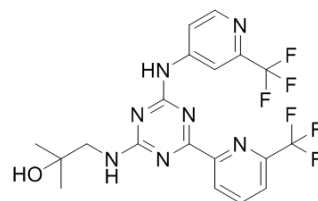


Data Sheet

Product Name:	Enasidenib
Cat. No.:	HY-18690
CAS No.:	1446502-11-9
Molecular Formula:	C ₁₉ H ₁₇ F ₆ N ₇ O
Molecular Weight:	473.38
Target:	Isocitrate Dehydrogenase (IDH)
Pathway:	Metabolic Enzyme/Protease
Solubility:	10 mM in DMSO



BIOLOGICAL ACTIVITY:

Enasidenib is a first-in-class, oral, potent, reversible, selective inhibitor of the **IDH2** mutant enzymes.

IC₅₀ & Target: IDH2^[1]

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-Kit⁺ population in the peripheral blood at 2wks^[2].

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].

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.

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

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