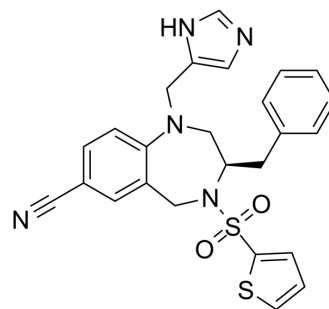


BMS-214662

Cat. No.:	HY-16111		
CAS No.:	195987-41-8		
Molecular Formula:	C ₂₅ H ₂₃ N ₅ O ₂ S ₂		
Molecular Weight:	489.61		
Target:	Farnesyl Transferase		
Pathway:	Metabolic Enzyme/Protease		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (204.24 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.0424 mL	10.2122 mL	20.4244 mL
	5 mM	0.4085 mL	2.0424 mL	4.0849 mL
	10 mM	0.2042 mL	1.0212 mL	2.0424 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (5.11 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (5.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BMS-214662 is a potent and selective farnesyl transferase inhibitor with potent antitumor activity with an IC₅₀ of 1.35 nM.

IC₅₀ & Target

IC₅₀: 1.35 nM (farnesyl transferase), 1.3 μM (Ras-CVLL), 2.3 μM (K-Ras)^[1]

In Vitro

BMS-214662 is over 1000-fold selective for farnesyl transferase, having IC₅₀ values for inhibition of geranylgeranylation of Ras-CVLL and K-Ras of 1.3 and 2.3 μM, respectively^[1]. BMS-214662 shows good potency in inhibiting H-ras-transformed rodent cells, A2780 human ovarian carcinoma tumor cells, and HCT-116 human colon carcinoma tumor cells. BMS-214662 is the most potent apoptotic FTI known and demonstrates broad spectrum yet robust cell-selective cytotoxic activity against a panel of cell lines with diverse histology^[2].

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

In Vivo

Tumors from BMS-214662-treated mice have increased numbers of apoptotic cells as compared with the nontreated control mice. The AIs in HCT-116 tumors are increased 4-10-fold in BMS-214662-treated mice as compared with nontreated controls. BMS-214662 is significantly cytotoxic to both HCT-116 and EJ-1 tumor cells; the doses of BMS-214662 required to kill 90% of clonogenic tumor cells are approximately 75 and 100 mg/kg for HCT-116 and EJ-1 tumors^[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

The hydrochloride salt of BMS-214662 is dissolved in DMSO with dilutions made using either water or RPMI 1640 plus 10% fetal bovine serum. BMS-214662 is added at various concentrations. The cells are incubated at 37°C for 72 h, at which time MTS in combination with phenazine methosulfate is added. After an additional 3 h, the absorbance is measured at 492 nm, and the growth inhibition results are eventually expressed as IC₅₀^[2].

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

Animal Administration ^[2]

Mice: BMS-214662 is dissolved in ethanol, followed by dilution with water to a final ethanol concentration of 10%. Mice implanted with HCT-116 xenografts are administered a single dose of BMS-214662 at 250 mg/kg i.v., 300 mg/kg i.p., or 400 mg/kg p.o. An additional group receives 400 mg/kg BMS-214662 daily for 2 days (administered p.o. on day 1 and i.p. on day 2). Nontreated mice with time-matched HCT-116 tumors served as controls. Tumors are collected at 24 h after dose, processed following standard methods, sectioned, and stained with H&E. Serial sections of each tumor are processed for in situ apoptotic cell labeling by the TUNEL method^[2].

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

REFERENCES

[1]. Hunt JT, et al. Discovery of (R)-7-cyano-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1,4-benzodiazepine (BMS-214662), a farnesyltransferase inhibitor with potent preclinical antitumor activity. *J Med Chem.* 200

[2]. Rose WC, et al. Preclinical antitumor activity of BMS-214662, a highly apoptotic and novel farnesyltransferase inhibitor. *Cancer Res.* 2001 Oct 15;61(20):7507-17.

Caution: Product has not been fully validated for medical applications. For research use only.

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