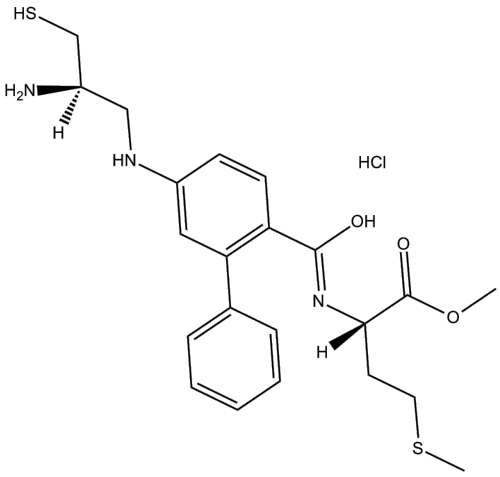
Product Data Sheet

Product Name: FTI 277 HCl
Cat. No.: GC16310

Chemical Properties

Cas. No.	180977-34-8		
Chemical Name	(Z)-5-(((R)-2-amino-3-mercaptopropyl)amino)-N-((S)-1-methoxy-4-(methylthio)-1-oxobutan-2-yl)-[1,1'-biphenyl]-2-carbimidic acid hydrochloride		
SMILES	COC([C@](/N=C(O)/C1=C(C2=CC=CC=C2)C=C(NC[C@](N)([H])CS)C=C1)([H])CCSC)=O.Cl		
Formula	$C_{22}H_{30}ClN_3O_3S_2$	M.Wt	484.07
Solubility	≥ 100mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Product Data Sheet

Cell lines	MDA-MB-231 (breast cancer cells)
Preparation Method	H-Ras and N-Ras are mainly located on the inner side of the cell membrane. To collect membrane fractions, cells were treated with FTI 277 HCl (50μM) for 24h and EGF (10ng/ml) for 30min prior to lysis. The level of Ras-GTP was measured by Ras assay reagent. The cells were treated with 10ng/ml EGF for 30min and lysed in Mg^{2+} lysis/wash buffer. Raf-1 RBD-agarose was added to the lysates and incubated for 45min at 4°C. The bead pellet was washed 3 times with MLB buffer, boiled in 2× Laemmli sample buffer, and subjected to immunoblot analysis with anti-H-Ras or anti-N-Ras antibodies.
Reaction Conditions	50μM; 24h
Applications	FTI 277 HCl inhibited the EGF-induced activation of H-Ras, but not that of N-Ras, in membrane fractions of MDA-MB-231 cells.

Animal experiment [2]:

Animal models	SCID mice inoculated with HT29 cells
Preparation Method	HT29 cells (1.5×10^6 cells) were inoculated into the spleen of SCID mice. After inoculation, FTI 277 HCl (1 and 5mg/kg/day) was administered daily for 3 weeks i.p. to SCID mice.
Dosage form	1 and 5mg/kg/day; 3 weeks; i.p.

Product Data Sheet

Applications	FTI 277 HCl treatment significantly reduced relative spleen weight and splenic primary tumor volume and also significantly reduced relative liver weight and liver metastasis volume. And no toxicity (diarrhea or loss of body weight) was detected in the FTI 277 HCl treatment group.

References:
[1] LEE K H, KOH M, MOON A. Farnesyl transferase inhibitor FTI-277 inhibits breast cell invasion and migration by blocking H-Ras activation[J]. Oncology Letters, 2016, 12(3): 2222-2226.
[2] NAM J S, INO Y, SAKAMOTO M, et al. Ras farnesylation inhibitor FTI-277 restores the E-cadherin/catenin cell adhesion system in human cancer cells and reduces cancer metastasis[J]. Japanese Journal of Cancer Research, 2002, 93(9): 1020-1028.

Background

FTI 277 HCl is a potent and selective farnesyltransferase (FTase) inhibitor with an IC_{50} value of 0.5nM, exhibiting approximately 100-fold greater selectivity over geranylgeranyltransferase I (GGTase I)[1]. FTase-mediated farnesylation is the first irreversible and rate-limiting step for Ras membrane association, and is an obligatory modification for the biological activity of oncogenic Ras[2]. FTI 277 HCl is commonly used in research on the function of farnesyltransferase and the role of Ras-mediated signaling pathways in diseases such as cancer[3,4].

In vitro, treatment of vascular smooth muscle cells (VSMCs) with FTI 277 HCl (20μM) for 10 days significantly inhibited β-glycerophosphate (βGP)-induced mineral deposition, reduced the mRNA expression of Runx2 and Msx2, and up-regulated the expression of MGP[5]. Pretreatment of breast cancer MDA-MB-231 cells with FTI 277 HCl (50μM) for 24h inhibited epidermal growth factor (EGF)-induced activation of H-Ras in the membrane fraction, but did not inhibit the activation of N-Ras[6].

In vivo, administration of FTI 277 HCl (1 and 5mg/kg/day) via intraperitoneal injection in SCID mice inoculated with human colon cancer HT29 cells for 3 weeks significantly reduced relative spleen weight and primary splenic tumor volume, as well as relative liver weight and liver metastasis volume, without causing significant toxicity[7]. In mice treated with FTI 277 HCl (25mg/kg) via intraperitoneal injection before L-arginine-induced pancreatitis, samples were harvested 72h after the

first dose of L-arginine. FTI 277 HCl administration significantly reduced L-arginine-induced myeloperoxidase (MPO) levels and the number of extravascular neutrophils in the pancreas[8].

References:

[1] LERNER E C, QIAN Y, BLASKOVICH M A, et al. Ras CAAX peptidomimetic FTI-277 selectively blocks oncogenic Ras signaling by inducing cytoplasmic accumulation of inactive Ras-Raf complexes[J]. Journal of Biological Chemistry, 1995, 270(45): 26802-26806.
[2] COX A D, DER C J, PHILIPS M R. Targeting RAS membrane association: back to the future for anti-RAS drug discovery?[J]. Clinical Cancer Research, 2015, 21(8): 1819-1827.
[3] MAZZOCCA A, GIUSTI S, HAMILTON A D, et al. Growth inhibition by the farnesyltransferase inhibitor FTI-277 involves Bcl-2 expression and defective association with Raf-1 in liver cancer cell lines[J]. Molecular Pharmacology, 2003, 63(1): 159-166.
[4] BERNHARD E J, KAO G, COX A D, et al. The farnesyltransferase inhibitor FTI-277 radiosensitizes H-ras-transformed rat embryo fibroblasts[J]. Cancer Research, 1996, 56(8): 1727-1730.
[5] PONNUSAMY A, SINHA S, HYDE G D, et al. FTI-277 inhibits smooth muscle cell calcification by up-regulating PI3K/Akt signaling and inhibiting apoptosis[J]. PLoS One, 2018, 13(4): e0196232.
[6] LEE K H, KOH M, MOON A. Farnesyl transferase inhibitor FTI-277 inhibits breast cell invasion and migration by blocking H-Ras activation[J]. Oncology Letters, 2016, 12(3): 2222-2226.
[7] NAM J S, INO Y, SAKAMOTO M, et al. Ras farnesylation inhibitor FTI-277 restores the E-cadherin/catenin cell adhesion system in human cancer cells and reduces cancer metastasis[J]. Japanese Journal of Cancer Research, 2002, 93(9): 1020-1028.
[8] MERZA M, AWLA D, HWAIZ R, et al. Farnesyltransferase regulates neutrophil recruitment and tissue damage in acute pancreatitis[J]. Pancreas, 2014, 43(3): 427-435.