

Product Data Sheet

Product Name: OSMI-1
Cat. No.: GC14870

Chemical Properties

Cas. No. 1681056-61-0

Chemical Name (R)-N-(furan-2-ylmethyl)-2-(2-methoxyphenyl)-2-(2-oxo-1,2-dihydroquinoline-6-sulfonamido)-N-(thiophen-2-ylmethyl)acetamide

SMILES O=C(N(CC1=CC=CS1)CC2=CC=CO2)[C@H](NS(C3=CC(C=C4)=C(C=C3)NC4=O)(=O)=O)C5=CC=CC=C5OC

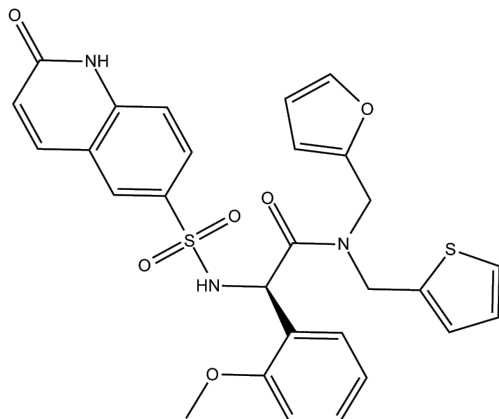
Formula $C_{28}H_{25}N_3O_6S_2$ M.Wt 563.64

Solubility 20mg/mL in DMSO, 25mg/mL in DMF Storage Store at -20°C, protect from light

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

Cell experiment [1]:

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Cell lines	Tamoxifen-sensitive (TamS) and tamoxifen-resistant (TamR) MCF7 breast cancer cells
Preparation Method	TamS and TamR cells were collected on ice following 24 h of treatment with 40 μ M dose of OSMI-1 compound, or DMSO. Samples were immediately fixed in 100% ice-cold methanol and placed in - 20 °C for storage. Samples were washed in cold PBS and stained with 1.5 μ g/ml Hoechst 33258 in PBS for 30 min at 37 °C. Cell cycle analysis was then performed on LSR II flow cytometer.
Reaction Conditions	40 μ M for 24 h
Applications	OSMI-1 decreased the number of cells in S-Phase and also caused a modest, but not significant, accumulation of cells in the G2-M phase
Animal experiment [2]:	
Animal models	HCT116 xenograft models on Five-week-old female BALB/c-Foxn1nu/ArcGem nude mice
Preparation Method	HCT116 xenograft models were injected subcutaneously with 5×10^6 cells in the flanks of each mouse. After 7 days, tumor-bearing mice (tumor volume approximately 90-110 mm ³) were randomized into various treatment groups (n = 4/group) as follows: Group 1—mice were administered DMSO as a vehicle control; Group 2—mice were administered TRAIL (500 μ g/kg/daily, Intraperitoneal); Group 3—mice were administered OSMI-1 (1 mg/kg/daily, Intravenous); Group 4—mice were coadministered TRAIL and OSMI-1 for 21 consecutive days.

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Dosage form 1 mg/kg/daily, i.v.

Applications The tumor size in mice treated with TRAIL or OSMI-1 alone was slightly reduced compared with the control group but was significantly reduced (5-fold) in the TRAIL and OSMI-1 combination group.

References:

[1]: Barkovskaya A, Seip K, Prasmickaite L, et al. Inhibition of O-GlcNAc transferase activates tumor-suppressor gene expression in tamoxifen-resistant breast cancer cells[J]. Scientific reports, 2020, 10(1): 1-10.

[2]: Lee S J, Lee D E, Choi S Y, et al. OSMI-1 enhances TRAIL-induced apoptosis through ER stress and NF-κB signaling in colon cancer cells[J]. International journal of molecular sciences, 2021, 22(20): 11073.

Background

OSMI-1 is an O-GlcNAc transferase (OGT) small molecule inhibitor that does not significantly affect other glycosyltransferases [1]. OSMI-1 inhibited full length human OGT (ncOGT) with an IC50 value of 2.7 μM [2].

OSMI-1 ranging from 10 to 100 μM treated inhibited global O-GlcNAcylation in Chinese hamster ovary (CHO) cells with the maximal effect being achieved at 50 μM [2]. 50 μM OSMI-1 treated CHO cells decreased viability by about 50% after 24 h [2]. OSMI-1 (40 μM) decreased total-O-GlcNAc by 30% in both TamS and TamR cell lines [1]. TamR cells were significantly more sensitive to OSMI-1 than the parental TamS cells, with OSMI-1-EC50 value of ~15 μM in TamR and ~40 μM in TamS by activity for proliferation assay [1]. OSMI-1 (40 μM, 24 h) increased expression of OGT and DDIT3 in both TamS and TamR cells while ERα is downregulated [1]. The levels of intracellular and secreted HBsAg, but not HBeAg, in the supernatants, increased in primary human hepatocytes (PHHs) and HepG2.2.15 cells after OSMI-1 treatment [3].

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OSMI-1 reduced osteoclast differentiation in vivo by disrupting the translocation of NF- κ B p65 and nuclear factor of activated T cells c1 (NFATc1) into the nucleus by controlling their PTM O-GlcNAcylation. OSMI-1 treatment effectively inhibited lipopolysaccharide (LPS)-induced formation of TRAP-positive osteoclasts in the calvarial surface compared to the mice injected with the vehicle, while OSMI-1 significantly reduced the number of TRAP-specific mature osteoclasts in the calvarial surfaces and sections [4]. The tumor size in mice treated with TRAIL or OSMI-1 alone was slightly reduced compared with the control group but was significantly reduced (5-fold) in the TRAIL and OSMI-1 combination group on HCT116 Xenograft in Nude Mice. Compared with vehicle-treated xenograft mice, the levels of ER stress-related proteins, such as IRE1 α , PERK, p-JNK, CHOP, and DR5, were increased when either TRAIL or OSMI-1 was administered alone, whereas these effects were even greater for the combination treatment [5].

References:

- [1]. Barkovskaya A, Seip K, Prasmickaite L, et al. Inhibition of O-GlcNAc transferase activates tumor-suppressor gene expression in tamoxifen-resistant breast cancer cells[J]. Scientific Reports, 2020, 10(1): 1-10.
- [2]. Ortiz-Meoz R F, Jiang J, Lazarus M B, et al. A small molecule that inhibits OGT activity in cells[J]. ACS Chemical Biology, 2015, 10(6): 1392-1397.
- [3]. Wang X, Lin Y, Liu S, et al. O-GlcNAcylation modulates HBV replication by regulating cellular autophagy at multiple levels[J]. The FASEB Journal, 2020, 34(11): 14473-14489.
- [4]. Kim M J, Kim H S, Lee S, et al. Hexosamine Biosynthetic Pathway-Derived O-GlcNAcylation Is Critical for RANKL-Mediated Osteoclast Differentiation[J]. International Journal of Molecular Sciences, 2021, 22(16): 8888.
- [5]. Lee S J, Lee D E, Choi S Y, et al. OSMI-1 enhances TRAIL-induced apoptosis through ER stress and NF- κ B signaling in colon cancer cells[J]. International journal of molecular sciences, 2021, 22(20): 11073.

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