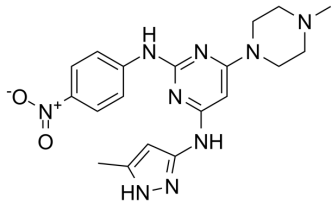
AKI603

Cat. No.:	HY-123159
CAS No.:	1432515-73-5
Molecular Formula:	$C_{19}H_{23}N_9O_2$
Molecular Weight:	409.45
Target:	Aurora Kinase
Pathway:	Cell Cycle/DNA Damage; Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (305.29 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4423 mL	12.2115 mL	24.4230 mL
5 mM	0.4885 mL	2.4423 mL	4.8846 mL
10 mM	0.2442 mL	1.2212 mL	2.4423 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: 6.25 mg/mL (15.26 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

AKI603 is an inhibitor of Aurora kinase A (AurA), with an IC_{50} of 12.3 nM. AKI603 is developed to overcome resistance mediated by BCR-ABL-T315I mutation. AKI603 exhibits strong anti-proliferative activity in leukemic cells[1][2].

IC_{50} & Target

Aurora A
12.3 nM (IC_{50})

In Vitro

AKI603 (0.039-0.6 μM; 48 hours) extensively inhibits proliferation of leukemia cells[1].
AKI603 (0.039-0.6 μM; 48 hours) significantly inhibits the phosphorylation of AurA in NB4, K562, and Jurkat cell lines in a dose-dependent manner while the level of total AurA protein is not changed[1].
AKI603 inhibits the proliferation and colony formation of imatinib resistant CML cells[1].
AKI603 (0.3-0.6 μM; 48 hours) inhibits cell proliferation and colony formation capacities in imatinib-resistant CML cells by inducing cell cycle arrest with polyploidy accumulation[1].

Inhibition of AurA by AKI603 induces leukemia cell senescence in both BCR-ABL wild type and T315I mutation cells[1].
AKI603 exhibits inhibitory activities on breast cancer cell proliferation, such as SUM149 (IC_{50}=2.04), BT549 (IC_{50}=0.86), MCF-7 (IC_{50}=0.97), MCF-7-Epi (IC_{50}=21.01), Sk-br-3 (IC_{50}=0.73), MDA-MB-231 (IC_{50}=3.49), MDA-MB-453 (MTT, IC_{50}=0.18; Cell counting, IC_{50}=0.19), MDA-MB-468 (MTT, IC_{50}=0.15; Cell counting, IC_{50}=0.17)[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	U937 cells, HL-60 cells, NB4 cells, KBM5 cells, K562 cells, Jurkat cells
Concentration:	0.039 μM, 0.078 μM, 0.16 μM, 0.3 μM, 0.6 μM
Incubation Time:	48 hours
Result:	Inhibited all the tested cell lines.

Western Blot Analysis[1]

Cell Line:	NB4 cells, K562 cells, Jurkat cells
Concentration:	0.039 μM, 0.078 μM, 0.16 μM, 0.3 μM, 0.6 μM
Incubation Time:	48 hours
Result:	Inhibited the phosphorylation of AurA Thr288 (p-AurA).

Cell Cycle Analysis[1]

Cell Line:	K562, K562/G, 32D-p210 and 32D-T315I cells
Concentration:	0.3 μM, 0.6 μM
Incubation Time:	48 hours
Result:	Induced polyploidization in the tested cells.

In Vivo

AKI603 (12.5-25 mg/kg; i.p.; every 2 days; for 14 days) abrogates the growth of xenografted KBM5-T315I cells in nude mice[1].
AKI603 exhibits moderate oral bioavailability (rat 28.7%) and C_{max} (rat 202.4 μg/L) following oral administration (rat 25 mg/kg)[3].
AKI603 exhibits terminal elimination half-life (rat 8.9 h) following intravenous administration (rat 2.5 mg/kg)[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female BALB/c nude mice, with KBM5-T315I cells xenografted[1]
Dosage:	12.5 mg/kg, 25 mg/kg
Administration:	Intraperitoneal injection, every 2 days, for 14 days
Result:	Significantly inhibited the growth of tumors.

Animal Model:	SD rats (220-280 g)[3]
Dosage:	2.5 mg/kg for i.v.; 25 mg/kg for p.o. (Pharmacokinetic Analysis)
Administration:	Intravenous injection, oral administration
Result:	Oral bioavailability (28.7%), C_{max} (202.4 μg/L), $T_{1/2}$ (8.9 h)

REFERENCES

[1]. Le-Xun Wang, et al. Aurora A Kinase Inhibitor AKI603 Induces Cellular Senescence in Chronic Myeloid Leukemia Cells Harboring T315I Mutation. Sci Rep. 2016 Nov 8;6:35533.

[2]. Fei-Meng Zheng, et al. A novel small molecule aurora kinase inhibitor attenuates breast tumor-initiating cells and overcomes drug resistance. Mol Cancer Ther. 2014 Aug;13(8):1991-2003.

[3]. Zhenzhen Zhao, et al. Determination of a novel Aurora-A (AurA) kinase AKI603 by UPLC-MS/MS and its application to a bioavailability study in rat. J Pharm Biomed Anal. 2016 Jun 5;125:303-9.

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