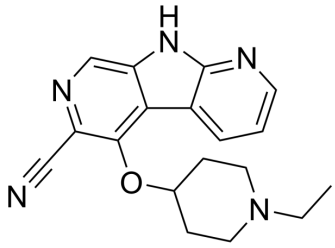
GDC-0425

Cat. No.:	HY-19926
CAS No.:	1200129-48-1
Molecular Formula:	$C_{18}H_{19}N_5O$
Molecular Weight:	321.38
Target:	Checkpoint Kinase (Chk)
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

H_2O : 25 mg/mL (77.79 mM; ultrasonic and adjust pH to 3 with HCl)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1116 mL	15.5579 mL	31.1158 mL
	5 mM	0.6223 mL	3.1116 mL	6.2232 mL
	10 mM	0.3112 mL	1.5558 mL	3.1116 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

GDC-0425 (RG-7602) is an orally available, highly selective small molecule ChK1 inhibitor. GDC-0425 can be used for the research of various malignancies[1][2].

IC_{50} & Target

Chk1

In Vitro

MEK inhibition either by pharmacologic inhibitors or RNAi-mediated gene silencing significantly protected cells from reduced viability upon GDC-0425 treatment[3].

GDC-0425 (3 μM; 24 hours) treatment results the hyperphosphorylation of Chk1[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[3]

Cell Line:	Chk1-positive breast cancer cell lines
Concentration:	0.001, 0.01, 0.1, 1, 10 mM

Incubation Time:	72 hours
Result:	Reduced cell proliferation.

Cell Viability Assay[3]

Cell Line:	U-2 OS cells
Concentration:	3 μM
Incubation Time:	24 hours
Result:	Led to hyperphosphorylation of Chk1.

In Vivo

GDC-0425 exhibits partial suppression of tumor growth. The Gemcitabine/GDC-0425 combination results in significant tumor regression in all tested models[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	NCr nude mice bearing xenografts of both osteosarcoma and triple-negative breast cancer models (143B PML BK TK, HCC1806, and HCC70 cell lines)[3]
Dosage:	For the 4-arm study, mice were treated with vehicle, Gemcitabine 120 mg/kg, GDC-0425 75 mg/kg alone, or Gemcitabine and GDC-0425 combination for 15 days. For 6-arm studies of HCC1806 and HCC70 models, mice were treated with vehicle, Gemcitabine 120 mg/kg, GDC-0425 50 mg/kg, GDC-0425 75 mg/kg alone, or Gemcitabine and GDC-0425 combination.
Administration:	Orally administrated at 24, 48, and 72 hours after gemcitabine administration by intraperitoneal injection.
Result:	Exhibited partial suppression of tumor growth upon treatment with either Gemcitabine or GDC-0425 alone. Notably, the Gemcitabine/GDC-0425 combination resulted in significant tumor regression in all tested models.

REFERENCES

[1]. Xiao Ding, et al. A supported liquid extraction LC-MS/MS method for determination of concentrations of GDC-0425, a small molecule Checkpoint kinase 1 inhibitor, in human plasma. Biomed Chromatogr. 2016 Dec;30(12):1984-1991.

[2]. Jeffrey R Infante, et al. Phase I Study of GDC-0425, a Checkpoint Kinase 1 Inhibitor, in Combination with Gemcitabine in Patients with Refractory Solid Tumors. Clin Cancer Res. 2017 May 15;23(10):2423-2432.

[3]. Ho-June Lee, et al. Ras-MEK Signaling Mediates a Critical Chk1-Dependent DNA Damage Response in Cancer Cells. Mol Cancer Ther. 2017 Apr;16(4):694-704.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA