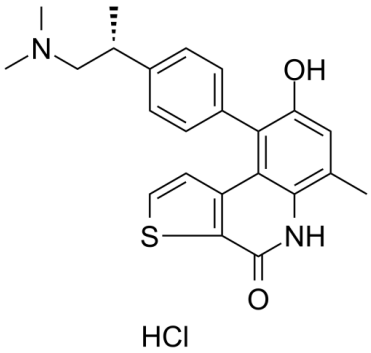
Data Sheet

Product Name:	OTS964 (hydrochloride)
Cat. No.:	CS-5121
CAS No.:	1338545-07-5
Molecular Formula:	C23H25ClN2O2S
Molecular Weight:	428.97
Target:	Apoptosis; CDK; TOPK
Pathway:	Apoptosis; Cell Cycle/DNA Damage
Solubility:	DMSO : ≥ 83.33 mg/mL (194.26 mM)



BIOLOGICAL ACTIVITY:

OTS964 hydrochloride is an orally active, high affinity and selective **TOPK** (T-lymphokine-activated killer cell-originated protein kinase) inhibitor with an **IC_{50}** of 28 nM[1]. OTS964 hydrochloride is also a potent inhibitor of the cyclin-dependent kinase **CDK11**, which binds to CDK11B with a **K_d** of 40 nM[2]. IC50 & Target: IC50: 28 nM (TOPK)[1]

Kd: 40 nM (CDK11B)[2] **In Vitro:** OTS964 hydrochloride (10 nM; 48 hours) suppresses cancer cell proliferation[1].

OTS964 hydrochloride (10 nM; 48 hours) increases cancer cell death[1].

OTS964 (0.1-2 μM; 24 and 48 hours) increases the expression of LC3-II and decreases the expression of P62, both in a dose-dependent manner[3]. **In Vivo:** OTS964 hydrochloride (intravenously; 40 mg/kg on days 1, 4, 8, 11, 15, and 18) makes tumors shrinking even after the treatment and finally revealing complete regression[1].

OTS964 hydrochloride (oral administration; 50 or 100 mg/kg/day for 2 weeks) ultimately achieves complete tumor regression[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]**$CD34^+$ 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 Administration: For intravenous administration, OTS-964 (OTS964) is formulated in 5% glucose[1].;For oral administration, OTS-964 (OTS964) is prepared in a vehicle of 0.5% methylcellulose[1].[1]Mice[1]

A549 (1×10^7 cells) or LU-99 cells (5×10^6 or 1×10^7 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 mm^3 or when LU-99 xenografts have reached an average volume of 150 or 200 mm^3, animals are randomized into groups of six mice. The starting tumor volume of 150 mm^3 is used for LU-99 xenografts when tumors are monitored for a longer time period (>14 days), because LU-99 cells grow very rapidly, and thus the starting volume of 200 mm^3 prevents longer observation considering animal ethics (for example, 200 mm^3 of inoculated LU-99 tumor reaches an average tumor volume of about 1100 mm^3, whereas A549 tumor reaches about 490 mm^3 on day 15). For intravenous administration, three LU-99 xenograft mice are **intravenously** treated with liposomal **OTS-964 (40 mg/kg)** into the tail vein or vehicle at days 1, 4, 8, and 11, and tumors are collected on day 12. For **oral administration**, **OTS-964** is treated at **50 or 100 mg/kg** once every day for 2 weeks. An administration volume of 10 mL/kg of body weight is used for both administration routes. Concentrations are indicated in the main text and figures. 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 ofcytokinesis. Sci Transl Med. 2014 Oct 22;6(259):259ra145.

[2]. Lin A, et al. Off-target toxicity is a common mechanism of action of cancer drugs undergoing clinical trials. Sci Transl Med. 2019 Sep 11;11(509).

[3]. Lu H, et al. TOPK inhibits autophagy by phosphorylating ULK1 and promotes glioma resistance to TMZ. Cell Death Dis. 2019 Aug 5;10(8):583.

CAIndexNames:

Thieno[2,3-c]quinolin-4(5H)-one, 9-[4-[(1R)-2-(dimethylamino)-1-methylethyl]phenyl]-8-hydroxy-6-methyl-, hydrochloride (1:1)

SMILES:

OC1=CC(C)=C2C(C3=C(SC=C3)C(N2)=O)=C1C4=CC=C([C@@H](C)CN(C)C)C=C4.Cl

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