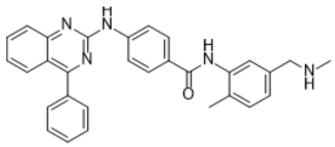
BMS-833923

Cat. No.:	HY-13809
CAS No.:	1059734-66-5
Molecular Formula:	$C_{30}H_{27}N_5O$
Molecular Weight:	473.57
Target:	Smo; Apoptosis
Pathway:	Stem Cell/Wnt; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (105.58 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1116 mL	10.5581 mL	21.1162 mL
	5 mM	0.4223 mL	2.1116 mL	4.2232 mL
	10 mM	0.2112 mL	1.0558 mL	2.1116 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.28 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BMS-833923 (XL-139) is an orally biocompatible Smoothened (Smo) inhibitor with anti-tumor activity. It can inhibit the binding of BODIPY cyclopamine to SMO in a dose-dependent manner with an IC_{50} of 21 nM[1].

In Vitro

BMS-833923 inhibits the expression of downstream effectors in the HH pathway (GLI1 and PTCH1) wild-type SMO and activated mutant forms of SMO expressing cells (IC_{50}: 6-35 nM)[1].
BMS-833923 (2.5-10 μM, 48 h) inhibits cell proliferation of both A549 and H1299 cells[2].
BMS-833923 (3 μM) inhibits osteoblast differentiation and mineralization of hMSCs, determined by decreased ALP activity and downregulation of osteoblast-related gene expression[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

RT-PCR[3]

Cell Line:	human MSCs
Concentration:	3 μM
Incubation Time:	48 h
Result:	Inhibited gene expression of ALP, ON, COL1A1, GLI1, and PTCH1.

In Vivo

BMS-833923 (15 mg/kg, oral gavage, daily) alone or together with Selumetinib (HY-50706) (10 mg/kg, oral gavage, daily) reduces tumor metastasis and the post-extravasation tumor growth in orthotopic mouse model of pancreatic cancer metastasis[4].

BMS-833923 (30 mg/kg, p.o., seven consecutive days) alone or together with Gemcitabine (HY-17026) (40 mg/kg, i.p., at the 1st, 4th and 7th day) reduces tumor volume (to 60% and 32% respectively) in a nu/nu mice xenograft model of cholangiocarcinoma[5].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Du J, et al. Disruption of SHH signaling cascade by SBE attenuates lung cancer progression and sensitizes DDP treatment. Sci Rep. 2017 May 15;7(1):1899.

[2]. AlMuraikhi N, et al. Hedgehog Signaling Inhibition by Smoothened Antagonist BMS-833923 Reduces Osteoblast Differentiation and Ectopic Bone Formation of Human Skeletal (Mesenchymal) Stem Cells. Stem Cells Int. 2019 Nov 21;2019:3435901.

[3]. Gu D, et al. Simultaneous Inhibition of MEK and Hh Signaling Reduces Pancreatic Cancer Metastasis. Cancers (Basel). 2018 Oct 26;10(11):403.

[4]. Riedlinger D, et al. Hedgehog pathway as a potential treatment target in human cholangiocarcinoma. J Hepatobiliary Pancreat Sci. 2014 Aug;21(8):607-15.

[5]. Steven B, et al. Abstract B192: Preclinical characterization of BMS-833923 (XL139), a hedgehog (HH) pathway inhibitor in early clinical development. Molecular Cancer Therapeutics: December 2009; Volume 8, Issue 12, Supplement 1.

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