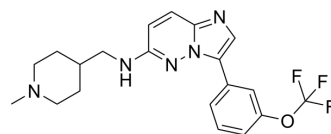


SGI-1776

Cat. No.:	HY-13287		
CAS No.:	1025065-69-3		
Molecular Formula:	C ₂₀ H ₂₂ F ₃ N ₅ O		
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	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro	DMSO : 125 mg/mL (308.32 mM; Need ultrasonic)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	Preparing Stock Solutions	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	<ol style="list-style-type: none"> 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 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 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 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.
IC₅₀ & Target	Ki: 7 nM (Pim-1), 363 nM (Pim-2), 69 nM (Pim-3) ^[4]
In Vitro	SGI-1776 (2.5, 5 μM) inhibits Pim-1 protein expression and Pim-1 kinase activity in SACC cells. SGI-1776 (2.5, 5 μM) causes cell cycle arrest and reduces cell proliferation in SACC-83 and SACC-LM cells. SGI-1776 (5 μM) inhibits cell migration and invasiveness in both SACC-83 and SACC-LM cells. SGI-1776 (0, 2.5, or 5 μM) induces apoptosis via Caspase-3 activation ^[1] .

SGI-1776 (5 μM) exerts inhibitory effects on both lipid accumulation and TG synthesis without affecting the number of adipocytes. SGI-1776 (5 μM) inhibits adipogenesis particularly at an early phase of differentiation. SGI-1776 (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 shows the significant activity against HO-8910 cells in a dose-dependent manner, with IC_{50} of (5.2 \pm 0.6) μM , and the inhibiting effect of SGI-1776 is sharply increased from 1.25 μM to 20 μM in vitro. SGI-1776 inhibits the migration and invasion of HO-8910 cells in a dose-dependent manner, and the inhibiting migration and invasion rate of 5 μM . SGI-1776 (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 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 (75, 200 mg/kg, p.o.) shows potent and sustained antitumor activity in a dose dependent manner in MV-4-11 xenografts^[4].

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

PROTOCOL

Kinase Assay ^[1]

SACC-83 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) \times 100%.

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Animal Administration ^[4]

The conditions for animal room environment and photoperiod are 20-25 $^{\circ}\text{C}$, 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 \times 10⁶). The treatments start when the tumor size reach 80-150 mm³. 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 mm³ 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 \times 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 mm³ or when they lose \geq 20% initial body weight; if the body weight loss \geq 15%, treatment is stopped at first until mice regain body weight. Mice are euthanized when body weight loss is still \geq 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.
- J Med Chem. 2021 Oct 21.
- eNeuro. 2019 Aug 22;6(4):ENEURO.0003-19.2019.

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

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