Product Data Sheet

Product Name: BMS-509744
Cat. No.: GC10455

Chemical Properties

Cas. No.	439575-02-7		
Chemical Name	N-(5-((5-(4-acetylpiperazine-1-carbonyl)-4-methoxy-2-methylphenyl)thio)thiazol-2-yl)-4-(((3,3-dimethylbutan-2-yl)amino)methyl)benzamide		
SMILES	CC1=C(SC(S2)=CN=C2NC(C3=CC=C(CNC(C(C)(C)C)C)C=C3)=O)C=C(C(N4CCN(C(C)=O)CC4)=O)C(OC)=C1		
Formula	$C_{32}H_{41}N_5O_4S_2$	M.Wt	623.83
Solubility	DMSO : 21.9 mg/mL (35.11 mM; Need ultrasonic and warming)	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	BMS-509744		

Protocol

Cell experiment [1]:

Cell lines	Jurkat T cells and A549 lung carcinoma cells
Preparation method	This compound is soluble in DMSO. 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.

Caution: Product has not been fully validated for medical applications. For research use only.
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Reacting condition	0.1 ~ 10 μM
Applications	In Jurkat T-cells, BMS-509744 dose-dependently inhibited tyrosine phosphorylation of phospholipase Cγ1 (PLCγ1) induced by anti-CD3 antibodies. In A549 lung carcinoma cells, Itk expression of which was not evident, BMS-509744 did not exhibit significant inhibition on cellular tyrosine or PLCγ1 phosphorylation induced by epidermal growth factors, at the concentration even up to 10 μM.

Animal experiment [1]:

Animal models	Mice
Dosage form	5, 25 and 50 mg/kg; s.c. or i.p.; b.i.d., for 3 days
Applications	In mice treated with anti-CD3 antibodies, BMS-509744 at the dose of 50 mg/kg inhibited IL-2 production by 50%. In a mouse model of ovalbumin-induced allergy/asthma, BMS-509744 dose-dependently reduced total cell and eosinophil infiltration into the lung, which indicated reduced lung inflammation. The reduction reached statistical significance at the dose of 25 mg/kg administered subcutaneously.
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.

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References:

[1]. Lin, T.A., et al., Selective Itk inhibitors block T-cell activation and murine lung inflammation. Biochemistry, 2004. 43(34): p. 11056-62.

Background

BMS-509744 is a selective inhibitor of ITK with IC50 value of 15 nM [1].
ITK (IL-2-inducible T cell kinase) is an enzyme and plays an important role in T cell receptor signaling. It has been reported that ITK involves in the Th2-mediated inflammatory process and thus be regarded as a promising target for Th2-mediated inflammatory/immunosuppressive diseases treatment, such as asthma, rhinitis, allergies and atopic dermatitis [2].
BMS-509744 is a potent ITK inhibitor and is different from the reported ITK inhibitor RO5191614. When tested with human and murine cells, administration of BMS-509744 reduced TCR-induced functions by functioning on PLCgamma1 tyrosine phosphorylation, calcium mobilization, IL-2 secretion and T-cell proliferation [2]. In wild-typr HIV1 infected cells, BMS-509744 treatment blocked its infectivity and replication by inhibiting ITK, while has no effect on Nef-defective HIV1 infected cells [3].
In mouse model of ovalbuim-induced allergy/asthma, administration of BMS-509744 suppressed the production of IL-2 and significantly diminished lung inflammation by inhibiting ITK activity [2].
References:
[1].Kutach, A.K., et al., Crystal structures of IL-2-inducible T cell kinase complexed with inhibitors: insights into rational drug design and activity regulation. Chem Biol Drug Des, 2010. 76(2): p. 154-63.
[2].Lin, T.A., et al., Selective Itk inhibitors block T-cell activation and murine lung inflammation. Biochemistry, 2004. 43(34): p. 11056-62.
[3].Tarafdar, S., J.A. Poe, and T.E. Smithgall, The accessory factor Nef links HIV-1 to Tec/Btk kinases in an Src homology 3 domain-dependent manner. J Biol Chem, 2014.

289(22): p. 15718-28.

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