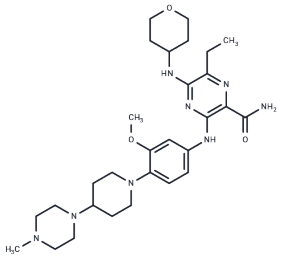
Data Sheet (Cat.No.T4409)

TargetMol

Gilteritinib

Chemical Properties



CAS No. : 1254053-43-4

Formula: C29H44N8O3

Molecular Weight: 552.71

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Gilteritinib (ASP2215) is a potent inhibitor of FMS-related tyrosine kinase 3 (FLT3) and AXL tyrosine kinase receptors (IC50 = 0.29 nM and <1 nM, respectively). In preclinical studies, gilteritinib demonstrated strong antileukemic and antitumor effects. Gilteritinib is currently in several Phase 3 clinical trials for acute myeloid leukemia.
Targets(IC50)	FLT,c-Kit,TAM Receptor
In vitro	Gilteritinib (ASP2215) has been tested against 78 tyrosine kinases, demonstrating strong inhibitory effects on FLT3, leukocyte tyrosine kinase (LTK), anaplastic lymphoma kinase (ALK), and AXL kinases, reducing their activity by over 50% at a concentration of 1 nM. Particularly, Gilteritinib exhibits an IC50 of 0.29 nM for FLT3, making it approximately 800 times more effective against FLT3 than against c-KIT, for which the IC50 is 230 nM. Furthermore, it significantly inhibits eight out of the tested kinases at concentrations up to 5 nM, including TRKA, ROS, RET, and MER, in addition to those previously mentioned. In cell-based assays, Gilteritinib effectively suppresses the growth of MV4-11 and MOLM-13 cells, which naturally express FLT3-ITD mutations, with mean IC50 values of 0.92 nM and 2.9 nM, respectively, upon 5-day treatment. This antiproliferative effect correlates with the reduction of FLT3 phosphorylation and the downstream inhibition of ERK, STAT5, and AKT phosphorylation. A study exploring its impact on AXL inhibition in MV4-11 cells that express exogenous AXL revealed dose-dependent decreases in phosphorylated AXL levels following 4 hours of treatment, highlighting Gilteritinib's potent inhibitory action on both FLT3 and AXL signaling pathways.
In vivo	In MV4-11 xenografted mice, administration of Gilteritinib (ASP2215) orally at 10 mg/kg for four days markedly elevates its tumor concentration, achieving levels over 20-fold higher than in plasma. A 28-day course of Gilteritinib treatment demonstrates dose-dependent suppression of MV4-11 tumor growth, with complete regression observed at dosages exceeding 6 mg/kg. Additionally, Gilteritinib significantly reduces tumor presence in the bone marrow and extends the survival of mice that have undergone intravenous transplant with MV4-11 cells.
Kinase Assay	The kinase inhibitory activity of Gilteritinib is tested against a panel of 78 tested kinases using ATP concentrations that are approximately equal to the Km value for each kinase in a TK-ELISA or off-chip mobility shift assay. Initially, two concentrations of Gilteritinib (1 nM and 5 nM) are tested to assess each compound's inhibitory effect on TK activity. Further studies are then conducted using a dose range of Gilteritinib to determine IC50 values for kinases in which activity is inhibited by >50% with 1 nM Gilteritinib as well as

	for c-KIT. TK-ELISA and MSA assays are used to conduct IC50 studies for FLT3, LTK, AXL, and c-KIT; the HTRF KinEASE-TK assay is performed to assess the IC50 value of echinoderm microtubule-associated protein-like 4-ALK (EML4-ALK)
Cell Research	Gilteritinib is dissolved in DMSO and stored, and then diluted with appropriate media before use.The effect of Gilteritinib on MV4-11 and MOLM-13 cells is assessed using the CellTiter-Glo Luminescent Cell Viability Assay. Subsequent studies are conducted to examine the effect of Gilteritinib and Quizartinib on Ba/F3 cells expressing either FLT3-ITD, FLT3-D835Y, FLT3-ITD-D835Y, FLT3-ITD-F691 L, or FLT3-ITD-F691I. MV4-11 and MOLM-13 cells are treated with DMSO or increasing concentrations of Gilteritinib (0.01, 0.1, 1, 10, and 100 nM) for 5 days, and cell viability is measured using CellTiter-Glo
Animal Research	MiceAntitumor activity is evaluated in nude mice transplanted with MV4-11 AML cells. The pharmacokinetics in xenografted mice is also investigated. MV4-11 xenografted-mice are treated with oral administration of Gilteritinib at 10 mg/kg for 4 days. Treatment of Gilteritinib for 28 days results in dose-dependent inhibition of MV4-11 tumor growth and induces complete tumor regression at more than 6 mg/kg

Solubility Information

Solubility	DMSO: 1 mg/mL (1.81 mM),Sonication is recommended. Ethanol: 4 mg/mL (7.24 mM),Sonication is recommended. H2O: Insoluble, 10% DMSO+90% Saline: 0.2 mg/mL (0.36 mM),Solution. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8093 mL	9.0463 mL	18.0927 mL
5 mM	0.3619 mL	1.8093 mL	3.6185 mL
10 mM	0.1809 mL	0.9046 mL	1.8093 mL
50 mM	0.0362 mL	0.1809 mL	0.3619 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.

Reference

Mori M, et al. Gilteritinib, a FLT3/AXL inhibitor, shows antileukemic activity in mouse models of FLT3 mutated acute myeloid leukemia. Invest New Drugs. 2017 Oct;35(5):556-565.

Zhang Y, Wang P, Wang Y, et al.Sitravatinib as a potent FLT3 inhibitor can overcome gilteritinib resistance in acute myeloid leukemia.Biomarker Research.2023, 11(1): 1-16.

Huang F, Liang J, Lin Y, et al.Repurposing of Ibrutinib and Quizartinib as potent inhibitors of necroptosis. Communications Biology.2023, 6(1): 972.

Zhu R, et al. FLT3 tyrosine kinase inhibitors synergize with BCL-2 inhibition to eliminate FLT3/ITD acute leukemia cells through BIM activation. Signal Transduct Target Ther. 2021 May 24;6(1):186.

Hu C, Zhang Y, Yang J, et al.Ningetinib, a novel FLT3 inhibitor, overcomes secondary drug resistance in acute myeloid leukemia.Cell Communication and Signaling.2024, 22(1): 1-14.

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