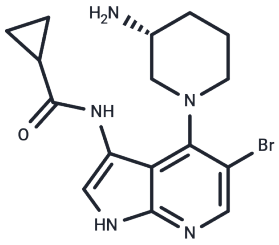
Data Sheet (Cat.No.T7300)

TargetMol

GDC-0575

Chemical Properties



CAS No. : 1196541-47-5

Formula: C16H20BrN5O

Molecular Weight: 378.27

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	GDC-0575 (ARRY-575) is a highly-selective oral small-molecule Chk1 inhibitor(IC50 of 1.2 nM).
Targets(IC50)	Chk
In vitro	GDC-0575 demonstrates markedly higher efficacy in inducing DNA damage, replication stress, and cell death compared to V158411, LY2603618, and MK-8776 in a panel of melanoma cell lines[1].
In vivo	CHK1 inhibitor (CHK1i) GDC-0575 enhances AraC-mediated killing of AML cells both in vitro and in vivo, thus abrogating any potential chemoresistance mechanisms involving DNA repair. Importantly, this combination of drugs does not affect normal long-term hematopoietic stem/progenitors[2].
Animal Research	For in vivo experiments, aliquots of GDC-0575 (10 mg/mL) were stored at ?20℃and diluted in 100 mM sodium citrate buffer immediately prior to each experiment. GDC-0575 was used at 1.8 mg/ml for female mice (~25 g) and 2.6 mg/ml for male mice (~35 g) via oral gavage (final concentration 7.5 mg/kg). For in vitro experiments, aliquots of GDC-0575 (100 μM) were stored at ?20 ℃ and used at a final concentration of 100 nM. AraC (Cytosine β-D-arabinofuranoside C1768, Sigma) was used at 10 mg/kg (commonly used in clinical practice) for in vivo and at 100 nM and 500 nM for in vitro experiments. For in vivo experiments, toxicity of GDC-0575 was assessed in non-engrafted NSG mice using a range of concentrations of GDC-0575 in combination with AraC. 7.5 mg/kg GDC-0575 was the highest concentration to have no significant or lasting adverse effects in mice. Similarly, for in vitro experiments, 100 nM GDC-0575 in combination with 500 nM AraC was the highest concentration non-cytotoxic to MS5 stoma cell. ATR inhibitor was used at a final concentration of 0.5 μM[2].

Solubility Information

Solubility	DMSO: 50 mg/mL (132.18 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (5.29 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one.*

In vivo Formulation	*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	2.6436 mL	13.2181 mL	26.4361 mL
5 mM	0.5287 mL	2.6436 mL	5.2872 mL
10 mM	0.2644 mL	1.3218 mL	2.6436 mL
50 mM	0.0529 mL	0.2644 mL	0.5287 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

Oo Z Y , Stevenson A J , Proctor M A , et al. Endogenous replication stress marks melanomas sensitive to CHK1 inhibitors in vivo[J]. Clinical Cancer Research, 2018:clincanres.2701.2017.
Tullio A D , Rouault-Pierre K , Abarrategi A , et al. The combination of CHK1 inhibitor with G-CSF overrides cytarabine resistance in human acute myeloid leukemia[J]. Nature Communications, 2017, 8(1):1679.