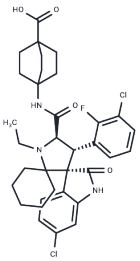
Data Sheet (Cat.No.T14303)

TargetMol

Alrizomadlin

Chemical Properties



CAS No. : 1818393-16-6

Formula: C34H38Cl2FN3O4

Molecular Weight: 642.59

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	Alrizomadlin is an orally active MDM2 inhibitor. APG-115 shows significant dose-dependent inhibitory effects on TP53wt AML cell lines. The IC50 values are 26.8 nM for MOLM-13 cells and 165.9 nM for MV-4-11 cells. , OCI-AML-3 cells 315.6 nM. Alrizomadlin blocks the interaction of MDM2 and p53 and induces cell cycle arrest and apoptosis in a p53-dependent manner.
Targets(IC50)	Apoptosis,Mdm2,E1/E2/E3 Enzyme,MDM-2/p53
In vitro	**METHODS**: CD4 T cells isolated from mouse spleen were exposed to 250 nM APG-115 for 3, 6, and 24 hours, and the effect of APG-115 on T cell viability and activation was investigated. **RESULTS** APG-115 treatment did not induce apoptosis of CD4+ T cells, but promoted CD4+ T cell activation, as evidenced by an increase in the proportion of CD25highCD62Llow cells and an increase in cell size. In addition, treatment did not lead to an increase in the number of regulatory T cells (Tregs), demonstrating a positive activation effect on effector T cells. [1] **METHODS**: Different concentrations of APG-115 (0.001-100μM) were used to treat TP53wt AML cell lines, including MOLM-13, MV-4-11, OCI-AML-3, and HL-60 and SKM-1 cells with TP53 mutations or deletions. , the treatment time is 72 hours, and cell viability, cell cycle and apoptosis analysis are detected. **RESULTS** APG-115 showed significant dose-dependent inhibitory effect on TP53wt AML cell line, with IC50 values of 26.8 nM for MOLM-13 cells, 165.9 nM for MV-4-11 cells, and 315.6 nM for OCI-AML-3 cells; APG -115 treatment caused a significant increase in the proportion of MOLM-13 cell apoptosis, reaching a maximum of 96.8% (1 μM concentration), and caused cell cycle arrest in the G0/G1 phase. [2]
In vivo	**METHODS**: APG-115 was orally administered to TRP53-/- knockout C57BL/6J mice at 10 or 50 mg/kg daily or every other day (Q2D) to observe the effect of APG-115 on tumor growth in mice. **RESULTS** APG-115 can effectively activate the p53 pathway, affect macrophage polarization (reduce M2 type, increase M1 type), and increase PD-L1 expression on tumor cells, regulate the immune microenvironment, and enhance anti-tumor immune response. [1] **METHODS**: APG-115 was administered to mice orally (PO), 20 mg/kg, once every two days for 21 days; daily administration: 50 mg/kg, for 7 days; daily administration changes High dose: 100 mg/kg for 7 days to observe the in vivo therapeutic effect of

In vivo	APG-115. **RESULTS** Administration of APG-115 significantly reduced leukemia burden and prolonged survival in mice in the TP53 wild-type systemic MOLM-13 AML model. Compared with the control group, the median survival time of the APG-115 treatment group was extended by approximately 18.5 days. [2]

Solubility Information

Solubility	DMSO: 81.67 mg/mL (127.1 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: 5 mg/mL (7.78 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	1.5562 mL	7.781 mL	15.562 mL
5 mM	0.3112 mL	1.5562 mL	3.1124 mL
10 mM	0.1556 mL	0.7781 mL	1.5562 mL
50 mM	0.0311 mL	0.1556 mL	0.3112 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

Fang DD, et al. MDM2 inhibitor APG-115 synergizes with PD-1 blockade through enhancing antitumor immunity in the tumor microenvironment. J Immunother Cancer. 2019 Nov 28;7(1):327.
Fang DD,et al. MDM2 inhibitor APG-115 exerts potent antitumor activity and synergizes with standard-of-care agents in preclinical acute myeloid leukemia models. Cell Death Discov. 2021 May 3;7(1):90.
Hanjie Yi ea al, A novel small molecule inhibitor of MDM2-p53 (APG-115) enhances radiosensitivity of gastric adenocarcinoma, J Exp Clin Cancer Res. 2018 May 2;37(1):97.
Chen H, et al. Restoration of p53 using the novel MDM2-p53 antagonist APG115 suppresses dedifferentiated papillary thyroid cancer cells. Oncotarget. 2017 Jun 27;8(26):43008-43022.