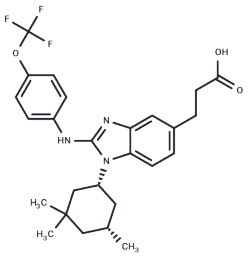
Data Sheet (Cat.No.TQ0042)

TargetMol

BAY-1436032

Chemical Properties



CAS No. : 1803274-65-8

Formula: C26H30F3N3O3

Molecular Weight: 489.53

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	BAY-1436032 is a novel, selective and orally available inhibitor of pan-mutant isocitrate dehydrogenase 1 (IDH1).
Targets(IC50)	Dehydrogenase,Isocitrate Dehydrogenase (IDH)
In vitro	BAY-1436032 inhibits intracellular (R)-2-hydroxyglutarate (R-2HG) production in mouse hematopoietic cells expressing IDH1R132H or IDH1R132C (IC50s: 60 and 45?nM). R-2HG levels are not reduced in IDH2R140Q and IDH2R172K expressing mouse hematopoietic cells by BAY-1436032 at concentrations up to 10?μM. Colony growth is inhibited by 50% at a concentration of 0.1?μM BAY-1436032, while concentrations up to 100?μM do not suppress colony growth of patient-derived IDH1 wild-type AML cells. On morphologic evaluation myelomonocytic differentiation of myeloid progenitors is strongly induced by BAY-1436032.
In vivo	Long-term exposure to once-daily oral BAY-1436032 reveals nearly complete suppression of R-2HG production with 150?mg/kg BAY1436032. White blood cell counts constantly increase in vehicle-treated mice and, at a lower rate, in animals receiving 45?mg/kg BAY-1436032, while they remain constant in the 150?mg/kg cohort. Hemoglobin levels are slightly lower in the vehicle and 45?mg/kg groups as compared to the 150?mg/kg cohort at day 60, while platelet counts are significantly reduced in the vehicle and 45?mg/kg BAY-1436032 treated mice compared to the 150?mg/kg cohort at day 60. All mice receiving 150?mg/kg BAY-1436032 survive with minimal hCD45+ cell load in their peripheral blood until the end of observation at day 150 after treatment start, while vehicle-treated animals die from leukemia with a median survival of 91 days. Mice treated with 45?mg/kg BAY-1436032 display intermediate levels of CD14/CD15 expression.
Cell Research	Colony-forming cell (CFC) units are assayed in methylcellulose supplemented with 10?ng/mL IL-3, 10?ng/mL GM-CSF, 50?ng/ mL SCF, 50?ng/mL FLT3-ligand and 3?U/mL EPO. Vehicle or BAY-1436032 is added to methylcellulose containing 1 × 10^5 human mononuclear cells, which are plated in duplicate. Colonies are evaluated microscopically 10 to 14 days after plating by standard criteria.
Animal Research	NSG mice are used and transplanted with primary acute myeloid leukemia (AML) cells from a patient with IDH1R132C mutant AML. Per condition 10 mice are treated with vehicle, 45 or 150?mg/kg body weight BAY-1436032 once daily by oral gavage for 150 days starting 17 days after transplantation. Finally, serum R-2HG levels and human

Animal Research	CD45+ (hCD45+) cells are measured.

Solubility Information

Solubility	DMSO: 120 mg/mL (245.13 mM),Sonication and heating are recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4 mg/mL (8.17 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0428 mL	10.2139 mL	20.4278 mL
5 mM	0.4086 mL	2.0428 mL	4.0856 mL
10 mM	0.2043 mL	1.0214 mL	2.0428 mL
50 mM	0.0409 mL	0.2043 mL	0.4086 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Chaturvedi A, et al. Pan-mutant-IDH1 inhibitor BAY1436032 is highly effective against human IDH1 mutant acute myeloid leukemia in vivo. Leukemia. 2017 Oct;31(10):2020-2028.