Product Data Sheet

Product Name: Voreloxin
Cat. No.: GC13544

Chemical Properties

Cas. No.	175414-77-4		
Chemical Name	7-[(3S,4S)-3-methoxy-4-(methylamino)pyrrolidin-1-yl]-4-oxo-1-(1,3-thiazol-2-yl)-1,8-naphthyridine-3-carboxylic acid		
SMILES	CNC1CN(CC1OC)C2=NC3=C(C=C2)C(=O)C(=CN3C4=NC=CS4)C(=O)O		
Formula	$C_{18}H_{19}N_5O_4S$	M.Wt	401.44
Solubility	<4.01 mg/mL in DMSO, <2.51 mg/mL in EtOH, <2.49 mg/mL in Water	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Voreloxin		

Protocol

Cell experiment [1]:

Cell lines	SK-BR-3, ScaBER, PANC-1, KB, HCT116, SKOV3, GT3TKB, Hs746T, Calu-6, NCI-H460, PA-1, MES-SA, SBC-3, SBC-3/ETP and PC-14 cells

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Preparation method	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reaction Conditions	0.04 ~ 1.155 μM; 72 hrs
Applications	Voreloxin exhibited broad anti-proliferative activity in 15 cell lines, including 4 drug-resistant lines, with the IC50 values ranging from 0.04 to 1.155 μM.

Animal experiment [2]:

Animal models	Mice implanted with P388 leukemia cells
Dosage form	3.13, 12.5 or 50 mg/kg; i.p.; on days 1 and 5 after tumor implantation
Applications	In mice implanted with P388 leukemia cells, Voreloxin (50 mg/kg, i.p.) showed potent antitumor activity.

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Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Hoch U, Lynch J, Sato Y, Kashimoto S, Kajikawa F, Furutani Y, Silverman JA. Voreloxin, formerly SNS-595, has potent activity against a broad panel of cancer cell lines and in vivo tumor models. Cancer Chemother Pharmacol. 2009;64(1):53-65.

[2]. Tsuzuki Y, Tomita K, Shibamori K, Sato Y, Kashimoto S, Chiba K. Synthesis and structure-activity relationships of novel 7-substituted 1,4-dihydro-4-oxo-1-(2-thiazolyl)-1,8-naphthyridine-3-carboxylic acids as antitumor agents. Part 2. J Med Chem. 2004;47(8):2097-109.

Background

Voreloxin, formerly known as SNS-595 or AG-7352, is a novel naphthyridine analog, which is structurally related to the quinolone antibiotics, a chemical class not previously used for the treatment

of cancer.

In vitro: In vitro studies demonstrated voreloxin has broad anti-proliferative activity in 11 tumor cell lines, with IC50 values ranging from 0.04 to 0.97 μM. Similar activity was observed in vitro in drug-resistant cell lines, including those that overexpress P-glycoprotein [2].

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In vivo: After a single intravenous dose, voreloxin concentrations in tumor were correlated with induction of the apoptosis marker caspase-3. Administration of voreloxin at 20 mg/kg weekly inhibited tumor growth (86%). Voreloxin demonstrated strong dose-dependent tumor growth inhibition (63–88%) in 10 of 11 solid tumor xenograft models [2].

Clinical trial: Voreloxin showed an acceptable safety profile with clinical activity in patients with relapsed/refractory solid tumors. The maxmum tolerence dose was schedule-dependent. Voreloxin is now in clinical studies of ovarian cancer and acute myeloid leukemia [3].

References:

[1] Tsuzuki Y, Tomita K, Shibamori K, Sato Y, Kashimoto S, Chiba K. Synthesis and structure-activity relationships of novel 7-substituted 1,4-dihydro-4-oxo-1-(2-thiazolyl)-1,8-naphthyridine-3-carboxylic acids as antitumor agents. Part 2. J Med Chem. 2004;47(8):2097-109.
[2] Hoch U, Lynch J, Sato Y, Kashimoto S, Kajikawa F, Furutani Y, Silverman JA. Voreloxin, formerly SNS-595, has potent activity against a broad panel of cancer cell lines and in vivo tumor models. Cancer Chemother Pharmacol. 2009;64(1):53-65.
[3] Advani RH, Hurwitz HI, Gordon MS, Ebbinghaus SW, Mendelson DS, Wakelee HA, Hoch U, Silverman JA, Havrilla NA, Berman CJ, Fox JA, Allen RS, Adelman DC. Voreloxin, a first-in-class anticancer quinolone derivative, in relapsed/refractory solid tumors: a report on two dosing schedules. Clin Cancer Res. 2010;16(7):2167-75.

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