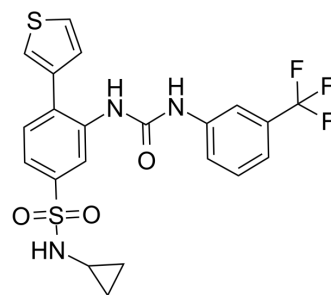


AGI-6780

Cat. No.:	HY-15734		
CAS No.:	1432660-47-3		
Molecular Formula:	C ₂₁ H ₁₈ F ₃ N ₃ O ₃ S ₂		
Molecular Weight:	481.51		
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 : ≥ 29 mg/mL (60.23 mM)
 * "≥" means soluble, but saturation unknown.

Concentration	Mass		
	1 mg	5 mg	10 mg
1 mM	2.0768 mL	10.3840 mL	20.7680 mL
5 mM	0.4154 mL	2.0768 mL	4.1536 mL
10 mM	0.2077 mL	1.0384 mL	2.0768 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (5.19 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (5.19 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AGI-6780 that potently and selectively inhibits the tumor-associated mutant IDH2^{R140Q} with IC₅₀ of 23±1.7 nM. AGI-6780 is less potent against IDH2^{WT} with IC₅₀ of 190±8.1 nM.

IC₅₀ & Target

IC₅₀: 23±1.7 nM (IDH2^{R140Q}), 190±8.1 nM (IDH2^{WT})^[1]

In Vitro

AGI-6780 is tested in both human glioblastoma U87 and TF-1 cells expressing IDH2^{R140Q}, as well as against IDH1^{R132H} for 48 h incubation, with IC₅₀ of 11±2.6 nM, 18±0.51 nM, and >1 mM, respectively. Treatment of TF-1^{R140Q} cells with AGI-6780, at concentrations that lower 2HG to near-normal physiologic levels, restore expression of both HBG and KLF1 genes and the color change associated with differentiation. AGI-6780 can reverse the IDH2^{R140Q}-induced differentiation block in TF-1 cells.

Pretreatment with AGI-6780 (0.2 μ M and 1 μ M) markedly decreased the intracellular concentration of (R)-2-hydroxyglutarate in the TF1^{R140Q} cells and restored their ability to undergo EPO-induced differentiation^[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay ^[1]

AGI-6780 is prepared as 10 mM stock in DMSO and diluted to 50X final concentration in DMSO, for a 50 μ L reaction mixture. IDH enzyme activity converting alpha-ketoglutarate to 2-hydroxyglutarate is measured using a NADPH depletion assay. In the assay the remaining cofactor is measured at the end of the reaction with the addition of a catalytic excess of diaphorase and resazurin, to generate a fluorescent signal in proportion to the amount of NADPH remaining. IDH enzyme activity in the direction of isocitrate to alpha-ketoglutarate conversion is measured by direct coupling of the NADPH production to conversion of resazurin to resorufin by diaphorase. In both cases, resorufin is measured fluorometrically at Ex544 Em590^[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay ^[1]

Cells are sorted from fresh or frozen bone marrow aspirates and blood samples after labelling with PE-CD34, APC-CD38, PE-CD14, FITC-CD3 (clone HIT3a) and PECy7-CD19 (clone SJ25C1) antibodies using a MoFlow cell sorter. Unfractionated nucleated blood or bone marrow cells are plated in Methocult H4434 methylcellulose medium at 10⁴ cells/dish, in duplicate dishes per condition. AGI-6780 (5 mM) is directly added to the medium. Dishes are incubated in a humidified incubator at 37°C and colonies containing at least 30 cells are counted after 13 days^[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Metab. 2020 Dec 8;S1550-4131(20)30655-0.
- Clin Cancer Res. 2018 Apr 1;24(7):1705-1715.
- Cell Commun Signal. 2020 Apr 3;18(1):55.
- Oncol Rep. 2018 Aug;40(2):635-646.
- bioRxiv. April 09, 2021.

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REFERENCES

[1]. Wang F, et al. Targeted inhibition of mutant IDH2 in leukemia cells induces cellular differentiation. Science. 2013 May 3;340(6132):622-6.

Caution: Product has not been fully validated for medical applications. For research use only.

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