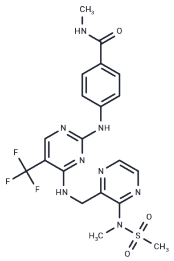
Data Sheet (Cat.No.T1996)

TargetMol

Defactinib

Chemical Properties



CAS No. : 1073154-85-4

Formula: C20H21F3N8O3S

Molecular Weight: 510.49

Storage: Store at low temperature
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	Defactinib (VS-6063) is a second-generation inhibitor of FAK that inhibits FAK phosphorylation at the Tyr397 site. Defactinib has potential antitumor activity.
Targets(IC50)	FAK
In vitro	**METHODS**: Thyroid cancer cell lines TT, K1, BCPAP and TPC1 were treated with Defactinib (1-50 μM) for 24 h and cell viability was measured by MTS assay. **RESULTS**: Defactinib reduced cell viability in a dose-dependent manner in TT, K1, BCPAP and TPC1 cell lines with IC50s of 1.98 μM, 10.34 μM, 23.04 μM and >50 μM, respectively. [1] **METHODS**: Taxane-sensitive cell line HeyA8 and Taxane-resistant cell line HeyA8-MDR were treated with Defactinib (0.001-10 mM) for 1-48 h, and target protein expression levels were detected by Western Blot. **RESULTS**: Defactinib statistically significantly inhibited the expression of pFAK (Tyr397) in a dose-dependent manner. pFAK (Tyr397) expression was inhibited by Defactinib within 3 h and was gradually restored within 48 h. Defactinib was also shown to inhibit pFAK (Tyr397) expression in a dose-dependent manner. [2]
In vivo	**METHODS**: To assay antitumor activity in vivo, Defactinib (25 mg/kg orally twice daily) and PTX (2 mg/kg intraperitoneally once weekly) were administered to thymus-free nude mice bearing SKOV3ip1, SKOV3-TR, HeyA8 or HeyA8-MDR xenografts for 35 or 28 days. **RESULTS**: In the HeyA8 model, PTX monotherapy resulted in an 87.4% reduction in tumor weight, and combination therapy resulted in the greatest reduction in tumor weight, 97.9% compared with PTX. In the SKOV3ip1 model, tumor weight was reduced by 92.7% in the combination group compared to PTX.Treatment with PTX alone was ineffective in the HeyA8 MDR model and the SKOV3-TR model, but treatment with Defactinib resulted in a reduction in tumor weight of 42.6% and 67.1%, respectively, with the combination leading to an even greater reduction in tumor growth. [2]
Kinase Assay	Cell-free Kinase Activity Assays: IC50 values for TG101348 are determined commercially using the InVitrogen kinase profiling service for a 223 kinase screen that included JAK2 and JAK2V617F or Carna Biosciences for the screen of all Janus kinase family members including JAK1 and Tyk2. ATP concentration is set to approximately the Km value for each kinase.

Cell Research	Ovarian cancer cells are treated with increasing concentrations of VS-6063 for 96 hours and then subjected to the MTT assay. Results are confirmed with triplicate experiments. (Only for Reference)

Solubility Information

Solubility	DMSO: 50 mg/mL (97.95 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 (9.79 mM),Suspension. *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	1.9589 mL	9.7945 mL	19.589 mL
5 mM	0.3918 mL	1.9589 mL	3.9178 mL
10 mM	0.1959 mL	0.9795 mL	1.9589 mL
50 mM	0.0392 mL	0.1959 mL	0.3918 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

O'Brien S, et al. FAK inhibition with small molecule inhibitor Y15 decreases viability, clonogenicity, and cell attachment in thyroid cancer cell lines and synergizes with targeted therapeutics. Oncotarget. 2014 Sep 15;5(17):7945-59.

Su Y, Li R, Ning X, et al. Discovery of 2, 4-diarylaminopyrimidine derivatives bearing dithiocarbamate moiety as novel FAK inhibitors with antitumor and anti-angiogenesis activities. European Journal of Medicinal Chemistry. 2019 May 18;177:32-46

Li R, Gong L, Sun J, et al.Discovery of 2, 4-diarylaminopyrimidine derivatives bearing sulfonamide moiety as novel FAK inhibitors.Bioorganic Chemistry.2024: 107134.

Kang Y, et al. Role of focal adhesion kinase in regulating YB-1-mediated paclitaxel resistance in ovarian cancer. J Natl Cancer Inst. 2013 Oct 2;105(19):1485-95.

Su Y, Li R, Ning X, et al. Discovery of 2, 4-diarylaminopyrimidine derivatives bearing dithiocarbamate moiety as novel FAK inhibitors with antitumor and anti-angiogenesis activities[J]. European Journal of Medicinal Chemistry. 2019 May 18;177:32-46.

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