Product Name: Dovitinib (TKI-258, CHIR-258)

Revision Date: 6/30/2016

Chemical Properties

Product Name: Dovitinib (TKI-258, CHIR-258)
Cas No.: 405169-16-6
M.Wt: 392.43
Formula: C21H21FN6O

Chemical Name: (3Z)-4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1,3-dihydrobenzimidazol-2-ylidene]quinolin-2-one

Canonical SMILES: CN1CCN(CC1)C2=CC3=C(C=C2)NC(=C4C(=C5NC(=NC4=O)C=CC=C5F)N)N3

Solubility: >36.4mg/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.

Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: FGFR
Pathways: Tyrosine Kinase >> FGFR

Description:

Dovitinib (TKI258, CHIR-258) is a multitargeted receptor tyrosine kinase inhibitor against FLT3, KIT, FGFR, VEGFR, PDGFRα and PDGFRβ with IC50 of 1 nM, 2 nM, 8-9 nM, 8-13 nM, 210 nM and 27 nM, respectively [1].
The viability of ZNF198-FGFR1 or BCR-FGFR1 cells was specifically inhibited by TKI258 with IC50 values of 150 nM or 90 nM. The phosphorylation of ERK and STAT5 genes was inhibited by TKI258.
TKI258 also specifically inhibited proliferation and survival of the FGFR1OP2-FGFR1-positive KG1 and KG1A cell lines, increasing levels of apoptosis [2]. In hepatocellular carcinoma (HCC) cells, the combination of TKI258 and tigatuzumab restored the sensitivity of HCC cells to TRAIL- and tigatuzumab-induced apoptosis. TKI258 inhibited phosphorylation of STAT3 and subsequently reduced the protein levels of Mcl-1, Survivin and Cyclin D1. Co-treatment of TRAIL and TKI258 increased the activity of SHP-1 [3]. Inhibition of FGFR3 with TKI258 decreased Waldenström macroglobulinemia (WM) cell survival, increased apoptosis, and induced cell cycle arrest. TKI258 reduced the interaction of WM to bone marrow element, and reversed its proliferation. TKI258 had an additive effect with other drugs [4]. In vivo, the combination of tigatuzumab and TKI258 inhibited Huh-7 xenograft tumor growth [3]. TKI258 reduced WM tumor progression [4].

Reference:

Protocol

Cell experiment:

Cell lines
Human multiple myeloma (MM) cell lines and B9 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.

Reacting conditions
100 nM CHIR-258; 48-96 h.

Applications
Dovitinib is a receptor tyrosine kinases inhibitor. Dovitinib selectively inhibits the growth of human myeloma cell lines and B9 cells expressing wild-type (WT) or activated mutant FGFR3. Dovitinib also causes cytostatic and cytotoxic effects and inhibits downstream extracellular signal-regulated kinase (ERK) 1/2 phosphorylation.
Animal experiment [3]:

Animal models 6- to 8-week-old female BNX mice bearing 3 ×10^7 KMS11 cells.
Dosage form 10, 30, or 60 mg/kg for 21 days by gavage.
Applications Dovitinib causes antitumor effect and inhibits tumor growths by 48%, 78.5%, and 94% in the 10 mg/kg, 30 mg/kg, and 60 mg/kg treatment arms, respectively. Weight loss, as a marker of significant toxicity, is not observed in any of the treatment groups. Dovitinib completely inhibits FGFR3 at the 60 mg/kg dose. CHIR-258 induces both cytostatic and cytotoxic responses.
Preparation method Dissolved in dimethyl sulfoxide (DMSO) at a stock concentration of 20 mM. For animal experiments: formulated in 5 mM citrate buffer.
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.

Reference:

Caution
FOR RESEARCH PURPOSES ONLY.
NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.