(S,R)-GSK321

Cat. No.: HY-128888B

CAS No.: 1816272-18-0

Molecular Formula: $C_{28}H_{28}FN_5O_3$

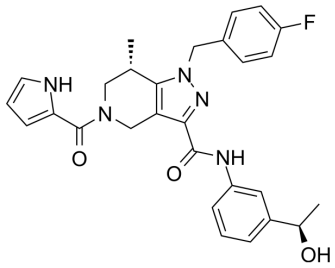
Molecular Weight: 501.55

Target: Isocitrate Dehydrogenase (IDH)

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (199.38 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9938 mL	9.9691 mL	19.9382 mL
	5 mM	0.3988 mL	1.9938 mL	3.9876 mL
	10 mM	0.1994 mL	0.9969 mL	1.9938 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

(S,R)-GSK321 is a potent, selective mutant IDH1 inhibitor with IC_{50} values of 2.9, 3.8, 4.6 and 46 nM for R132G, R132C, R132H and WT IDH1, respectively, and >100-fold selectivity over IDH2. (S,R)-GSK321 induces decrease in intracellular 2-HG, abrogation of the myeloid differentiation block and induction of granulocytic differentiation at the level of leukemic blasts and more immature stem-like cells. (S,R)-GSK321can be used for research of acute myeloid leukemia (AML) and other cancers[1].

IC_{50} & Target

IDH1

In Vitro

(S,R)-GSK321 (0.1-10000 nM; 24 h) inhibits intracellular 2-HG production in HT1080 cells with an EC_{50} value of 85 nM[1].
(S,R)-GSK321 (0-5 μM; 48 h; HT1080 fibrosarcoma cells) leads to reduction of histone H3K9 dimethylation (H3K9me2)[1].
(S,R)-GSK321 (3 μM; 22 d) decreases intracellular 2-HG in a dose-dependent manner (R132G, 0.13-fold; R132C, 0.15-fold; R132H, 0.29-fold)[1].
(S,R)-GSK321 (3 μM; 15 d) affects proliferation of primary IDH1 mutant AML cells[1].
(S,R)-GSK321 (3 μM; 9 d) induces differentiation in primary IDH1 mutant AML blasts and immature stem-like cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	IDH1 mutant AML cells
Concentration:	3 μM
Incubation Time:	15 days
Result:	Increased in cell numbers (2-fold to 15-fold) in IDH1 mutant AML cells.

Cell Cycle Analysis[1]

Cell Line:	IDH1 mutant AML cells
Concentration:	3 μM
Incubation Time:	15 days
Result:	Decreased in quiescent (G0)-phase cells and increased in G1-phase in R132G IDH1.

Western Blot Analysis[1]

Cell Line:	HT1080 fibrosarcoma cells
Concentration:	0, 0.5 and 5 μM
Incubation Time:	48 hours
Result:	Induced markedly decreased H3K9me2 levels.

In Vivo

(S,R)-GSK321 (150 mg/kg; i.p.; daily, for 15 d; male CD-1 mice with IDH1 mutant AML xenograft) reduces leukemic blasts in vivo[1].

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

Animal Model:	Male CD-1 mice with IDH1 mutant AML xenograft[1]
Dosage:	150 mg/kg
Administration:	Intraperitoneal injection; daily, for 15 days
Result:	Decreased in 2HG in IDH1-mutant AML cells. Decreased in the percentage of blast cells ($^{SSClow}CD45^{low/+}$) and a relative increase in mature lymphoid and granulocytic/monocytic cells.

REFERENCES

[1]. Okoye-Okafor UC, et, al. New IDH1 mutant inhibitors for treatment of acute myeloid leukemia. Nat Chem Biol. 2015 Nov;11(11):878-86.

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