

Product Data Sheet

Product Name: OTS514

Cat. No.: GC12304

Chemical Properties

Cas. No. 1338540-63-8

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

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

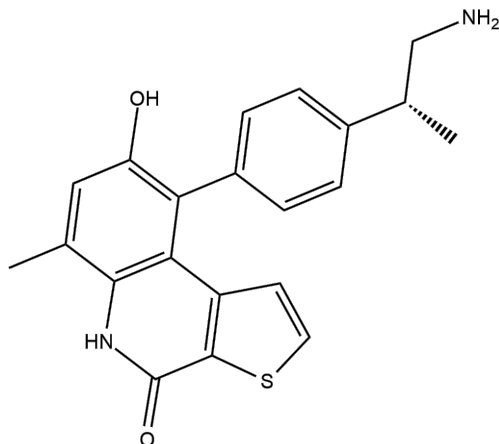
Formula $C_{21}H_{20}N_2O_2S$ M.Wt 364.46

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.

Structure



Protocol

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

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Cell experiment: CD34+ HSCs are cultured in RPMI supplemented with 20% fetal bovine serum and 1× StemSpan CC100. Cells are treated with OTS514 (20 or 40 nM) or OTS-964 (100 or 200 nM) for 48 hours. Collected cells are washed with phosphate-buffered saline (PBS) and resuspended in 100 µL of PBS followed by staining with CD41a antibody for 20 min at room temperature. Finally, the cells are washed with PBS again and then analyzed for CD41a staining by flow cytometry on the BD FACSCalibur. Expression of STAT5 is examined by Western blot with an anti-STAT5 antibody[1].

Animal experiment: Mice[1]A549 (1×10⁷ cells) or LU-99 cells (5×10⁶ or 1×10⁷ cells) are injected subcutaneously in the left flank of female BALB/cSLC-nu/nu mice. When A549 xenografts have reached an average volume of 200 mm³ or when LU-99 xenografts have reached an average volume of 150 or 200 mm³, animals are randomized into groups of six mice. The in vivo antitumor effect of OTS514 is first investigated in a xenograft model of A549 cells (TOPK-positive lung cancer cells). OTS514 is administered to mice bearing A549 cells after the tumor size reaches about 200 mm³. Mice are intravenously treated with OTS514 (1, 2.5, and 5 mg/kg) once a day for 2 weeks. The tumor size is measured as a surrogate marker of drug response, and the percentage of tumor growth inhibition (TGI) is calculated. The antitumor effect of OTS514 is further investigated in another lung cancer xenograft model of LU-99 cells. OTS514 is administered to mice bearing LU-99 cancer cells after the tumor size reaches about 200 mm³. Mice are intravenously treated with OTS514 (5 mg/kg) once a day for 2 weeks. Tumor volumes are determined using a caliper. The weight of the mice is determined as an indicator of tolerability on the same days[1].

References:

[1]. Matsuo Y, et al. TOPK inhibitor induces complete tumor regression in xenograft models of human cancer through inhibition of cytokinesis. Sci Transl Med. 2014 Oct 22;6(259):259ra145.

Background

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OTS514, a thieno[2,3-c]quinolone compound, is a highly potent TOPK inhibitor with an IC₅₀ value of 2.6 nM. The compound can inhibit TOPK kinase activity. 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 OTS514 strongly inhibited the growth of the TOPK-positive cancer cell lines with low IC₅₀ values ranging from 1.5 to 14 nM. While in HT29 cells, in which TOPK expression was little detectable, the IC₅₀ value was 170 nM. Intravenous administration of free OTS514 at 1, 2.5, and 5mg/kg once a day for 2 weeks resulted in tumor growth Inhibition (TGI) of 5.7, 43.3, and 65.3% on day 15, respectively, without anybody weight loss. However, this inhibition also cause dysfunction in the differentiation process of hematopoietic stemcells (HSCs) to WBCs and RBCs but may enhance the differentiation of HSCs to megakaryocytes and platelets.

The antitumor effect of OTS514 in lung cancer xenograft model of LU-99 cells has also been investigated. OTS514 was administered to mice bearing LU-99 cancer cells after the tumor size reached about 200mm³. Intravenous administration of OTS514 (5 mg/kg) once a day for 2 weeks achieved good growth-suppressive effect with TGI of 104% without any body weight loss. However, the antitumor effect of OTS514 against LU-99 xenograft caused a significant reduction of WBCs.

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. Y. Nakamura, Y. Matsuo, S. Hisada, et al. Tricyclic compounds and PBK inhibitors containing the same. Patent WO/2011/123419 (2011)

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