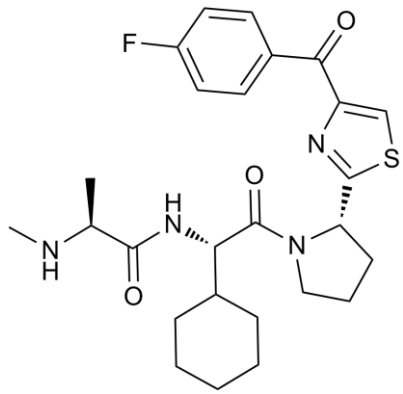
Product Name: LCL161

Revision Date: 6/30/2016

Product Data Sheet

Chemical Properties



Product Name:	LCL161
Cas No.:	1005342-46-0
M.Wt:	500.63
Formula:	C26H33FN4O3S
Synonyms:	LCL-161;LCL 161
Chemical Name:	(2S)-N-[(1S)-1-cyclohexyl-2-[(2S)-2-[4-(4-fluorobenzoyl)-1,3-thiazol-2-yl]pyrrolidin-1-yl]-2-oxoethyl]-2-(methylamino)propanamide
Canonical SMILES:	CC(C(=O)NC(C1CCCCC1)C(=O)N2CCCC2C3=NC(=CS3)C(=O)C4=CC=C(C=C4)F)NC
Solubility:	>25.1mg/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 :	IAP
Pathways:	Apoptosis >> IAP

Description:

LCL161 is a small molecular antagonist of the inhibitor of apoptosis (IAP) with IC50 value of 10.23 μM in Hep3B cells [1].
IAP is a family of proteins which are firstly found in virus and to inhibit the apoptosis of the infected hosts. It contains eight proteins in human. Since they were always found to overexpress

in variety of malignant tumors, the IAP are thought to be appropriate targets in cancer therapy. SMAC (second mitochondria-derived activator of caspases) is the first-identified antagonist of IAP. It binds to XIAP within the BIR2/3 domain through its N-terminal segment. As a mimetic of SMAC, LCL161 is designed to be the inhibitor of both XIAP and cIAP1/2 [1].
LCL161 showed significant inhibition of cell proliferation and viability in two human hepatocellular carcinoma (HCC) cells, Hep3B and PLC5. The IC50 values were 10 and 19 μM, respectively. However, LCL161 had no effect in the two other HCC cell lines, Sk-Hep1 (IC50 value of 224 μM) and Huh-7 (IC50 value of 228 μM). The difference of the effects is found to dependent on the expression of Bcl-2 in cells. For the ALL cells, LCL161 exerted growth inhibition with IC50 values of 9.3 and 0.25 μM, respectively. LCL161 also showed effect on the ALCL cell line Karpas-299 with IC50 value of 1.6 μM [1, 2].
In vivo, LCL161 markedly affected the distribution of EFS in many solid tumor xenograft models. It also caused growth delay in some tumors such as osteosarcoma, neuroblastoma and glioblastoma at dose of 30 mg/kg orally. Besides that, LCL161 administration caused significant growth inhibition in EW-5 and BT-39 glioblastoma but not in BT-28. Moreover, the combination therapy of LCL161 and the adeno-associated virus bacteriophage-tumor necrosis factor-α (AAVP-TNF-α) has been reported to has synergistic anti-tumor effects and delayed treatment resistance in mice models of tumor xenografts [1, 2 and 3].

***Reference**:*

1.Chen K F, Lin J P, Shiau C W, et al. Inhibition of Bcl-2 improves effect of LCL161, a SMAC mimetic, in hepatocellular carcinoma cells. Biochemical pharmacology, 2012, 84(3): 268-277.
2.Houghton P J, Kang M H, Reynolds C P, et al. Initial testing (stage 1) of LCL161, a SMAC mimetic, by the Pediatric Preclinical Testing Program. Pediatric blood & cancer, 2012, 58(4): 636-639.
3.Yuan Z, Syrkin G, Adem A, et al. Blockade of inhibitors of apoptosis (IAPs) in combination with tumor-targeted delivery of tumor necrosis factor-α leads to synergistic antitumor activity. Cancer gene therapy, 2012, 20(1): 46-56.

Protocol

Cell experiment:

Cell lines	Hep3B, PLC5, Sk-Hep1 and Huh-7 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℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting conditions	0, 0.01, 0.05, 0.1, 0.5, 1, 5 and 10 μM; 24, 48 or 72 hrs
Applications	LCL161 showed significant inhibition of cell proliferation and viability in 2 human hepatocellular carcinoma (HCC) cells, Hep3B and PLC5. The IC50 values were 10 and 19 μM, respectively. However, LCL161 had no effect in 2 other HCC cell lines, Sk-Hep1 (IC50 value of 224 μM) and Huh-7 (IC50 value of 228 μM).

Animal experiment [3]:

Animal models	Huh-7 xeonograft nude mice
Dosage form	50 mg/kg; p.o.; q.d., for 20 days
Applications	Co-treatment with LCL161 and SC-2001 showed significant anti-tumor effect on Huh-7 tumors, without affecting body weight significantly.
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:
[1]. Chen K F, Lin J P, Shiau C W, et al. Inhibition of Bcl-2 improves effect of LCL161, a SMAC mimetic, in hepatocellular carcinoma cells. Biochemical pharmacology, 2012, 84(3): 268-277.

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.

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