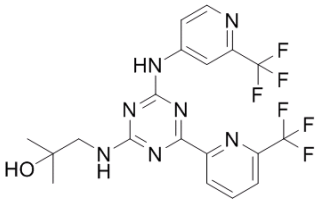
Data Sheet

Product Name:	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
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.

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