

Product Data Sheet

Product Name: OTS964

Cat. No.: GC16511

Chemical Properties

Cas. No. 1338545-07-5

Chemical Name (R)-9-(4-(1-(dimethylamino)propan-2-yl)phenyl)-8-hydroxythieno[2,3-c]quinolin-4(5H)-one

SMILES C[C@@H](CN(C)C)C1=CC=C(C2=C(O)C=CC3=C2C(C=CS4)=C4C(N3)=O)C=C1

Formula $C_{22}H_{22}N_2O_2S$ M.Wt 378.49

Solubility DMF: 30 mg/ml, DMSO: 30 mg/ml, DMSO:PBS(pH 7.2) (1:2): 0.25 mg/ml
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.

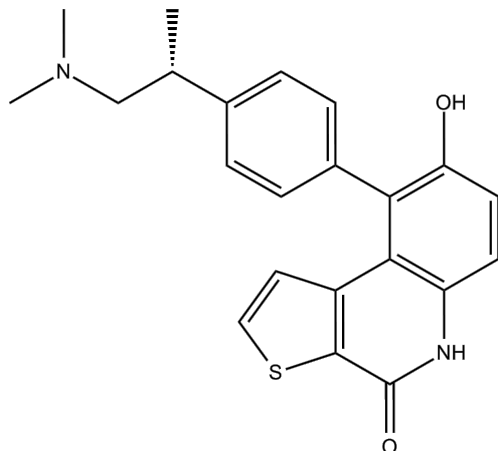
Caution: Product has not been fully validated for medical applications. For research use only.

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Address: 10292 Central Ave. #205, Montclair, CA, USA

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Structure



Protocol

Cell experiment [2]:

Cell lines AML-CD34+, MV4-11 and MOLM13 cell lines

Soluble in DMSO > 10 mM. General tips for obtaining a higher concentration:
Preparation method 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~ 48 hours

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Applications There is a significant decrease in the number of colonies per well in AML-CD34+ cells treated with 10 nM of OTS514 compared to untreated cells (41 vs 73, P = 0.01). OTS514 exhibits cytotoxic activity in AML cells but not in normal CD34+ cells. OTS514 also leads to 80% and 70% increase in apoptotic cell population in MV4-11 and MOLM13 cells that carried FLT3 mutations.

Animal experiment [1]:

Animal models LU-99 xenografts (female BALB/cSLC-nu/nu Mice)

Dosage form Intravenously treated with liposomal OTS964 (40 mg/kg)

Applications OTS514 induces irregular cell morphology with cytokinesis defects and significantly increases the number of LU-99 cells with the “intercellular bridge” which is one of the markers indicating impaired cell division.

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. Matsuo Y, Park JH2, Miyamoto T, et al. TOPK inhibitor induces complete tumor regression in xenograft models of human cancer through inhibition of cytokinesis. *ci Transl Med*. 2014 Oct 22;6(259):259ra145.
2. Alachkar H, Mutonga M, Malnassy G et al. T-LAK cell-originated protein kinase presents a novel therapeutic target in FLT3-ITD mutated acute myeloid leukemia. *Oncotarget*. 2015 Oct 20;6(32):33410-25.

Background

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OTS964{(R)-9-(4-(1-(dimethylamino)propan-2-yl)phenyl)-8-hydroxy-6-methylthieno[2,3-c] quinolin-4(5H)-one} is a potent TOPK inhibitor with an IC₅₀ value of 28 nM. It is a dimethylated derivative of OTS514. OTS964 can inhibit TOPK kinase activity with high affinity and selectivity. TOPK (T-lymphokine-activated killer cell-originated protein kinase) is a protein that is found in a wide range of human cancers and is believed to work as an oncogene, promoting tumor growth.

It has been reported that OTS964 inhibited the growth of TOPK-positive cells with low IC₅₀ values [A549 (31 nM), LU-99 (7.6 nM), DU4475 (53 nM), MDA-MB-231 (73 nM), T47D (72 nM), Daudi (25 nM), UM-UC-3 (32 nM), HCT-116(33nM), MKN1(38nM), MKN45(39nM), HepG2(19nM), MIAPaca-2 (30 nM), and 22Rv1 (50 nM)]. However, its growth inhibitory effect against TOPK-negative HT29 cancer cells was significantly weaker, with IC₅₀ value of 290 nM. Intravenous administration of OTS964 at 40 mg/kg on days 1, 4, 8, 11, 15, and 18 to mice bearing LU-99 lung cancer cells, a TGI of 44% was observed on day 22 without any body weight loss. The differentiation of HSCs to amegakaryocyte population was also enhanced by OTS964 treatment ¹.

References:

1. Matsuo Y, Park JH2, Miyamoto T, et al. TOPK inhibitor induces complete tumor regression in xenograft models of human cancer through inhibition of cytokinesis. *ci Transl Med*. 2014 Oct 22;6(259):259ra145.

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