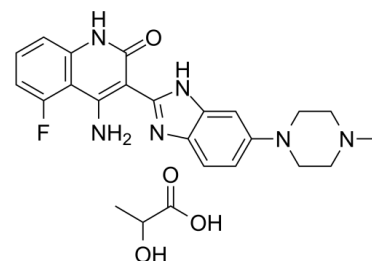


Data Sheet

Product Name:	Dovitinib (lactate)
Cat. No.:	CS-6230
CAS No.:	692737-80-7
Molecular Formula:	C ₂₄ H ₂₇ N ₆ O ₄
Molecular Weight:	482.51
Target:	FGFR
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : ≥ 30 mg/mL (62.17 mM)



BIOLOGICAL ACTIVITY:

Dovitinib(CHIR-258; TKI258) lactate is a potent inhibitor of fibroblast growth factor receptor 3 (**FGFR3**) with an **IC₅₀** of 5 nM. **IC₅₀** & Target: **IC₅₀**: 5 nM (FGFR3)^[1] **In Vitro**: Dovitinib potently inhibits FGFR3 with an **IC₅₀** of 5 nM in in vitro kinase assays and selectively inhibits the growth of B9 cells and human myeloma cell lines expressing wild-type or activated mutant FGFR3. Addition of interleukin 6 (IL-6) or insulin growth factor 1 or coculture on stroma does not confer resistance to dovitinib. In primary myeloma cells dovitinib inhibits downstream extracellular signal-regulated kinase (ERK) 1/2 phosphorylation with an associated cytotoxic response^[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 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 **IC₅₀** for SK-HEP1 cells, cells are plated at a density of 2×10⁴ 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. **IC₅₀** 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

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

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