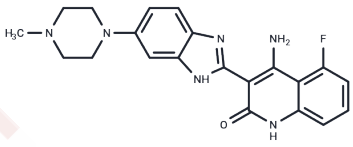
Data Sheet (Cat.No.T6289)

TargetMol

Dovitinib

Chemical Properties



CAS No. : 405169-16-6

Formula: C21H21FN6O

Molecular Weight: 392.43

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Dovitinib is an orally active, multi-targeted tyrosine kinase (RTK) inhibitor with anti-tumor effects.
Targets(IC50)	c-Fms,FGFR,FLT,c-Kit,PDGFR,VEGFR
In vitro	**METHODS**: FGFR3 cell lines (KMS11, KMS18, OPM2, H929) and FGFR3 cell lines were treated with Dovitinib (CHIR-258) (12.5, 25, 50, 100, 200, 300, 400 nM, 48 hours), and cell viability was detected by MTT. **RESULTS** Dovitinib inhibited the proliferation of KMS11 (FGFR3-Y373C), OPM2 (FGFR3-K650E), and KMS18 (FGFR3-G384D) cells with IC50 values of 90 nM (KMS11 and OPM2) and 550 nM, respectively. [1]
In vivo	**METHODS**: Dovitinib (CHIR-258) (10, 30, 60 mg/kg, orally, once a day, 21 days) was used to treat tumor xenograft model mice, and the growth of tumors in vivo was observed. **RESULTS** Significant anti-tumor effects were observed in all three dovitinib dose groups. The minimum effective dose was 10 mg/kg. The growth inhibition in the 10 mg/kg, 30 mg/kg and 60 mg/kg treatment groups was 48% respectively. , 78.5% and 94%. [1]
Kinase Assay	In vitro kinase assays: The inhibitory concentration of 50% (IC50) values for the inhibition of RTKs by Dovitinib are determined in a time-resolved fluorescence (TRF) or radioactive format, measuring the inhibition by Dovitinib of phosphate transfer to a substrate by the respective enzyme. The kinase domains of FGFR3, FGFR1, PDGFRβ, and VEGFR1-3 are assayed in 50 mM HEPES (N-2-hydroxyethylpiperazine-N′-2-ethanesulfonic acid), pH 7.0, 2 mM MgCl2, 10 mM MnCl2 1 mM NaF, 1 mM dithiothreitol (DTT), 1 mg/mL bovine serum albumin (BSA), 0.25 μM biotinylated peptide substrate (GGGGQDGKDYIVLPI), and 1 to 30 μM adenosine triphosphate (ATP) depending on the Km for the respective enzyme. ATP concentrations are at or just below Km. For c-KIT and FLT3 reactions the pH is raised to 7.5 with 0.2 to 8 μM ATP in the presence of 0.25 to 1 μM biotinylated peptide substrate (GGLFDDPSYVNVQNL). Reactions are incubated at room temperature for 1 to 4 hours and the phosphorylated peptide captured on streptavidin-coated microtiter plates containing stop reaction buffer (25 mM EDTA [ethylenediaminetetraacetic acid], 50 mM HEPES, pH 7.5). Phosphorylated peptide is measured with the DELFIA TRF system using a Europium-labeled antiphosphotyrosine antibody PT66. The concentration of Dovitinib for IC50 is calculated using nonlinear regression with XL-Fit data analysis software version 4.1 (IDBS). Inhibition of colony-stimulating factor-1 receptor (CSF-1R), PDGFRα, insulin receptor (InsR), and insulin-like growth factor receptor 1 (IGFR1) kinase activity is

Kinase Assay	determined at ATP concentrations close the Km for ATP.
Cell Research	Cell viability is assessed by 3-(4,5-dimethylthiazol)-2,5-diphenyl tetrazolium (MTT) dye absorbance. Cells are seeded in 96-well plates at a density of 5 × 103 (B9 cells) or 2 × 104 (MM cell lines) cells per well. Cells are incubated with 30 ng/mL aFGF and 100 μg/mL heparin or 1% IL-6 where indicated and increasing concentrations of Dovitinib. For each concentration of Dovitinib, 10 μL aliquots of drug or DMSO diluted in culture medium is added. For drug combination studies, cells are incubated with 0.5 μM dexamethasone, 100 nM Dovitinib, or both simultaneously where indicated. To evaluate the effect of Dovitinib on growth of MM cells adherent to BMSCs, 104 KMS11 cells are cultured on BMSC-coated 96-well plates in the presence or absence of Dovitinib. Plates are incubated for 48 to 96 hours. For assessment of macrophage colony-stimulating factor (M-CSF)-mediated growth, 5 × 103 M-NFS-60 cells/well are incubated with serial dilutions of Dovitinib with 10 ng/mL M-CSF and without granulocyte-macrophage colony-stimulating factor (GM-CSF). After 72 hours cell viability is determined using Cell Titer-Glo Assay. Each experimental condition is performed in triplicate. (Only for Reference)

Solubility Information

Solubility	DMSO: 15.63 mg/mL (39.83 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (2.55 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5482 mL	12.7411 mL	25.4823 mL
5 mM	0.5096 mL	2.5482 mL	5.0965 mL
10 mM	0.2548 mL	1.2741 mL	2.5482 mL
50 mM	0.051 mL	0.2548 mL	0.5096 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Trudel S, et al. CHIR-258, a novel, multitargeted tyrosine kinase inhibitor for the potential treatment of t(4;14) multiple myeloma. Blood. 2005 Apr 1;105(7):2941-8.
Huynh H, et al. Dovitinib demonstrates antitumor and antimetastatic activities in xenograft models of hepatocellular carcinoma. J Hepatol. 2012 Mar;56(3):595-601.
Trudel S, et al. CHIR-258, a novel, multitargeted tyrosine kinase inhibitor for the potential treatment of t(4;14) multiple myeloma. Blood. 2005 Apr 1;105(7):2941-8.
Chon HJ, et al. Traf2- and Nck-interacting kinase (TNIK) is involved in the anti-cancer mechanism of dovitinib in human multiple myeloma IM-9 cells. Amino Acids. 2016 Jul;48(7):1591-9.
Chon HJ, et al. Traf2- and Nck-interacting kinase (TNIK) is involved in the anti-cancer mechanism of dovitinib in human multiple myeloma IM-9 cells. Amino Acids. 2016 Jul;48(7):1591-9.