

IACS-010759

Chemical Properties

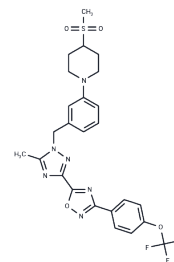
CAS No. : 1570496-34-2

Formula: C₂₅H₂₅F₃N₆O₄S

Molecular Weight: 562.56

Appearance: no data available

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



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,Others,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 EC ₅₀ 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

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: 30 mg/mL (53.3 mM), (< 1 mg/ml refers to the product slightly soluble or insoluble)
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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.

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

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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