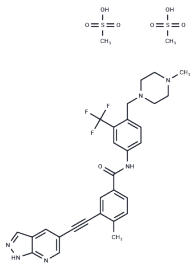
Data Sheet (Cat.No.T2429)

TargetMol

Olverembatinib dimesylate

Chemical Properties



CAS No. : 1421783-64-3

Formula: C29H27F3N6O·2CH4O3S

Molecular Weight: 724.77

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Olverembatinib dimesylate (GZD824 Dimesylate) is a novel orally bioavailable Bcr-Abl inhibitor for Bcr-Abl(WT) and Bcr-Abl(T315I).
Targets(IC50)	Bcr-Abl
In vitro	Administering 20 mg/kg of GZD824 daily inhibits tumor growth in syngeneic transplantation mice bearing Ba/F3 cells expressing Bcr-AblWT and BCR-AblT315I. Daily doses of 5 and 10 mg/kg GZD824 show a dose-dependent inhibition of tumor growth in xenograft models of K562 and KU812 tumors, without causing mortality or weight loss.
In vivo	GZD824 effectively inhibits the activation of Bcr-Abl and its downstream targets, Crk1 and STAT5, in leukemia cells in a concentration-dependent manner. Its efficacy in inhibiting the proliferation of Ba/F3 cells expressing the Bcr-Abl T315I mutation and another 14 Bcr-Abl mutations associated with resistance aligns closely with results from biochemical kinase inhibition and protein binding affinity experiments.
Kinase Assay	FRET-Based Z'-Lyte Assay Detecting Peptide Substrate Phosphorylation: The kinases ABL1, ABL1(E255K), ABL1 (G250E), ABL1(T315I), and ABL1(Y253F) are P3049, PV3864, PV3865, PV3866, and PV3863 are full-length human recombinant protein expressed in insect cells and histidine-tagged. Inhibition activities of inhibitors against Abl1 and its mutants are performed in 384-well plates using the FRET-based Z'-Lyte assay system. Briefly, the kinase substrate is diluted into 5 μL of kinase reaction buffer; and the kinase is added. Compounds (10 nL) with indicated concentrations are then delivered to the reaction by using Echo liquid handler, and the mixture is incubated for 30 min at room temperature. Then 5 μL of 2X ATP solution is added to initiate the reaction, and the mixture is further incubated for 2 h at room temperature. The resulting reactions contains 10 μM (for wild-type Abl1, and mutants Y253F, Q252H, M351T, and H396P) or 5 μM (for mutants E255K, G250E, T315I) of ATP, 2 μM of Tyr2 Peptide substrate in 50 mM HEPES (PH 7.5), 0.01% BRIJ-35, 10 mM MgCl2, 1 mM EGTA, 0.0247 μg/mL Abl1, and inhibitors as appropriate. Then, 5 μL of development reagent is added, and the mixture is incubated for 2 h at room temperature before 5 μL of stop solution is added. Fluorescence signal ratio of 445 nm (Coumarin)/520 nm (fluorescin) is examined on an EnVision Multilabel Reader. The data are analyzed using Graphpad Prism5. The data are the mean value of three experiments.
Cell Research	Cells in the logarithmic phase are plated in 96-well culture dishes. Twenty-four hours later, cells are treated with the corresponding compounds or vehicle control at the

indicated concentration for 72 h. CCK-8 is added into the 96-well plates (10 μL/well) and incubated with the cells for 3 h. OD450 and OD650 are determined by a microplate reader. Absorbance rate (A) for each well is calculated as OD450 - OD650. The cell viability rate for each well is calculated as V% = (As - Ac)/(Ab - Ac) × 100%, and the data were further analyzed using Graphpad Prism5. The data are the mean value of the three experiments. As is the absorbance rate of the test compound well, Ac is the absorbance rate of the well without either cell or test compound, and Ab is the absorbance rate of the well with cell and vehicle control.(Only for Reference)

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: 92 mg/mL (126.94 mM),Sonication is recommended. DMSO: 93 mg/mL (128.32 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.3797 mL	6.8987 mL	13.7975 mL
5 mM	0.2759 mL	1.3797 mL	2.7595 mL
10 mM	0.138 mL	0.6899 mL	1.3797 mL
50 mM	0.0276 mL	0.138 mL	0.2759 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.

Reference

Ren X, et al. J Med Chem. 2013, 56(3), 879-894.