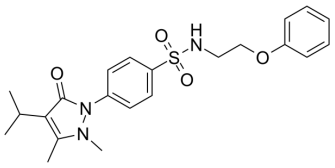
BC-LI-0186

Cat. No.:	HY-136265
CAS No.:	695207-56-8
Molecular Formula:	$C_{22}H_{27}N_3O_4S$
Molecular Weight:	429.53
Target:	Aminoacyl-tRNA Synthetase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (291.02 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3281 mL	11.6406 mL	23.2813 mL
	5 mM	0.4656 mL	2.3281 mL	4.6563 mL
	10 mM	0.2328 mL	1.1641 mL	2.3281 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.84 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BC-LI-0186 is a potent and selective inhibitor of Leucyl-tRNA synthetase (LRS; LeuRS) and Ras-related GTP-binding protein D (RagD) interaction (IC_{50}=46.11 nM). BC-LI-0186 competitively binds to the RagD interacting site of LRS (K_d=42.1 nM) and has on effects on LRS-Vps34, LRS-EPRS, RagB-RagD association, mTORC1 complex formation or the activities of 12 kinases. BC-LI-0186 can effectively suppress the activity of cancer-associated MTOR mutants and the growth of rapamycin-resistant cancer cells. BC-LI-0186 is a promising agent for lung cancer research[1][2].

IC_{50} & Target

IC50: 46.11 nM (LeuRS and RagD interaction)[1]
Kd: 42.1 nM (LeuRS and RagD interaction)[1]

In Vitro

BC-LI-0186 (0-20 μM; starved for 90 min in the leucine-free medium and then in the serum-free media for 15 min) inhibits

phosphorylation of S6K in a dose- and time-dependent manner, but it has no effects on hosphorylation of AKT (S473)[1].
BC-LI-0186 (0-20 μM; 6 hours) induces cleaved poly (ADP-ribose) polymerase (PARP) and caspase-3 and an increase of p62 in A549 and H460 cells[1].
BC-LI-0186 exhibits cytotoxic effect at nanomolar concentration in NSCLC cells, it exhibits IC_{50} values of 98 nM, 206 nM, 55 nM, 78 nM, 83 nM, 86 nM, 102 nM, 109 nM, 128 nM, and 206 nM in A549, H460, H2228, H1703, SNU1330, H1650, H2009, H358, H2279, H460, and H596 cells, respectively[1].
BC-LI-0186 overcome acquired rapamycin resistance and inhibits the mTORC1 pathway in isogenic HCT116 cell lines that harbored either M TOR WT (HCT116 MW) or S2035I mutations (HCT116 MM), it exhibits little changed efficacy between the wild-type and mutant cells (GI_{50}: 39.49 nM and 42.03 nM, EC_{50}: 105.03 nM and 100.45 nM)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	NSCLC cells
Concentration:	0 μM, 0.1 μM, 0.2 μM,1 μM, 2 μM, 5 μM, 10 μM, 20 μM
Incubation Time:	Starved for 90 min in the leucine-free medium and then in the serum-free media for 15 min
Result:	Suppressed leucine-mediated mTORC1 activation in NSCLC cells.

In Vivo

BC-LI-0186 (intraperitoneal injection; 50 mg/kg; alone or combines with cisplatin alone; 2 weeks; bid for 5 days per week) exhibits antitumor effects and significantly reduces tumor size compared with treatment with vehicle in an LSL K-ras G12D lung cancer animal model[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	K-ras mouse lung cancer modelan LSL K-ras G12D lung cancer animal model[1]
Dosage:	50 mg/kg
Administration:	Intraperitoneal injection; 50 mg/kg; alone or combines with cisplatin alone; 2 weeks; bid for 5 days per week
Result:	Showed activated caspase-3-positive cells higher in the BC-LI-0186-treated group than in the vehicle or cisplatin-treated group. Reduced p-S6 and p-AKT level whereas cisplatin alone has minimal effect on both p-S6 and p-AKT expression. Showed a slight (not statistically significant) increase in body weight during the treatment period. Exhibited a specific inhibition of mTORC1 and not mTORC2.

REFERENCES

[1]. Jong Hyun Kim, et al. Control of leucine-dependent mTORC1 pathway through chemical intervention of leucyl-tRNA synthetase and RagD interaction. Nat Commun. 2017 Sep 29;8(1):732.

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