SGI-1776 free base

Cat. No.: HY-13287

CAS No.: 1025065-69-3

Molecular Formula: $C_{20}H_{22}F_3N_5O$

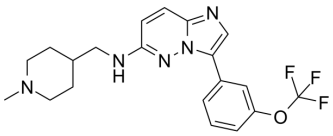
Molecular Weight: 405.42

Target: Pim; Autophagy; Apoptosis

Pathway: JAK/STAT Signaling; Autophagy; Apoptosis

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 : 125 mg/mL (308.32 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4666 mL	12.3329 mL	24.6658 mL
5 mM	0.4933 mL	2.4666 mL	4.9332 mL
10 mM	0.2467 mL	1.2333 mL	2.4666 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: ≥ 2.08 mg/mL (5.13 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.13 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SGI-1776 free base is an inhibitor of Pim kinases, with IC_{50}s of 7 nM, 363 nM, and 69 nM for Pim-1, -2 and -3, respectively.

IC_{50} & Target

Ki: 7 nM (Pim-1), 363 nM (Pim-2), 69 nM (Pim-3)[4]

In Vitro

SGI-1776 free base (2.5, 5 μM) inhibits Pim-1 protein expression and Pim-1 kinase activity in SACC cells. SGI-1776 free base (2.5, 5 μM) causes cell cycle arrest and reduces cell proliferation in SACC-83 and SACC-LM cells[1].
SGI-1776 free base (5 μM) inhibits cell migration and invasiveness in both SACC-83 and SACC-LM cells. SGI-1776 free base (0,

	2.5, or 5 μM) induces apoptosis via Caspase-3 activation[1]. SGI-1776 free base (5 μM) exerts inhibitory effects on both lipid accumulation and TG synthesis without affecting the number of adipocytes[2]. SGI-1776 free base (5 μM) inhibits adipogenesis particularly at an early phase of differentiation[2]. SGI-1776 free base (5 μM) decreases the expression of C/EBP-α and PPAR-γ and the phosphorylation levels of STAT-3 during adipocyte differentiation, and downregulates the protein and/or mRNA expression of FAS, leptin and RANTES during adipocyte differentiation[2]. SGI-1776 free base shows the significant activity against HO-8910 cells in a dose-dependent manner, with IC_{50} of (5.2±0.6) μM, and the inhibiting effect of SGI-1776 free base is sharply increased from 1.25 μM to 20 μM in vitro[3]. SGI-1776 free base inhibits the migration and invasion of HO-8910 cells in a dose-dependent manner, and the inhibiting migration and invasion rate of 5 μM[3]. SGI-1776 free base (2.5, 5 and 10 μM) decreases Pim-1 kinase activity of HO-8910 cells in a dose-dependent manner. Furthermore, the down-regulation of Pim-1 expression by SGI-1776 free base significantly inhibits cell viability, arrests cell in G1 phase, and inhibits the migration and invasion[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SGI-1776 free base (75, 200 mg/kg, p.o.) shows potent and sustained antitumor activity in a dose dependent manner in MV-4-11 xenografts in mice[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	SACC-83 free base and SACC-LM cells of 0 μM, 2.5 μM and 5 μM groups after SGI-1776 exposure are harvested. 6 samples of SACC cells are diluted in Kinase buffer and pipetted into the wells which is pre-coated with a substrate corresponding to recombinant p21waf1. It contains threonine residues that can be efficiently phosphorylated by Pim-1. After undergoing the procedure, measure absorbance in each well is quantitated by spectrophotometry at dual wavelengths of 450/540 nm. It reflects the relative amount of Pim-1 activity in the 6 groups of SACC cells. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [3]	Cells are seeded in a 96-well plate at a density of 5 000 cells/well. After incubation for 24 h, different concentrations of SGI-1776 (0.625, 1.25, 2.5, 5, 10, 20, 40 μM) are added to each well and cultured for 48 h. The medium is removed and then incubated with 5 mg/L MTT for 4 h. Next, the supernatant is removed after centrifugation. Finally, 100 μL of DMSO is added and an absorbance at 570 nm wavelength (A570) is measured by enzyme-labeling instrument. Relative cell proliferation inhibition rate (IR)=(1-average A570 of the experimental group/average A570 of the control group)×100%. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	The conditions for animal room environment and photoperiod are 20-25°C, 40%-70% humidity, and 12 hours of light/12 hours of dark cycle. Each mouse is inoculated subcutaneously at the right flank with MV-4-11 tumor cells (5×10^6). The treatments start when the tumor size reach 80-150 mm^3. Mice are randomized to treatment groups based on their tumor sizes; tumor size is measured in 2 dimensions using a caliper, and the volume is expressed in mm^3 using the formula: $V = 0.5\ a \times b^2$ where a and b are the long and short diameters of the tumor, respectively. Pretreatment randomization ensures that each group has approximately the same mean tumor size. Mice are treated with vehicle (5% dextrose), SGI-1776 or cytarabine (ara-C). SGI-1776 and ara-C are formulated in 5% dextrose. SGI-1776 is administered by oral gavage (PO) on a daily × 5/week or twice/week schedule; ara-C is administered by intraperitoneal injection 3 times/week for 3 consecutive weeks. Animals are euthanized when their measured tumor size is greater than 3000 mm^3 or when they lose ≥ 20% initial body weight; if the body weight loss ≥ 15%, treatment is stopped at first until mice regain body weight. Mice are euthanized when body weight loss is still ≥ 20% even after stopping treatment. T/C value (in %) is an indication of antitumor efficacy, where T and C are the mean tumor volume of the treated and control groups, respectively, on a given day. The differences between the mean tumor sizes for comparing groups is analyzed using the ANOVA test, where $P \leq 0.05$ is considered to be statistically significant. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Death Dis. 2018 Feb 22;9(3):307.
- Cell Chem Biol. 2023 Nov 16:S2451-9456(23)00384-7.
- J Med Chem. 2021 Oct 21.

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REFERENCES

[1]. Hou X, et al. Biochemical changes of salivary gland adenoid cystic carcinoma cells induced by SGI-1776. Exp Cell Res. 2017 Mar 15;352(2):403-411.

[2]. Park YK, et al. The novel anti-adipogenic effect and mechanisms of action of SGI-1776, a Pim-specific inhibitor, in 3T3-L1 adipocytes. Int J Mol Med. 2016 Jan;37(1):157-64

[3]. Xie J, et al. SGI-1776, an imidazo pyridazine compound, inhibits the proliferation of ovarian cancer cells by inactivating Pim-1. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2014 Jul;39(7):649-57

[4]. Chen LS, et al. Mechanisms of cytotoxicity to Pim kinase inhibitor, SGI-1776, in acute myeloid leukemia. Blood, 2011, 118(3), 693-702.

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