

Product Data Sheet

Product Name: GDC-0941

Cat. No.: GC10816

Chemical Properties

Cas. No. 957054-30-7

Chemical Name 4-[2-(1H-indazol-4-yl)-6-[(4-methylsulfonylpiperazin-1-yl)methyl]thieno[3,2-d]pyrimidin-4-yl]morpholine

SMILES CS(=O)(=O)N1CCN(CC1)CC2=CC3=C(S2)C(=NC(=N3)C4=C5C=NNC5=CC=C4)N6CCOCC6

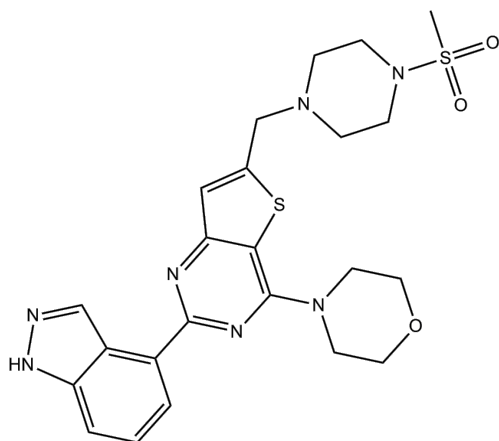
Formula $C_{23}H_{27}N_7O_3S_2$ M.Wt 513.64

Solubility $\geq 25.7\text{mg/mL}$ in DMSO, $\geq 3.59\text{mg/mL}$ in EtOH with ultrasonic and warming
Storage Store at -20°C

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	Daoy cells
Preparation Method	Daoy cells were cultured in Dulbecco Modified Eagle Medium (DMEM) supplemented with L-glutamine, 1mM sodium pyruvate (PAA), 1% penicillin/streptomycin (Invitrogen), and 10% fetal bovine serum (FBS), at 37°C and 5% CO ₂ . 2.5×10 ³ Daoy cells were seeded in 96-well plates and treated with different concentrations of GDC-0941 (0, 1, 2, 5, and 10μM) for 48 hours. MTS reagent was added and absorbance was measured at 490nm.
Reaction Conditions	0, 1, 2, 5, and 10μM; 48h
Applications	GDC-0941 treatment significantly inhibited the cell viability of Daoy cells in a concentration-dependent manner.

Animal experiment [2]:

Animal models	Female MMTV-neu mice
Preparation Method	Female MMTV-neu mice at 10 weeks of age were treated with GDC-0941 (50mg/kg) or vehicle (0.5% hydroxypropyl methylcellulose containing 0.1% Tween 80) by gavage once daily until the tumors became palpable. The median tumor-free survival time was recorded as T(50). At 15 weeks after treatment, 4-5 mice in each group were sacrificed, and a fourth pair of normal-looking mammary fat pads (MFP) were isolated for immunohistochemical analysis.
Dosage form	50mg/kg/day for 15 weeks; p.o.
Applications	GDC-0941 treatment resulted in a significant decrease in the levels of p-Akt-S473 and Ki-67 in the mouse mammary tissue.

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References:

- [1] Ehrhardt M, Craveiro R B, Holst M I, et al. The PI3K inhibitor GDC-0941 displays promising in vitro and in vivo efficacy for targeted medulloblastoma therapy[J]. *Oncotarget*, 2014, 6(2): 802.
- [2] Wang J, Zhang Y, Xiao Y, et al. Boosting immune surveillance by low-dose PI3K inhibitor facilitates early intervention of breast cancer[J]. *American journal of cancer research*, 2021, 11(5): 2005.

Background

GDC-0941 is an oral, potent, selective pan-inhibitor of class I PI3K, with IC₅₀ values of 3nM, 33nM, 3nM, and 75nM for p110 α , p110 β , p110 δ , and p110 γ , respectively^[1]. GDC-0941 inhibits the AKT signaling pathway by suppressing PI3K expression, mainly including the inhibition of AKT phosphorylation as well as phosphorylation levels of AKT downstream proteins^[2]. GDC-0941 has been widely used in both cell and animal models to inhibit the progression of cancer, and has been employed in the development of combined therapies targeting tumors^[3].

In vitro, GDC-0941 treatment for 96 hours significantly inhibited the viability of U87MG, PC3 and MDA-MB-361 cells, with IC₅₀ values of 0.95 μ M, 0.28 μ M and 0.72 μ M, respectively^[4]. Treatment with 10 μ M GDC-0941 for 48 hours significantly inhibited the proliferation of Daoy cells and induced cell apoptosis, causing the cells to undergo cell cycle arrest^[5]. GDC-0941 (1 μ M) treatment for 18 hours inhibited hypoxia-induced HIF-1 α and HIF-2 α expression and HIF activity in thyroid cancer cells^[6].

In vivo, GDC-0941 treatment via oral administration at a dose of 50mg/kg/day for 15 weeks resulted in a significant reduction in the levels of p-Akt-S473 and Ki-67 in the mammary tissues of MMTV-neu mice, delaying tumor occurrence and prolonging the tumor-free survival period^[7]. Oral administration of 100mg/kg/day dose of GDC-0941 for 2 weeks can inhibit tumor growth in RIP1-Tag2 mice without affecting tumor blood vessels^[8].

References:

- [1] Sarker D, Ang J E, Baird R, et al. First-in-human phase I study of pictilisib (GDC-0941), a potent pan-class I phosphatidylinositol-3-kinase (PI3K) inhibitor, in patients with advanced solid tumors[J]. *Clinical cancer research*, 2015, 21(1): 77-86.

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- [2] Chen H, Cheng M, Gao P, et al. GDC-0941 activates integrin linked kinase (ILK) expression to cause resistance to GDC-0941 in breast cancer by the tumor necrosis factor (TNF)- α signaling pathway[J]. Bioengineered, 2022, 13(4): 10944-10955.
- [3] Usman M W, Gao J, Zheng T, et al. Macrophages confer resistance to PI3K inhibitor GDC-0941 in breast cancer through the activation of NF- κ B signaling[J]. Cell death & disease, 2018, 9(8): 809.
- [4] Folkes A J, Ahmadi K, Alderton W K, et al. The identification of 2-(1 H-indazol-4-yl)-6-(4-methanesulfonyl-piperazin-1-ylmethyl)-4-morpholin-4-yl-thieno [3, 2-d] pyrimidine (GDC-0941) as a potent, selective, orally bioavailable inhibitor of class I PI3 kinase for the treatment of cancer[J]. Journal of medicinal chemistry, 2008, 51(18): 5522-5532.
- [5] Ehrhardt M, Craveiro R B, Holst M I, et al. The PI3K inhibitor GDC-0941 displays promising in vitro and in vivo efficacy for targeted medulloblastoma therapy[J]. Oncotarget, 2014, 6(2): 802.
- [6] Burrows N, Babur M, Resch J, et al. GDC-0941 inhibits metastatic characteristics of thyroid carcinomas by targeting both the phosphoinositide-3 kinase (PI3K) and hypoxia-inducible factor-1 α (HIF-1 α) pathways[J]. The journal of clinical endocrinology & metabolism, 2011, 96(12): E1934-E1943.
- [7] Wang J, Zhang Y, Xiao Y, et al. Boosting immune surveillance by low-dose PI3K inhibitor facilitates early intervention of breast cancer[J]. American journal of cancer research, 2021, 11(5): 2005.
- [8] Soler A, Figueiredo A M, Castel P, et al. Therapeutic benefit of selective inhibition of p110 α PI3-kinase in pancreatic neuroendocrine tumors[J]. Clinical Cancer Research, 2016, 22(23): 5805-5817.

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