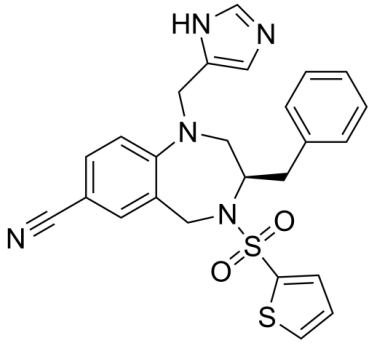
Data Sheet

Product Name:	BMS-214662
Cat. No.:	CS-6471
CAS No.:	195987-41-8
Molecular Formula:	$C_{25}H_{23}N_5O_2S_2$
Molecular Weight:	489.61
Target:	Farnesyl Transferase; Ras
Pathway:	GPCR/G Protein; MAPK/ERK Pathway; Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 100 mg/mL



BIOLOGICAL ACTIVITY:

BMS-214662 is a **farnesyl transferase** inhibitor. BMS-214662 can effectively block the localization and function of Ras protein in the cell membrane by inhibiting the pro-group modification of Ras protein, thereby exerting anti-tumor activity. BMS-214662 has an **IC_{50}** value of 1.3 nM for H-Ras and 8.4 nM for K-Ras. BMS-214662 can be used to study Ras-related tumor diseases[1][2]. 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 IC_{50} 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]. ***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].

PROTOCOL (Extracted from published papers and Only for reference)

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 IC_{50}s[2]. **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].

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. 2000 Oct 5;43(20):3587-95.

[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.

CAIndexNames:

1H-1,4-Benzodiazepine-7-carbonitrile, 2,3,4,5-tetrahydro-1-(1H-imidazol-5-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-, (3R)-

SMILES:

N#CC1=CC=C(N(CC2=CN=CN2)C[C@@H](CC3=CC=CC=C3)N(S(=O)(C4=CC=CS4)=O)C5)C5=C1

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