Ro3280

Cat. No.: HY-15161

CAS No.: 1062243-51-9

Molecular Formula: $C_{27}H_{35}F_2N_7O_3$

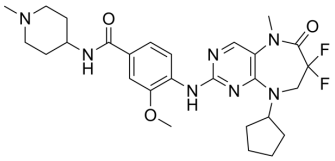
Molecular Weight: 543.61

Target: Polo-like Kinase (PLK)

Pathway: Cell Cycle/DNA Damage

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 (183.96 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8396 mL	9.1978 mL	18.3955 mL
	5 mM	0.3679 mL	1.8396 mL	3.6791 mL
	10 mM	0.1840 mL	0.9198 mL	1.8396 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 (4.60 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.60 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.60 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ro3280 is a potent, highly selective inhibitor of PLK1 with an IC_{50} and a K_d of 3 nM and 0.09 nM, respectively, and nearly has no effect on PLK2 and PLK3.

IC_{50} & Target

PLK1 0.09 nM (Kd)	ALK 230 nM (Kd)	CAMKK1 1100 nM (Kd)	CAMKK2 87 nM (Kd)
DAPK1 100 nM (Kd)	DAPK3 70 nM (Kd)	FER 53 nM (Kd)	GAK 87 nM (Kd)

	MYLK 170 nM (Kd)	PTK2 84 nM (Kd)	PTK2B 130 nM (Kd)	RPS6KA6 (KinDom.2) 560 nM (Kd)
	TTK 51 nM (Kd)			
In Vitro	Ro3280 (RO3280) inhibits PLK1 activity in NB4 and K562 cells, with an IC_{50}s of 13.45 nM and 301 nM, respectively. RO3280 shows inhibitory activities against the growth of six leukemia cells, with IC_{50}s of 186 nM, 175 nM, 74 nM, 797 nM, 120 nM and 162 nM for U937, HL60, NB4, K562, MV4-11 and CCRF cell lines, respectively. RO3280 also suppresses the growth of primary ALL and AML cells, with IC_{50}s of 35.49-110.76 nM, and 52.80-147.50 nM, respectively. RO3280 (50 or 100 nM) induces apoptosis and cell cycle disorder in acute leukemia cells[1]. Ro3280 shows potent activity in H82, H69, A549 lung cancer cell lines with EC_{50}s of 6 nM, 7 nM and 82 nM. Ro3280 also inhibits several other cancer cell lines, with low concentration[2]. RO3280 is cytotoxic to 5637 and T24 human bladder cancer cells, with IC_{50}s of appr 100 nM. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			
In Vivo	Ro3280 (RO3280, 40 mg/kg, i.v.) inhibits 72% tumor growth in a mouse xenograft model implanted with HT-29 colorectal cancer cells, and when dosed more frequently, RO3280 completely suppresses the tumor growth[2]. RO3280 (30 mg/kg, once every 5 days, i.p.) shows significant anti-bladder cancer activities in a nude mouse model[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			

PROTOCOL

Cell Assay [1]	Leukemia cells or primary leukemia cells (2×10^4) are seeded in 96-well plates overnight and incubated with DMSO, or increasing concentrations of RO3280 (0.05-120 μM) for 24 h. The same volume of DMSO added to the vehicle treated wells. Each drug concentration is replicated four times. Then, 10 μL CCK8 solution is added to each well, incubated at 37°C for 2-4 h and the optical density (OD) values are measured at 450 nm using a scanning multi-well spectrophotometer. Relative survival rate is calculated from the absorbance values compared with the control group. The proliferation of cells is calculated as a percentage of the DMSO-treated control wells with 50% inhibitory concentration (IC_{50}) values derived after plotting proliferation values on a logarithmic curve. The IC_{50} of PLK1 inhibitor is calculated by Graph Prism software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Briefly, mice (female, 4-5 weeks of age) are used in the assay. Cells (5×10^6 cells in 150 μL) are suspended in RPMI 1640 and injected subcutaneously into the flank of each BALB/c nude mouse. On day 5, tumour size is measured, the animals are randomized into two groups (n = 15 per group), and RO3280 (40 mg/kg, once every 5 days) treatment is initiated by intraperitoneal injection. The control group is treated with vehicle (1.5% DMSO in PBS). The drug (or vehicle) treatment is performed for 40 days. The length and width of the resulting tumours (in millimetres) are measured every 3 days with callipers. The tumour diameter is measured, and the volume (length × $width^2$ × 0.52) is calculated. The mice are humanely killed on day 45, and the tumours are dissected and weighed. Western blot and immunohistochemistry assays are also performed with these sections. Then, the tumours are fixed, embedded and cut into 3μmthick sections, which are subsequently stained with haematoxylin and eosin to permit the observation of the tumour margin[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Theranostics. 2022; 12(8): 3911-3927.
- Cancer Lett. 2020 Oct 28;491:50-59.
- J Photochem Photobiol B. 2022 May 20;232:112477.
- Mol Pharm. 2023 Feb 22.

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REFERENCES

[1]. Wang NN, et al. Molecular targeting of the oncoprotein PLK1 in pediatric acute myeloid leukemia: RO3280, a novel PLK1 inhibitor, induces apoptosis in leukemia cells. Int J Mol Sci. 2015 Jan 7;16(1):1266-92.

[2]. Chen S, et al. Identification of novel, potent and selective inhibitors of Polo-like kinase 1. Bioorg Med Chem Lett. 2012 Jan 15;22(2):1247-50.

[3]. Zhang Z, et al. Targeted inhibition of Polo-like kinase 1 by a novel small-molecule inhibitor induces mitotic catastrophe and apoptosis in human bladder cancer cells. J Cell Mol Med. 2017 Apr;21(4):758-767.

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