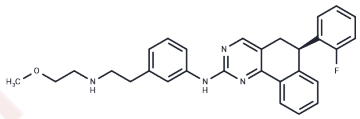
Data Sheet (Cat.No.TQ0228)

TargetMol

Derazantinib

Chemical Properties



CAS No. : 1234356-69-4

Formula: C29H29FN4O

Molecular Weight: 468.57

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	Derazantinib (ARQ-087) is a potent, ATP-competitive, orally active tyrosine kinase inhibitor with IC50 values of 4.5/1.8/4.35/3.4 nM for chondrocyte FGFR1/FGFR2/FGFR3/FGFR4, respectively.
Targets(IC50)	FGFR
In vitro	**METHODS**: COS-1 cells ectopically expressing FGFR1, FGFR2, FGFR3, or FGFR4 were treated with derazantinib (ARQ-087) (0.1, 0.3, 1.1, 3.3, 10 μM, 2 hours) and stimulated with 100 pM FGF1/2/7 for 15 minutes. Total and phosphorylated FGFRs were assessed by Western blot analysis. **RESULTS** Derazantinib inhibited phosphorylation of FGFR1, FGFR2, FGFR3, and FGFR4 with IC50 values of 0.123 μM, 0.185 μM, 0.463 μM, and >10 μM, respectively, together with EC. [1]
In vivo	**METHODS**: Derazantinib (ARQ-087) (25, 50, 75 mg/kg) treated SNU-16 and NCI-H716 xenograft athymic mouse models; Derazantinib (50, 100, 150 mg/kg) treated Ba/F3-FGFR2 xenograft athymic mouse models Thymic mouse model; Derazantinib (75 mg/kg) treated Ba/F3-INSR xenograft athymic mouse model; both were administered orally and the in vivo anti-tumor effect of Derazantinib was evaluated. **RESULTS** Derazantinib showed potent tumor growth inhibition in the Ba/F3-FGFR2 model but failed to inhibit the growth of the Ba/F3-INSR model; in the SNU-16 xenograft study, 75 mg/kg and 50 mg /kg treatment achieved TGI of 83% and 69%, respectively; in the NCI-H716 human cecum model, 50 mg/kg and 75 mg/kg showed significant TGI of 68% and 96%, respectively. [1]
Kinase Assay	Derazantinib is titrated in DMSO utilizing a 3-fold dilution scheme and then diluted 10-fold further in deionized water for a final DMSO concentration of 10%. A volume (2.5 μL) of these dilutions or vehicle is added to each well of a reaction plate. FGFR1 or FGFR2 is added to assay buffer to each well in a volume of 17.5 μL for a final concentration of 0.50 or 0.25 nM, respectively. After a 30-minute pre-incubation period, ATP and substrate are added in assay buffer (5 μL) for final concentrations of 0-1,000 μM ATP and 80 nM biotinylated-PYK2, for a final reaction volume of 25 μL. The plates are incubated for 60 minutes at room temperature and then stopped in the dark by the addition of 10 μL stop/detection mixture prepared in assay buffer containing EDTA [1].
Cell Research	Cells are seeded at 3000-5000 cells per well with 130 μL media in 96-well tissue culture-treated plates. The cells are incubated overnight and subsequently treated with 3-fold serial dilutions of Derazantinib starting at 100 μM. The cells are returned to a 37°C

Cell Research	humidified incubator for 72 hours. Cell proliferation is measured using the MTS assay [1].
Animal Research	Female NCr nu/nu mice (SNU-16) or CB17 SCID mice (NCI-H716) with well established (400 mg) subcutaneous tumors are given a single oral dose of Derazantinib or vehicle control. Plasma and tumor samples are collected 4 hours post single dose. Derazantinib is administered orally. The dosing volume for all groups is 10 mL/kg or 0.1 mL/10 g body weight [1].

Solubility Information

Solubility	DMSO: 100 mg/mL (213.42 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: < 10 mg/mL (21.34 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+90% (20% SBE-β-CD in Saline): < 10 mg/mL (21.34 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+90% Saline: < 10 mg/mL (21.34 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+90% Corn oil: < 10 mg/mL (21.34 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. *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	2.1342 mL	10.6708 mL	21.3415 mL
5 mM	0.4268 mL	2.1342 mL	4.2683 mL
10 mM	0.2134 mL	1.0671 mL	2.1342 mL
50 mM	0.0427 mL	0.2134 mL	0.4268 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

Hall TG, et al. Preclinical Activity of ARQ 087, a Novel Inhibitor Targeting FGFR Dysregulation. PLoS One. 2016 Sep 14;11(9):e0162594.

Balek L, et al. ARQ 087 inhibits FGFR signaling and rescues aberrant cell proliferation and differentiation in experimental models of craniosynostoses and chondrodysplasias caused by activating mutations in FGFR1, FGFR2 and FGFRBone. 2017 Dec;105:57-66.

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