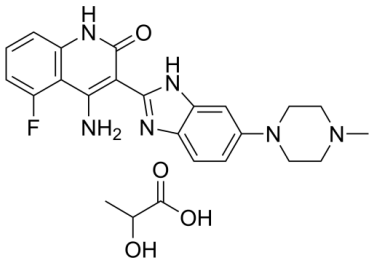
Data Sheet

Product Name:	Dovitinib (lactate)
Cat. No.:	CS-6230
CAS No.:	692737-80-7
Molecular Formula:	$C_{24}H_{27}FN_6O_4$
Molecular Weight:	482.51
Target:	c-Kit; FGFR; FLT3; PDGFR; VEGFR
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 25 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

Dovitinib lactate (TKI258 lactate) is a multi-targeted tyrosine kinase inhibitor with **IC_{50}**s of 1, 2, 8/9, 10/13/8, 27/210 nM for **FLT3**, **c-Kit**, **FGFR1/3**, **VEGFR1/2/3** and **PDGFRα/β**, respectively[1]. IC50 & Target: IC50: 5 nM (FGFR3)[1] ***In Vitro:*** Dovitinib potently inhibits the FGF-stimulated growth of WT and F384L-FGFR3-expressing B9 cells with IC_{50} values of 25 nM. B9-MINV cells are resistant to the inhibitory activity of Dovitinib at concentrations up to 1 μM. Dovitinib inhibits cell proliferation of KMS11 (FGFR3-Y373C), OPM2 (FGFR3-K650E), and KMS18 (FGFR3-G384D) cells with IC_{50} of values of 90 nM (KMS11 and OPM2) and 550 nM, respectively[1]. Treatment of SK-HEP1 cells with dovitinib results in G2/M cell cycle arrest, inhibition of colony formation in soft agar and blockade of bFGF-induced cell migration. Dovitinib inhibits basal expression and FGF-induced phosphorylation of FGFR-1, FRS2-α and ERK1/2 [2]. ***In Vivo:*** Dovitinib (10 mg/kg, 30 mg/kg, 60 mg/kg, p.o.) shows significant antitumor effect in the KMS11-bearing mice model, and the growth inhibition is 48%, 78.5%, and 94% in the 10 mg/kg, 30 mg/kg, and 60 mg/kg treatment arms, respectively, compared with the placebo-treated mice[1]. Dovitinib demonstrates significant antitumor and antimetastatic activities in HCC xenograft models. Dovitinib potently inhibits tumor growth of six HCC lines. Inhibition of angiogenesis correlates with inactivation of FGFR/PDGFR-β/VEGFR-2 signaling pathways. Dovitinib also causes dephosphorylation of retinoblastoma, upregulation of p-histone H2A-X and p27, and downregulation of p-cdk-2 and cyclin B1, which results in a reduction in cellular proliferation and the induction of tumor cell apoptosis[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]To determine IC_{50} for SK-HEP1 cells, cells are plated at a density of 2×10^4 cells per dish. After 48 h, cells are treated with 0, 0.01, 0.1, 1, 5, 10, 50, 100 μM dovitinib in DMEM containing 1% FBS for 24 h. Cell viability is determined with Cell Proliferation Assay. IC_{50} is calculated by nonlinear regression analysis using GraphPad Prism software[2]. **Animal Administration:** [2]Mice: Six HCC lines (06-0606, 26-0808A, 26-1004, 25-0705A, 5-1318, 21-0208) are used to establish tumors in male SCID mice. or dose-esponse experiments, mice bearing the 06-0606 xenografts re orally given vehicle (5% dextrose) or two doses of dovitinib (50 and 75 mg/kg) daily for 14 days. For time-dependent inhibition of dovitinib targets, mice bearing 06-0606 tumors are given orally 200 μL of either vehicle (n=6) or 50 mg/kg/day of dovitinib (n=10)[2].

References:

[1]. Trudel S, et al. CHIR-258, a novel, multitargeted tyrosine kinase inhibitor for the potential treatment of t(4;14) multiple myeloma. Blood. 2005, 105(7), 2941-2948.

[2]. Huynh H, et al. Dovitinib demonstrates antitumor and antimetastatic activities in xenograft models of hepatocellular carcinoma. J Hepatol. 2012, 56(3), 595-601.

CAIndexNames:

Propanoic acid, 2-hydroxy-, compd. with 4-amino-5-fluoro-3-[6-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone (1:1)

SMILES:

O=C(N1)C(C(NC2=C3)=NC2=CC=C3N4CCN(C)CC4)=C(N)C5=C1C=CC=C5F.O=C(O)C(C)O

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