KU 59403

Cat. No.: HY-18650

CAS No.: 845932-30-1

Molecular Formula: $C_{29}H_{32}N_4O_4S_2$

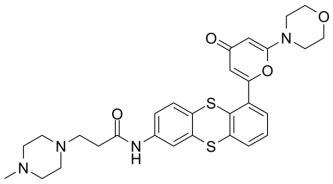
Molecular Weight: 564.72

Target: ATM/ATR

Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR

Storage: -20°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 10 mg/mL (17.71 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7708 mL	8.8539 mL	17.7079 mL
	5 mM	0.3542 mL	1.7708 mL	3.5416 mL
	10 mM	0.1771 mL	0.8854 mL	1.7708 mL

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

BIOLOGICAL ACTIVITY

Description

KU 59403 is a potent ATM inhibitor, with IC_{50} values of 3 nM, 9.1 μM and 10 μM for ATM, DNA-PK and PI3K, respectively[1].

IC_{50} & Target

IC50: 3 nM (ATM)[1].

In Vitro

KU 59403 (1 μM) enhances VP-16 (1 μM) cytotoxicity to a similar extent in HCT116 and HCT116-N7 cells, and in the p53 mutant SW620 cells and human breast cancer cell line, MDAMB-231, sensitisation is 11.9±4.7 and 3.8±1.8-fold respectively. Inhibition of IR-induced ATM activity by KU 59403 (1 μM) is approximately 50% in MDA-MB231 cells and >50% in HCT116 cells that have low ATM expression and activity[1].

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

Cell Viability Assay[1]

Cell Line:	LoVo, HCT116 and SW620 (human colon cancer), and U2OS (human osteosarcoma) and MDA-MB-231 (human breast cancer) cells.
Concentration:	1 μM.
Incubation Time:	16 hours.

Result:	Had at least 1000 times greater specificity for ATM over other members of the PI3K family tested. Enhanced camptothecin cytotoxicity in both cell lines with greater enhancement being observed in the LoVo compared to the SW620 cells. Significantly enhanced the cytotoxicity of fixed concentrations of VP-16 (0.1 and 1 μM) or NSC 123127 (10 or 100 nM) in these cell lines, with greater enhancement of VP-16 in SW620 cells and of NSC 123127 in LoVo cells.

In Vivo

KU59403 with a single daily dose of 12.5 mg/kg causes a significant sensitization[1].
Increasing the dose of KU59403 to 25 mg/kg given twice daily results in the greatest chemo-sensitisation with a 3-fold increase in BMY-40481-induced tumour growth delay in both SW620 and HCT116-N7 xenografts, in the absence of a significantly increased toxicity[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	CD-1 nude mice implanted with SW620 or HCT116-N7 human cancer cell lines at 1×10^7 cells per animal s.c. (n=5 per group)[1].
Dosage:	6, 12.5 and 25 mg/kg.
Administration:	I.P. twice daily (0 and 4 hours) and 12.5 mg/kg once daily.
Result:	Treatment with BMY-40481 alone causes a modest tumour growth delay of 4 days (time to RTV4=10.5 days). This delay is extended to 8.5 days when given with KU 59403 at 12.5 mg/kg i.p. twice daily for 5 days and 11.5 days (time to RTV4=18 days) when given with KU 59403 at 25 mg/kg i.p. twice daily for 5 days.

REFERENCES

[1]. Batey MA, et al. Preclinical evaluation of a novel ATM inhibitor, KU59403, in vitro and in vivo in p53 functional and dysfunctional models of human cancer. Mol Cancer Ther. 2013 Jun;12(6):959-67.

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