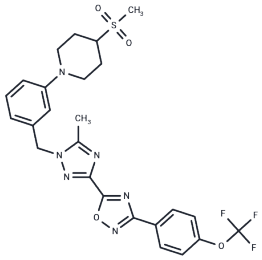
Data Sheet (Cat.No.T5337)

TargetMol

IACS-010759

Chemical Properties



CAS No. : 1570496-34-2

Formula: C25H25F3N6O4S

Molecular Weight: 562.56

Storage: 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	IACS-010759 is an orally bioavailable inhibitor of complex I of oxidative phosphorylation of the mitochondrial electron transport chain.
Targets(IC50)	Apoptosis,OXPHOS,Mitochondrial Metabolism
In vitro	Treatment of primary CLL cells with IACS-010759 greatly inhibited oxidative phosphorylation (OxPhos) but caused only minor cell death at 24 and 48 h [1]. KPS-tumor-derived murine cells were more sensitive to IACS-010759 compared to KP-tumor-derived cell lines [2]. Established AML cell lines were exposed to a range of IACS-010759 concentrations for 3-7 d, resulting in reduced viability with EC50 values of<3nM [3].
In vivo	In mice following intravenous (0.3mg per kg body weight (mg/kg)) and oral (1mg/kg) administration, IACS-010759 was characterized by low plasma clearance with a high volume of distribution, resulting in a prolonged terminal half-life (>24h) of IACS-010759 with sustained levels of compound in the plasma following oral dosing. Treatment with IACS-010759 at the 5 or 10mg/kg dose resulted in tumor regression with minimal body weight loss, whereas IACS-010759 at the 25mg/kg dose was not tolerated, and body weight loss, lethargy, and hypothermia were observed [3].
Cell Research	CLL cells were incubated with either dimethyl sulfoxide (control) or IACS-010759 (100 nM) for 24 h. A total of 10^6 cells were stained with MitoSOX Red and tetramethylrhodamine ethyl ester perchlorate and were analyzed using flow cytometry for mitochondrial reactive oxygen species (ROS) and mitochondrial outer membrane potential, respectively [1].
Animal Research	OCI-AML3 cells were expanded in RPMI medium + 5% or 10% fetal bovine serum (FBS) until ≥150 million cells were present. For OCI-AML3, 2 million cells in 200 µl of saline were injection into the tail vein of NSG mice. For the patient-derived models, 4030094 and S6-AP, cells were harvested from mice with advanced disease or resuscitated from frozen vials, washed and resuspended at 5 x 10^6 cells/ml in PBS. Mice were irradiated for 24 hours at 250 cGY before orthotopic implantation of 1 x 10^6 cells suspended in 200 µl of saline were into the tail vein of 6- to 8-week old female NSG mice. For OCI-AML3, treatment began when whole body luminescence averaged 5 x 10^7. For model 4030094, treatment for the efficacy began when animals reached 10% burden and for the PK/PD studies when the animals reached 80% disease burden as measured by human and mouse CD45 and viability (DAPI 62248) staining followed by flow cytometry with a Fortessa flow cytometer. Mice were randomized based on luminescence for the

Animal Research	OCI-AML3 model and by disease burden (hCD45+) for the patient-derived xenograft. Cohorts of mice were sacrificed 21 days after study drug initiation to collect spleen and bone marrow or followed for overall survival while continuing study drug [3].

Solubility Information

Solubility	DMSO: 51 mg/mL (90.66 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	2% DMSO+40% PEG300+5% Tween 80+53% Saline: 1 mg/mL (1.78 mM),Suspension. *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	1.7776 mL	8.8879 mL	17.7759 mL
5 mM	0.3555 mL	1.7776 mL	3.5552 mL
10 mM	0.1778 mL	0.8888 mL	1.7776 mL
50 mM	0.0356 mL	0.1778 mL	0.3555 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

Vangapandu HV, et al. Biological and metabolic effects of IACS-2010759, an OxPhos inhibitor, on chronic lymphocytic leukemia cells. Oncotarget. 2018 May 18;9(38):24980-241991.
Ren L, Meng L, Gao J, et al.PHB2 promotes colorectal cancer cell proliferation and tumorigenesis through NDUFS1-mediated oxidative phosphorylation.Cell Death & Disease.2023, 14(1): 44.
Lissanu Deribe Y, et al. Mutations in the SWI/SNF complex induce a targetable dependence on oxidative phosphorylation in lung cancer. Nat Med. 2018 Jul;24(7):1047-1057.
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Zheng J, Wang Q, Chen J, et al.Tumor mitochondrial oxidative phosphorylation stimulated by the nuclear receptor RORγ represents an effective therapeutic opportunity in osteosarcoma.Cell Reports Medicine.2024