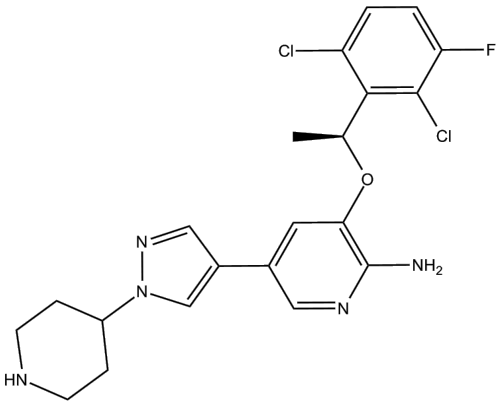
Product Data Sheet

Product Name: (S)-Crizotinib
Cat. No.: GC13136

Chemical Properties

Cas. No.	1374356-45-2		
Chemical Name	3-[(1S)-1-(2,6-dichloro-3-fluorophenyl)ethoxy]-5-(1-piperidin-4-ylpyrazol-4-yl)pyridin-2-amine		
SMILES	CC(C1=C(C=CC(=C1Cl)F)Cl)OC2=C(N=CC(=C2)C3=CN(N=C3)C4CCNCC4)N		
Formula	C21H22Cl2FN5O	M.Wt	450.34
Solubility	≥ 33.3mg/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



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Protocol

Cell experiment:[1]

Cell lines	BJ, H1437, H2122, H23, H358, H460, HCT116 and U2OS cells
Preparation method	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.
Reaction Conditions	BJ, SV40T, RASV12-cells (5 μM, 3h); U2OS cells (5 μM, 24h)
Applications	(S)-crizotinibthe selectively inhibited MTH1 catalytic activity with IC50 of 72 nM, while clinically used (R)-enantiomer of the drug was inactive with IC50 of 1375 nM. Furthermore, direct-binding assays (ITC) indicated a 16-fold higher affinity of the (S)-enantiomer towards MTH1 compared with (R)-enantiomer. By using Km concentrations of substrates, the average IC50 values for (S)-crizotinib and the MTH1 substrates 8-oxo-dGTP and 2-OH-dATP were 330 nM and 408 nM respectively. (S)-crizotinib efficiently inhibited colony formation of SW480 cells andKRAS-mutated PANC1 cells, similar to SCH51344. In addition, *in vitro* Kd measurements indicated that (S)-crizotinib was considerably less potent than the (R)-enantiomer against the established targets ALK,MET and ROS1. (S)-crizotinib did not lead to the detection of any significant effects on proliferation in SW480 cells and showed highest toxicity towards the SV40T and KRASV12 cells. (S)-crizotinib, in contrast to (R)-crizotinib, efficiently stabilized MTH1 validating the differential targeting within BJ-KRASV12 cells using a cellular thermal shift assay. (S)-crizotinib induced an increase in DNA single-strand breaks, activated DNA repair in human colon carcinoma cells, and effectively suppressed tumour growth in animal models as a result of disruption of nucleotide pool homeostasis via MTH1 inhibition.

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Animal experiment:[2]

Animal models	SCID mice (female, 5–6 weeks)
Dosage form	25 mg per kg,subcutaneously daily; 50 mg per kg, orally, daily
Applications	*In vivo* mouse xenograft studies showed (S)-crizotinib, but not the (R)-enantiomer, was able to impair overall tumour progression aswell as specifically reduce tumour volume by more than 50%.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

1. Huber KVM, Salah E, Radic B, et al. Stereospecific targeting of MTH1 by (S)-crizotinib as an anticancer strategy. NATURE,2014;508:222-227

Background

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References:

1. Huber KVM, Salah E, Radic B, et al. Stereospecific targeting of MTH1 by (S)-crizotinib as an anticancer strategy. NATURE,2014;508:222-227

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

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