Product Data Sheet

Product Name: TAK-960 hydrochloride
Cat. No.: GC37726

Chemical Properties

Cas. No.	1137868-96-2		
SMILES	O=C(NC1CCN(C)CC1)C2=CC(OC)=C(NC3=NC=C(N4C)C(N(C5CCCC5)CC(F)(F)C4=O)=N3)C=C2F.[H]Cl.[F,Cl,Br,I]		
Formula	$C_{27}H_{35}ClF_3N_7O_3$	M.Wt	598.06
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	TAK-960 hydrochloride		

Protocol

Kinase experiment:

The inhibitory activity of TAK-960 is assessed by the TR-FRET (fluorescence resonance energy transfer) assay, which measures the ATP-dependent phosphorylation of a biotinylated substrate peptide corresponding to residues 2,470 through 2,488 of the mTOR protein (Biotin-AGAGTVPESIHSFIGDGLV). A total of 288 kinases are screened for TAK-960 inhibition (1 μM) using HotSpot technology and IC50 values for the selected kinases are determined.

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Cell experiment:	Cells are seeded into 96-well plates at 3,000 to 30,000 cells per well in appropriate medium plus 10% fetal calf serum. After 24 hours, cells are treated with serial dilutions of TAK-960, and 72 hours later, the number of viable cells is assessed using the CellTiter-Glo Assay. Calculation of EC50 values and statistical analysis are done using GraphPad Prism software.
Animal experiment:	The suspension of HeLa cells (2×106 in 100?μL PBS) or H1299 cells (3×106 in 100?μL PBS) is subcutaneously inoculated into the right hind legs of 8-week-old nude mice (BALB/c nu/nu mice). The indicated dose of TAK-960 is orally administered to tumor-bearing mice. In the radiation treatment, tumor xenografts are locally irradiated with the indicated dose of 137Cs γ-rays using a Gammacell 40 Exactor.

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References:

[1]. Hikichi Y, et al. TAK-960, a novel, orally available, selective inhibitor of polo-like kinase 1, shows broad-spectrum preclinical antitumor activity in multiple dosing regimens. Mol Cancer Ther. 2012 Mar;11(3):700-9.
[2]. Inoue M, et al. PLK1 blockade enhances therapeutic effects of radiation by inducing cell cycle arrest at the mitotic phase. Sci Rep. 2015 Oct 27;5:15666.

Background

Polo-like kinases (Plks) are serine/threonine kinases with key roles in cell cycling. TAK-960 is an orally bioavailable, selective inhibitor of Plks with IC_{50} values of 0.8, 16.9, and 50.2 nM for Plk1, Plk2, and Plk3, respectively.[1,2] It exhibits greater than 20-fold selectivity for Plk1 over FAK, MLCK, and the tyrosine protein kinase Fes, and has minimal activity against a panel of 282 other kinases.[1,2] It inhibits the proliferation of various cancer cell lines, including MDR1-expressing tumors, and also prevents tumor growth in several human cancer cell xenograft models, including a disseminated model of AML- and MDR1-expressing hematological tumors.[1,2]

1.Hikichi, Y., Honda, K., Hikami, K., et al.TAK-960, a novel, orally available, selective inhibitor of polo-like kinase 1, shows broad-spectrum preclinical antitumor activity in multiple dosing regimensMol. Cancer Ther.11(3)700-709(2012) 2.Nie, Z., Feher, V., Natala, S., et al.Discovery of TAK-960: An orally available small molecule inhibitor of

polo-like kinase 1 (PLK1)Bioorg. Med. Chem. Lett.23(12)3662-3666(2013)

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