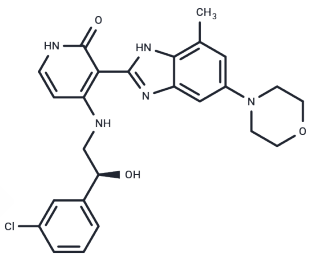
Data Sheet (Cat.No.T6419)

TargetMol

BMS-536924

Chemical Properties



CAS No. : 468740-43-4

Formula: C25H26ClN5O3

Molecular Weight: 479.96

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	BMS-536924 (BMS 536924) is an ATP-competitive IGF-1R/IR inhibitor with IC50 of 100 nM/73 nM, modest activity for Mek, Fak, and Lck with very little activity for Akt1, MAPK1/2.
Targets(IC50)	Apoptosis,FAK,MEK,IGF-1R,Src
In vitro	BMS-536924 also inhibits FAK and Lck with IC50 of 150 nM and 341 nM, respectively. BMS-536924 inhibits cellular proliferation and disrupts Akt and MAPK phosphorylation. [1] BMS-536924 inhibits IGF-I-stimulated IGF-1R signaling in MCF10A cells and blocks constitutive IGF-1R activity in CD8-IGF-1R-MCF10A. Preincubation of MCF10A cells with 1 μM BMS-536924 completely blocks the ability of IGF-I to stimulate IGF-1R phosphorylation. IGF-I stimulation results in increased phosphorylation of ERK1/2, GSK3β, and Akt. BMS-536924 inhibits this ligand-induced phosphorylation. Treatment of the CD8-IGF-1R-MCF10A cells with BMS-536924 results in a dose-dependent inhibition of phosphorylation with partial inhibition at 0.01 μM and 0.1 μM, but complete receptor inhibition at a concentration of 1 μM. Maximal inhibition of phosphorylated IGF-1R is observed as early as 10 minutes following incubation. BMS-536924 retains its ability to inhibit IGF-1R phosphorylation for up to 48 hours. Addition of BMS-536924 time-dependently inhibits Akt phosphorylation starting at 1 hour. By 48 hours, Akt activation is completely blocked. [2] Treatment with BMS-536924 shows antiproliferation activity in a panel of cancer cell lines including TC32, HT1080/S, SK-LMS-1, H513 and CTR cells. pIGF-1R/pIR is activated upon IGF-I/insulin stimulation and the activation is inhibited by BMS-536924 at similar potencies in Rh41 and Rh36 cell lines. The expression of programmed cell death 4 (PDCD4), cleavage of poly(ADP-ribose) polymerase (PARP) and caspase-3 are up-regulated in Rh41 cells treated with BMS-536924. [3]
In vivo	Oral administration of BMS-536924 at 100-300 mpk strongly inhibits IGR-1R Sal tumor model. Efficacy is also observed in the nonengineered Colo205 human colon carcinoma mode. Oral administration of 3 on a once a day schedule (100-300 mpk) or a twice a day schedule (50, 100 mpk) demonstrates antitumor activity in this tumor model. Oral glucose tolerance test (OGTT) shows 100 mpk (b.i.d.) causes a significant elevation in glucose levels after glucose challenge. The pharmacokinetic parameters of BMS-536924, administered orally in poly(ethylene glycol) 400 and water (80:20 v/v), are determined in mouse, rat, dog, and monkey. Good bioavailability is evident in all species. Significant nonlinear pharmacokinetics is observed in rodents at increasing p.o. dose. [1] BMS-536924 reduces the tumor xenografts volume of CD8-IGF-1R-MCF10A cells after two

In vivo	weeks' treatment (100 mg/kg) to 76%. [2] Oral administration of 70 mg/kg BMS-536924 significantly inhibits tumor growth (TGBC-1TKB cells) inoculated in nude mice. BMS-536924 up regulates apoptosis in xenografts tumors. The treatment doesn't have adverse effects on the body weight of mice or the glucose levels at the time of death, suggesting tolerable toxicity. [4]
Kinase Assay	IGF-I Pathway Activity: 1 × 106 pBabe-MCF10A cells are seeded onto 60-mm dishes. After 24 hours, the medium is changed to serum-free medium and incubated overnight at 37 °C for 24 hours. Cells are then pre-incubated with or without 1 uM BMS-536924 for 1 hour in serum free medium followed by stimulation with IGF-I (50 ng/mL) for 10 minutes. Cell monolayers are washed twice with PBS and harvested for immunoblot analysi
Cell Research	Cell proliferation is evaluated by [3H]thymidine incorporation after exposure to BMS-536924 for 72 hours. Cells are plated at an optimized density in 96-well plates, incubated overnight at 37 °C, and then exposed to a serial dilution of the drug. After a 72-hours incubation, cells are pulsed with 4 μCi/mL [3H]thymidine for 3 hours, trypsinized, harvested onto UniFilter-96 GF/B plates; scintillation is measured on a TopCount NXT. Results are expressed as an IC50. The mean IC50 and SD from multiple tests for each cell line are calculated. (Only for Reference)

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 89 mg/mL (185.43 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: 3.3 mg/mL (6.88 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	2.0835 mL	10.4175 mL	20.8351 mL
5 mM	0.4167 mL	2.0835 mL	4.167 mL
10 mM	0.2084 mL	1.0418 mL	2.0835 mL
50 mM	0.0417 mL	0.2084 mL	0.4167 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

Wittman M, et al. J Med Chem, 2005, 48(18), 5639-5643
Litzenburger BC, et al. Clin Cancer Res, 2009, 15(1), 226-237
Huang F, et al. Cancer Res, 2009, 69(1), 161-170
Hirokazu Ohashi, et al. Cancer Sci, 2012, 103(2), 252-261
Haluska P, et al, Mol Cancer THer, 2008, 7(9), 2589-2598.