Enasidenib

Cat. No.: HY-18690

CAS No.: 1446502-11-9

Molecular Formula: $C_{19}H_{17}F_6N_7O$

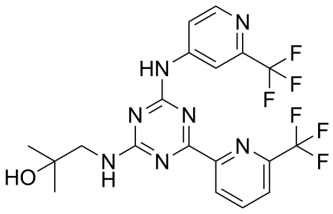
Molecular Weight: 473.38

Target: Isocitrate Dehydrogenase (IDH)

Pathway: Metabolic Enzyme/Protease

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (105.62 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1125 mL	10.5623 mL	21.1247 mL
	5 mM	0.4225 mL	2.1125 mL	4.2249 mL
	10 mM	0.2112 mL	1.0562 mL	2.1125 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.39 mM); Suspended solution; Need ultrasonic and warming
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (2.64 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.64 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Enasidenib is an oral, potent, reversible, selective inhibitor of the IDH2 mutant enzymes, with IC_{50}s of 100 and 400 nM against $IDH2^{R140Q}$ and $IDH2^{R172K}$, respectively.

IC_{50} & Target

IDH2

In Vitro

Enasidenib (AG-221) reverses the effects of mutant IDH2 on DNA methylation in mutant stem/progenitor cells. Enasidenib induces differentiation and impairs self-renewal of IDH2-mutant leukemia cells, effects that are further enhanced by

	simultaneous inhibition of $Flt3^{ITD}$. Enasidenib (AG-221) therapy induces differentiation of leukemic cells, with an increase in the $CD11b^+$ population and a decrease in the $c\text{-}Kit^+$ population in the peripheral blood at 2wks[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Treatment with Enasidenib (AG-221) significantly improves survival in an IDH2-mutant acute myeloid leukemia (AML) primary xenograft mouse model[1]. Enasidenib (AG-221), a mutant IDH2 inhibitor, remodels the epigenetic state of IDH2-mutant cells and induces alterations in self-renewal/differentiation in IDH2-mutant AML model in vivo. Enasidenib treatment (10mg/kg or 100mg/kg bid) leads to a reduction in 2-HG in vivo (96.7% below pre-treatment levels). Moreover, Enasidenib treatment restores megakaryocyte-erythroid progenitor (MEP) differentiation that is suppressed by mutant IDH2 expression (mean MEP% mean, 39% Veh vs 50% AG-221). Enasidenib therapy reverses the effects of mutant IDH2; a significant reduction is observed in DNA methylation, including 180 genes that have 20 or more hypomethylated differentially methylated cytosines (DMCs) following treatment. Enasidenib (100mg/kg bid) treatment of mice engrafted with Mx1-Cre $IDH2^{R140Q}Flt3^{ITD}$ AML cells markedly reduces 2-hydroxyglutarate (2-HG) levels consistent with on target inhibition. Enasidenib inhibits mutant IDH2-mediated 2-HG production[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2022 Aug 15;13(1):4785.
- Sci Adv. 2022 Sep 30;8(39):eabq5575.
- Cell Rep. 2022 Feb 15;38(7):110391.
- Oncogene. 2023 Feb 4.
- J Med Chem. 2023 Mar 23.

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REFERENCES

[1]. Exploring the Pathway: IDH Mutations and Metabolic Dysregulation in Cancer Cells: A Novel Therapeutic Target. MAY 29, 2015

[2]. Alan H. Shih, et al. AG-221, a Small Molecule Mutant IDH2 Inhibitor, Remodels the Epigenetic State of IDH2-Mutant Cells and Induces Alterations in Self-Renewal/Differentiation in IDH2-Mutant AML Model in Vivo. Blood 2014 124:437.

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