Data Sheet (Cat.No.T38266)

TargetMol

Nirogacestat dihydrobromide

Chemical Properties

CAS No. :	1962925-29-6
Formula:	C27H43Br2F2N5O
Molecular Weight:	651.47
Storage:	Keep away from moisture, 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	Nirogacestat dihydrobromide (PF-3084014 dihydrobromide) is an orally active, reversible, and non-competitive selective γ-secretase inhibitor with an IC50 value of 6.2 nM. It exerts its effects by inhibiting the Notch signaling pathway while minimizing gastrointestinal toxicity, making it suitable for the study of Notch receptor-dependent tumors.
Targets(IC50)	Gamma-secretase
In vitro	Method: Human T-ALL cell line HPB-ALL was treated with Nirogacestat dihydrobromide (0.001-10 μmol/L) for 72 h. NICD protein levels were detected by Western Blot, and Hes-1 and cMyc mRNA expression levels were measured by qRT-PCR. Result: Nirogacestat dihydrobromide dose-dependently reduced NICD protein levels in HPB-ALL cells and significantly downregulated the expression of Notch target genes Hes-1 and cMyc [1]. Method: Human T-ALL cell lines HPB-ALL, DND-41, TALL-1, and Sup-T1 were treated with Nirogacestat dihydrobromide for 7 days. Cell proliferation inhibition was assessed by Resazurin fluorescence assay. Result: Nirogacestat dihydrobromide inhibited the growth of multiple T-ALL cell lines [1]. Method: Human T-ALL cell line HPB-ALL was treated with Nirogacestat dihydrobromide (0.001-10 μmol/L) for 7 days. Cell cycle distribution was analyzed by flow cytometry (PI staining), and apoptosis was detected by Annexin V staining. Result: Nirogacestat dihydrobromide induced G_0-G_1 cell cycle arrest in HPB-ALL cells and increased the proportion of sub-G_1 cells, inducing apoptosis [1]. Method: Human T-ALL cell lines HPB-ALL and TALL-1 were treated with Nirogacestat dihydrobromide (1 μmol/L) for 7 days. Caspase-3 activity was measured using a Caspase-3 activity assay kit, and cleaved PARP and cleaved caspase-3 protein levels were detected by Western Blot. Result: Nirogacestat dihydrobromide significantly increased caspase-3 activity and induced the expression of cleaved PARP and cleaved caspase-3, indicating the induction of caspase-dependent apoptosis [1].
In vivo	Method: Nude mice bearing HPB-ALL xenografts were orally administered a single dose of Nirogacestat dihydrobromide (50 mg/kg). Tumor tissues were collected at different time points (4, 8, and 24 h) post-administration, and NICD protein levels were detected by Western Blot.

In vivo	Result: A >50% reduction in NICD was observed as early as 4 h after Nirogacestat dihydrobromide administration, and NICD inhibition reached 70%-80% at 24 h [1]. Method: Nude mice bearing HPB-ALL xenografts were orally administered Nirogacestat dihydrobromide (75 or 150 mg/kg, twice daily for 14 consecutive days). Tumor volume changes were measured using Vernier calipers. Result: Nirogacestat dihydrobromide inhibited tumor growth in a dose-dependent manner, with a tumor growth inhibition rate of ~92% in the 150 mg/kg dose group [1]. Method: Nude mice bearing HPB-ALL xenografts were orally administered Nirogacestat dihydrobromide (150 mg/kg, twice daily for 7 consecutive days). Tumor tissues were collected for immunohistochemical staining to detect NICD, cleaved caspase-3, and Ki67 expression. Result: Following Nirogacestat dihydrobromide treatment, perinuclear NICD staining in tumor tissues was reduced, cleaved caspase-3-positive cells were significantly increased, and Ki67-positive cells were decreased, indicating induction of apoptosis and inhibition of tumor cell proliferation [1].

Solubility Information

Solubility	DMSO: 64 mg/mL (98.24 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.535 mL	7.675 mL	15.3499 mL
5 mM	0.307 mL	1.535 mL	3.070 mL
10 mM	0.1535 mL	0.7675 mL	1.535 mL
50 mM	0.0307 mL	0.1535 mL	0.307 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

Wei P, et al. Evaluation of selective gamma-secretase inhibitor PF-03084014 for its antitumor efficacy and gastrointestinal safety to guide optimal clinical trial design. Mol Cancer Ther. 2010;9(6):1618-1628.