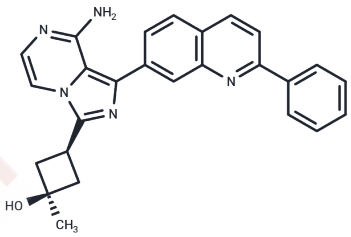
Data Sheet (Cat.No.T6017)

TargetMol

Linsitinib

Chemical Properties



CAS No. : 867160-71-2

Formula: C26H23N5O

Molecular Weight: 421.49

Storage: Store at low temperature
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	Linsitinib (OSI-906) belongs to small molecule inhibitors and is a dual IGF-1/IR inhibitor (IC50 = 35 and 75 nM, respectively) with selectivity, cell permeability, and oral activity. This compound is used in antitumor research and can effectively inhibit cell proliferation and induce apoptosis.
Targets(IC50)	IGF-1R
In vitro	**Methods**: In SW48 colon cancer cells, pretreatment with Linsitinib (1.0 or 10.0 μmol/L) for 48 hours was followed by treatment with Regorafenib (5 μmol/L) for 96 hours. **Results**: MTT assay showed cell viability decreased to 42±7%, indicating that Linsitinib could inhibit Regorafenib resistance.[1] **Methods**: In PC9, HCC827, and H1975 human lung cancer cells, treatment with Linsitinib (10 μmol/L) for 5 days inhibited cell proliferation as detected by MTT assay. **Results**: Combination with Gefitinib synergistically inhibited cell viability in PC9 and HCC827 cells and increased apoptosis rates in HCC827 and H1975 cells. Western blot confirmed that the mechanism involved inhibition of IGF-1R and downstream AKT/ERK phosphorylation. [2] **Methods**: In H295R and HAC15 human adrenocortical carcinoma cells, treatment with Linsitinib for 3 or 6 days resulted in dose- and time-dependent inhibition of cell proliferation as measured by DNA content. **Results**: IC50 values were 1.5×10^{-7} M and 2.9×10^{-8} M, respectively. Additionally, DNA fragmentation assay confirmed its ability to induce apoptosis.[3]
In vivo	**Methods**: In an AOM/DSS-induced C57BL/6J mouse colon cancer model, Linsitinib was orally administered in combination with Regorafenib. **Results**: The combination therapy significantly inhibited body weight loss, reduced tumor number (minimum 1±1), and prolonged survival (40%). [1]
Kinase Assay	Protein kinase biochemical assays: Protein kinase assays are either performed in-house by ELISA-based assay methods (IGF-1R,IR,EGFR and KDR) or at Upstate Inc.by a radiometric method with ATP at 100 μM concentration.In-house ELISA assays use poly (Glu:Tyr) as the substrate bound to the surface of 96-well assay plates and phosphorylation is detected using an antiphosphotyrosine antibody conjugated to horseradish peroxidase.The bound antibody is quantified using ABTS as the peroxidase substrate by measuring absorbance at 405 / 490 nm.All assays use purified recombinant kinase catalytic domains.Recombinant enzymes of human IGF-1R or EGFR

Kinase Assay	as an NH2-terminal glutathione S-transferase fusion protein in insect cells and are purified in house.IC50 values are determined from the sigmoidal dose-response plot of percent inhibition versus log10 compound concentration.A minimum of three measurements,performed in duplicate,are carried out with in-house assays unless otherwise indicated.OSI-906 at a concentration of 1 μM is profiled versus a panel of kinases using the ProfilerProTM Kinase Selectivity Assay Kit.
Cell Research	For assays of cell proliferation, cells are seeded into 96-well plates in appropriate media containing FCS 10% and incubated for 3 days in the presence of OSI-906 at various concentrations. Inhibition of cell growth is determined by luminescent quantitation of intracellular ATP content using CellTiterGlo. Data is presented as a fraction of maximal proliferation, calculated by dividing the cellular density in the presence of varying concentrations of OSI-906 by the cellular density of control cells treated with vehicle (DMSO) only.(Only for Reference)

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 96 mg/mL (227.76 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (7.83 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3725 mL	11.8627 mL	23.7254 mL
5 mM	0.4745 mL	2.3725 mL	4.7451 mL
10 mM	0.2373 mL	1.1863 mL	2.3725 mL
50 mM	0.0475 mL	0.2373 mL	0.4745 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

Guo, Yu et al. Linsitinib and aspirin as the IGF1-R antagonists, inhibit regorafenib-resistant chemotherapy in colon cancer. Saudi journal of biological sciences vol. 29,2 (2022): 872-877.
Chen F, Shi Q, Pei F, et al. A systems-level study reveals host-targeted repurposable drugs against SARS-CoV-2 infection. Molecular Systems Biology. 2021, 17(8): e10239
Yeo, Chang Dong et al. Inhibiting IGF-1R attenuates cell proliferation and VEGF production in IGF-1R over-expressing EGFR mutant non-small cell lung cancer cells. Experimental lung research vol. 43,1 (2017): 29-37.
Kang J, Guo Z, Zhang H, et al. Dual Inhibition of EGFR and IGF-1R Signaling Leads to Enhanced Antitumor Efficacy against Esophageal Squamous Cancer. International Journal of Molecular Sciences. 2022, 23(18): 10382
De Martino, Maria Cristina et al. IGF and mTOR pathway expression and in vitro effects of linsitinib and mTOR inhibitors in adrenocortical cancer. Endocrine vol. 64,3 (2019): 673-684.
Yang N, Fan Z, Sun S, et al.Discovery of highly potent and selective KRASG12C degraders by VHL-recruiting PROTACs for the treatment of tumors with KRASG12C-Mutation.European Journal of Medicinal Chemistry.2023: 115857.
Guan J, Borenäs M, Xiong J, et al.IGF1R Contributes to Cell Proliferation in ALK-Mutated Neuroblastoma with Preference for Activating the PI3K-AKT Signaling Pathway.Cancers.2023, 15(17): 4252.
Alhaddad H, Ospina O E, Khaled M L, et al.Spatial transcriptomics analysis identifies a tumor-promoting function of the meningeal stroma in melanoma leptomeningeal disease.Cell Reports Medicine.2024