adjusted to 37°C and monitored frequently for signs of neurological decline. To reduce the impacts of hypoglycemia and dehydration, cage floors are supplied with hydrogel and rodent chow and after 12 h, and every subsequent 4 h, mice are injected subcutaneously with 5% dextrose in 250 µL of saline. If mice undergo a 20% or greater weight loss they are removed from the study[2].

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References:

[1]. Xue CB, et al. Discovery of INCB3284, a Potent, Selective, and Orally Bioavailable hCCR2 Antagonist. ACS Med Chem Lett. 2011 Mar 31;2(6):450-4.
[2]. McMillin M, et al. Neuronal CCL2 is upregulated during hepatic encephalopathy and contributes to microglia activation and neurological decline. J Neuroinflammation. 2014 Jul 10;11:121.

Background

INCB 3284 dimesylate is a potent, selective and orally bioavailable human CCR2 antagonist, inhibiting monocyte chemoattractant protein-1 binding to hCCR2, with an IC50 of 3.7 nM. INCB 3284 dimesylate can be used in the research of acute liver failure.

INCB 3284 dimesylate is a pentent, selective and orally bioavailable human CCR2 antagonist, inhibiting monocyte chemoattractant protein-1 binding to hCCR2, with an IC50 of 3.7 nM. INCB 3284 also causes an IC50 of 4.7 nM in antagonism of chemotaxis activity, an IC50 of 84 μM in inhibition of the hERG potassium current. However, INCB 3284 has no effec on CCR1, CCR3, CCR5, CXCR3, and CXCR5, or additional GPCRs at a

concentration of 1 μM. Moreover, INCB 3284 potently inhibits CCR2-mediated signaling events such as intracellular calcium mobilization and ERK phosphorylation with IC50 values of 6 and 2.6 nM, respectively[1].

INCB 3284 (1 mg/kg/day, ip) reduces liver damage, and decreases microglia activation in AOM-treated mice via inhibition on CCR2. INCB 3284 also significantly reduces the pERK1/2 to tERK1/2 ratio, as well as G-protein signaling pathway activity and proinflammatory cytokine production in cortex lysates from mice administed with azoxymethane[2].

References:
[1]. Xue CB, et al. Discovery of INCB3284, a Potent, Selective, and Orally Bioavailable hCCR2 Antagonist. ACS Med Chem Lett. 2011 Mar 31;2(6):450-4.
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