KU-60019

Cat. No.: HY-12061

CAS No.: 925701-46-8

Molecular Formula: $C_{30}H_{33}N_3O_5S$

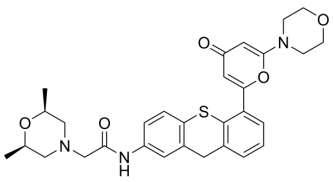
Molecular Weight: 548

Target: ATM/ATR

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

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 (182.48 mM; Need ultrasonic)
Ethanol : 10 mg/mL (18.25 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8248 mL	9.1241 mL	18.2482 mL
5 mM	0.3650 mL	1.8248 mL	3.6496 mL
10 mM	0.1825 mL	0.9124 mL	1.8248 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: ≥ 2.5 mg/mL (4.56 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.56 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KU-60019 is an improved ATM kinase-specific inhibitor with IC_{50} of 6.3 nM.

IC_{50} & Target

ATM	DNA-PKcs
6.3 nM (IC_{50})	1.7 μM (IC_{50})

In Vitro

KU-60019 is an improved analogue of KU-55933. KU-55933 has an IC_{50} of 13 nM and K_i of 2.2 nM in vitro and is highly specific for the ATM kinase using a panel of 60 protein kinases. KU-60019 is an improved inhibitor of the ATM kinase with an IC_{50} of 6.3 nM, approximately half that of KU-55933. The IC_{50} values for DNA-PKcs and ATR are 1.7 and >10 μM, respectively, almost 270-and 1600-fold higher than for ATM. KU-60019 is 10-fold more effective than KU-55933 at blocking radiation-induced

	phosphorylation of key ATM targets in human glioma cells. In human U87 glioma cells, KU-55933 completely inhibits phosphorylation of p53 (S15) at 10 μM but not at 3 μM, whereas γ-H2AX levels are only partly reduced with 10 μM 1 h after irradiation. By comparison, 3 μM KU-60019 completely inhibits p53 phosphorylation and partial inhibits at 1 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Despite PTEN-deficient control tumors reaching a 4-fold increase in size before PTEN wild-type controls, KU-60019-treated PTEN-deficient tumors display a statistically significant slowing in growth. This growth inhibition is especially evident at the start of the experiment (days 5-12) just after KU-60019 is administered (days 1-5)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cell growth is determined by AlamarBlue. U1242 cells are serially diluted, allowed to attach for 6 h and then exposed to KU-60019 at 3 μM. At days 1, 3 and 5 after seeding, AlamarBlue is added to the medium to the recommended final concentration. Plates are incubated for 1 h at 37°C and fluorescence determined on a FluoroCount plate reader (excitation 530 nm, emission 590 nm) and values taken as a measure of cell growth[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Cells (3×10^7) are implanted into male Fox Chase Severe Combined Immunodeficiency (SCID) mice. Administration of Doxycycline is started when tumors reach 100 mm^3 in volume and is performed every 48 hours up to removal of the animal from the experiment. Forty-eight hours after PTEN induction, animals are administered KU-60019 (100 mg/kg) for 5 consecutive days and measured until they reach a target 400 mm^3 volume. Measurements of tumor volume and body weight took place every 3 days using calipers. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Acta Biomater. 2021 Mar 31;S1742-7061(21)00201-4.
- Cell Rep. 2020 Jan 14;30(2):497-509.e4.
- Acta Pharmacol Sin. 2021 Jan 7.
- Oncogenesis. 2020 Feb 3;9(2):8.

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REFERENCES

[1]. Golding SE, et al. Improved ATM kinase inhibitor KU-60019 radiosensitizes glioma cells, compromises insulin, AKT and ERK prosurvival signaling, and inhibits migration and invasion. Mol Cancer Ther. 2009 Oct;8(10):2894-902.

[2]. McCabe N, et al. Mechanistic Rationale to Target PTEN-Deficient Tumor Cells with Inhibitors of the DNA Damage Response Kinase ATM. Cancer Res. 2015 Jun 1;75(11):2159-65.

Caution: Product has not been fully validated for medical applications. For research use only.

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