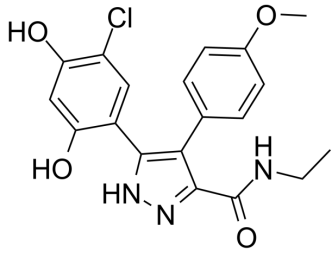
VER-49009

Cat. No.:	HY-15986
CAS No.:	558640-51-0
Molecular Formula:	$C_{19}H_{18}ClN_3O_4$
Molecular Weight:	387.82
Target:	HSP
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (257.85 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5785 mL	12.8926 mL	25.7852 mL
	5 mM	0.5157 mL	2.5785 mL	5.1570 mL
	10 mM	0.2579 mL	1.2893 mL	2.5785 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.75 mg/mL (7.09 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.75 mg/mL (7.09 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

VER-49009 is a Hsp90 inhibitor, with an IC_{50} of 25 nM and a K_d of 78 nM.

IC_{50} & Target

HSP90
25 nM (IC_{50})

In Vitro

VER-49009 is a Hsp90 inhibitor, with an IC_{50} of 25 nM. VER-49009 binds to the ATPase of full length yeast Hsp90 protein, with an IC_{50} of 140 nM[1]. VER-49009 inhibits Hsp90, with a K_d of 78 nM. VER-49009 also shows antiproliferative activities against various human cancer cells, with a mean GI_{50} of 685 ± 119 nM. VER-49009 suppressses the proliferation of human umbilical vein endothelial cells (HUVEC) with GI_{50} values of 444 ± 91.1 nM, and shows higher GI_{50}s against nontumorigenic human breast (MCF10a) and prostate (PNT2) epithelial cells. VER-49009 displays no differences in cellular activities of isogenic cell

	lines, and these activities are independent of NQO1 expression[2]. VER-49009 inhibits the proliferation (1, 2.5 μM), induces G2 phase arrest and reduces total Akt and phospho-Akt expression levels in CFSC cells (1-5 μM)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	VER-49009 (4 mg/kg, i.p.) results in clear depletion of ERBB2 at 3 and 8 h following the final dose, with client protein levels returning to normal by 24 h, in the athymic mice bearing well-established OVCAR3 human ovarian ascites tumors[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	Briefly, 5×10^3 cells/well are plated in 96-well culture plates. After an overnight incubation, the cells are treated with various concentrations of VER-49009 and VER-49009M (0, 1, 2.5, and 5 μM) for 24 h[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	In some studies, female NCr athymic mice are implanted i.p. with 10 million OVCAR3 ovarian carcinoma cells harvested from donor mice. This tumor mimics late-stage malignant disease. Once tumors are well established, mice are injected i.p. with 4 mg/kg VER-49009 or VER-50589 twice daily over 2 days (four doses total). Tumors are harvested at intervals after the last dose and snap frozen for pharmacodynamic analyses[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Dymock BW, et al. Novel, potent small-molecule inhibitors of the molecular chaperone Hsp90 discovered through structure-based design. J Med Chem. 2005 Jun 30;48(13):4212-5.

[2]. Sharp SY, et al. Inhibition of the heat shock protein 90 molecular chaperone in vitro and in vivo by novel, synthetic, potent resorcinylic pyrazole/isoxazole amide analogues. Mol Cancer Ther. 2007 Apr;6(4):1198-211.

[3]. Sun X, et al. Inhibition of hepatic stellate cell proliferation by heat shock protein 90 inhibitors in vitro. Mol Cell Biochem. 2009 Oct;330(1-2):181-5.

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