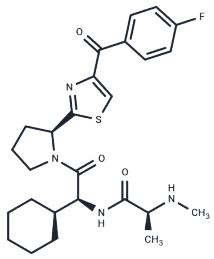
Data Sheet (Cat.No.T2080)

TargetMol

LCL161

Chemical Properties



CAS No. : 1005342-46-0

Formula: C26H33FN4O3S

Molecular Weight: 500.63

Storage: Keep away from direct sunlight,Store at low temperature,Store under nitrogen
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	LCL161 is a SMAC mimetic, an IAP antagonist with oral activity that inhibits XIAP (IC50=35 nM) in HEK293 cells and also inhibits cIAP1 (IC50=0.4 nM) in MDA-MB-231 cells. LCL161 has potential antitumor activity.
Targets(IC50)	IAP
In vitro	**METHODS**: MOLM13 cells were treated with LCL161 (1000-160,000 nM) and PKC412 (2.5-40 nM) for 3 days and cell viability was measured by trypan blue exclusion. **RESULTS**: LCL161 moderately inhibited cell growth when administered alone.Combined treatment of MOLM13-luc+ cells with LCL161 and PKC412 killed significantly more cells than either drug alone, and the Calcusyn Combination Index suggests a synergistic effect. [1] **METHODS**: NSCLC cells A549 and H460 were treated with LCL161 (10 μM) and paclitaxel (10 μM) for 48 h. Apoptosis was detected by flow cytometry. **RESULTS**: Apoptosis was significantly reduced in the LCL161/paclitaxel combination treatment group compared to cells treated with LCL161 or paclitaxel alone. [2]
In vivo	**METHODS**: To test the antitumor activity in vivo, LCL161 (50 mg/kg twice daily) and PKC412 (40 mg/kg once daily) were administered by gavage to NCr nude mice injected with Ba/F3-FLT3-ITD-luc+ tumor cells for seven days. **RESULTS**: LCL161 significantly enhanced the ability of PKC412 to inhibit the growth of Ba/F3-FLT3-ITD-luc+ cells in vivo.The difference between the inhibition of leukemia growth by PKC412 or LCL161 alone and the combination of PKC412+LCL161 was also significant.The percentage of spleen weights in mice treated with PKC412+LCL161 was smaller than that in mice treated with PKC412. Mice treated with PKC412+LCL161 had a smaller percent spleen weight than mice treated with the vector or either drug alone. [1]
Kinase Assay	CYP3A activity is assessed using the probe reactions, midazolam-1′-hydroxylation and testosterone 6β-hydroxylation. For reversible inhibition, incubations (37°C, 10 min) are composed of (final concentrations): potassium phosphate buffer (100 mM, pH 7.4), β-NADPH (1 mM), magnesium chloride (5 mM), microsomal protein (0.025 mg/mL), probe substrate (1 μM midazolam or 25 μM testosterone), LCL161 (0, 0.5, 1, 5, 10, 25, 50, or 100 μM) and organic solvent (0.2% acetonitrile for midazolam, 0.2% methanol for testosterone). After a 3-minute preincubation, the reactions are initiated by addition of β-NADPH and terminated by addition of acetonitrile (two volumes). Reactions are

Kinase Assay	previously shown to be linear with respect to time and protein concentration (results not shown) with midazolam and testosterone turnover of 8.7±1.3% (n=3) and 2.6±0.20%, respectively. Formation of 1′-hydroxymidazolam and 6β-hydroxytestosterone is determined by LC-MS/MS as described below[3].
Cell Research	In vitro testing is performed using DIMSCAN (Only for Reference)

Solubility Information

Solubility	DMSO: 93 mg/mL (185.77 mM),Sonication is recommended. Ethanol: 16 mg/mL (31.96 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.9975 mL	9.9874 mL	19.9748 mL
5 mM	0.3995 mL	1.9975 mL	3.995 mL
10 mM	0.1997 mL	0.9987 mL	1.9975 mL
50 mM	0.0399 mL	0.1997 mL	0.3995 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Weisberg E, et al. Smac mimetics: implications for enhancement of targeted therapies in leukemia. Leukemia. 2010 Dec;24(12):2100-9.
Chen H, Li Y, Wu J, et al. RIPK3 collaborates with GSDMD to drive tissue injury in lethal polymicrobial sepsis. Cell Death & Differentiation. 2020: 1-18
Yang C, et al. LCL161 increases paclitaxel-induced apoptosis by degrading cIAP1 and cIAP2 in NSCLC. J Exp Clin Cancer Res. 2016 Sep 30;35(1):158.
Knights AJ, et al. Cancer Immunol Immunother, 2013, 62(2), 321-335.
Chen H, Li Y, Wu J, et al. RIPK3 collaborates with GSDMD to drive tissue injury in lethal polymicrobial sepsis[J]. Cell Death & Differentiation. 2020: 1-18.