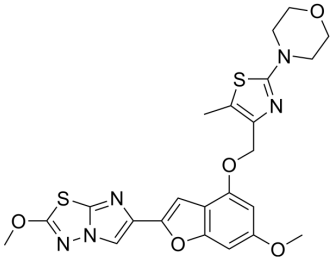
BMS-986120

Cat. No.:	HY-19837
CAS No.:	1478712-37-6
Molecular Formula:	$C_{23}H_{23}N_5O_5S_2$
Molecular Weight:	513.59
Target:	Protease Activated Receptor (PAR)
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 3.33 mg/mL (6.48 mM; ultrasonic and warming and heat to 80°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9471 mL	9.7354 mL	19.4708 mL
	5 mM	0.3894 mL	1.9471 mL	3.8942 mL
	10 mM	---	---	---

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

BIOLOGICAL ACTIVITY

Description

BMS-986120 is a first-in-class oral and reversible protease-activated receptor 4 (PAR4) antagonist, with IC_{50}s of 9.5 nM and 2.1 nM in human and monkey blood, respectively. BMS-986120 has potent and selective antiplatelet effects[1][2].

IC_{50} & Target

PAR4

In Vitro

BMS-986120 has high binding affinity to PAR4 expressed on HEK293 cells and inhibition of PAR4-induced calcium mobilization with an IC_{50} of 0.56 nM[3].

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

In Vivo

In monkeys, BMS-986120 (1 mg/kg) does not inhibit PA induced by PAR1-AP, ADP and collagen, supporting selectivity. BMS-986120 (0.2, 0.5, 1 mg/kg) reduces TW by 35±5, 49±4, and 83±4%, respectively. Maximum KBT and MBT increases are only 2.2-fold and 1.8-fold, respectively[1].

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PROTOCOL

Animal Administration [1]

Monkeys[1]

Individual anesthetized monkeys are given orally of BMS-986120 (BMS: 0.2, 0.5,1 mg/kg) or vehicle (n=8/group) 2 hour before a combination of thrombosis, BT and ex vivo biomarker experiments. Aspirin alone (ASA, 4 mg/kg/h IV) or in combination with BMS-986120 (0.5, 1 mg/kg) is also studied (n=8/group). Thrombus weight (TW) reduction, BT increase over vehicle in kidney (KBT) and mesenteric artery (MBT), and platelet aggregation (PA) inhibition are determined. Peak PA responses to activation peptides selective for PAR4 (PAR4-AP, 12.5 μM) and PAR1 (PAR1-AP, 18 μM), ADP (20 μM), and collagen (5 μg/mL) are determined by whole blood aggregometry[1].

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

REFERENCES

[1]. Pancras C Wong, et al. Abstract 175: A Novel Orally-Active Small-Molecule Antagonist of the Platelet Protease-Activated Receptor-4, BMS-986120, Inhibits Arterial Thrombosis With Limited Impact on Hemostasis in Cynomolgus Monkeys. Stroke. 2018;47:A175.

[2]. Wilson SJ, et al. PAR4 (Protease-Activated Receptor 4) Antagonism With BMS-986120 Inhibits Human Ex VivoThrombus Formation. Arterioscler Thromb Vasc Biol. 2018 Feb;38(2):448-456.

[3]. Wong PC, et al. Blockade of protease-activated receptor-4 (PAR4) provides robust antithrombotic activity with low bleeding. Sci Transl Med. 2017 Jan 4;9(371).

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