DHODH-IN-22

Cat. No.: HY-149031

CAS No.: 2450341-75-8

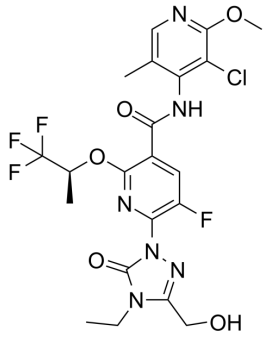
Molecular Formula: $C_{21}H_{21}ClF_4N_6O_5$

Molecular Weight: 548.88

Target: Dihydroorotate Dehydrogenase

Pathway: Metabolic Enzyme/Protease

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

DHODH-IN-22 is a potent, selective and orally active dihydroorotate dehydrogenase (DHODH) inhibitor with an IC_{50} value of 0.3 nM. DHODH-IN-22 can be used for researching acute myelogenous leukemia (AML)[1].

IC_{50} & Target

IC_{50}: 0.3 nM (human DHODH), 10 nM (mouse DHODH), 130 nM (rat DHODH), 4.2 nM (dog DHODH), 0.54 nM (monkey DHODH) [1]

In Vitro

DHODH-IN-22 (compound 29) exhibits antiproliferative activity against MOLM-13 and THP-1 cells[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	MOLM-13 and THP-1
Concentration:	0-30 nM
Incubation Time:	72 h
Result:	Exhibited antiproliferative activity against MOLM-13 and THP-1 cells with IC_{50}s of 0.4 nM and 1.4 nM, respectively.

In Vivo

DHODH-IN-22 (1.9-7.5 mg/kg; PO; QD for 5 days) significantly inhibits MOLM-13 tumor growth in mice, and exhibits no significant impact on body weight[1].

DHODH-IN-22 (2 mg/kg for IV and 10 mg/kg for PO; single dosage) has favorable pharmacokinetic property[1].

Pharmacokinetic Parameters of DHODH-IN-22 (compound 29) in mouse and rat[1].

	Mouse IV 2 mg/kg and PO 10 mg/kg	Rat IV 2 mg/kg and PO 10 mg/kg
CL (mL/min/kg)	7.3	7.6
V_{dss} (L/kg)	2.4	2.2

$t_{1/2}$ (ng/mL)	5	4
C_{max} (ng/mL)	3810	2193
t_{max} (h)	1.0	4.0
AUC_{0-inf} (ng/mL·h)	23046	23807
F (%)	110	106

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female NSG mice (implanted subcutaneously with 2×10^6 MOLM-13 tumor cells)[1]
Dosage:	1.9, 3.75 and 7.5 mg/kg
Administration:	PO; QD for 5 days
Result:	Significantly inhibited tumor growth with ΔTGI% of 71, 76, and 79% at 1.9, 3.75 and 7.5 mg/kg, respectively, and exhibited no significant impact on body weight over the course of 5 days.

Animal Model:	Rat and mouse[1]
Dosage:	2 mg/kg IV and 10 mg/kg PO
Administration:	IV or PO; single dosage (Pharmacokinetic analysis)
Result:	Exhibited low clearance and high oral bioavailability in both species.

REFERENCES

[1]. Cisar JS, et al. N-Heterocyclic 3-Pyridyl Carboxamide Inhibitors of DHODH for the Treatment of Acute Myelogenous Leukemia. J Med Chem. 2022 Aug 4.

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