

Product Data Sheet

Product Name: PI-103 Hydrochloride

Cat. No.: GC16379

Chemical Properties

Cas. No. 371935-79-4

Chemical Name 3-(4-morpholin-4-yl)pyrido[2,3]furo[2,4-b]pyrimidin-2-yl)phenol;hydrochloride

SMILES C1COCCN1C2=NC(=NC3=C2OC4=C3C=CC=N4)C5=CC(=CC=C5)O.Cl

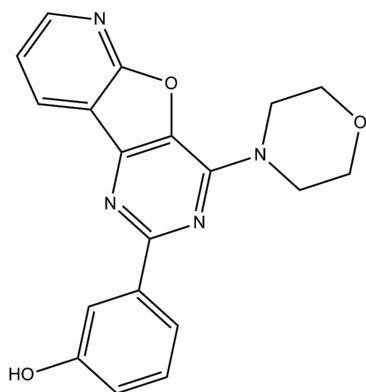
Formula $C_{19}H_{17}ClN_4O_3$ M.Wt 384.82

Solubility ≥ 19.25 mg/mL in DMSO 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 HCl



Protocol

Cell experiment [1]:

Cell lines Huh7 cells (human hepatocellular carcinoma cell line)

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

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Huh7 cells were maintained in Dulbecco's minimal essential medium (DMEM) supplemented with 10% heat-inactivated fetal bovine serum (FBS) at 37°C, 5% Preparation Method CO₂. Cells were treated with PI-103 Hydrochloride (2μM) at specified concentrations for designated time periods prior to epidermal growth factor (EGF; 2.5μM) stimulation or irradiation.

Reaction
Conditions 2μM; 1h pretreatment

Applications PI-103 Hydrochloride significantly inhibited EGF-stimulated phosphorylation of mTOR (Ser2448, 45% inhibition), S6K (Thr389, 87% inhibition), and AKT (Ser473, 88% inhibition), indicating potent dual inhibition of both mTORC1 and mTORC2 activity.

Animal experiment [2]:

Animal models Nude mice

Preparation Method Mice were implanted subcutaneously with MDA-MB-435S cells transfected with pGL4 luciferase reporter vector. One week after implantation, mice were treated with intraperitoneal administration of PI-103 Hydrochloride (10mg/kg) alone or in combination with Olaparib (10mg/kg) three times weekly for 2 weeks, followed by irradiation (3Gy per fraction, three times weekly). Mice were observed for 2 weeks post-treatment and analyzed via bioluminescence imaging.

Dosage form 10mg/kg; i.p.

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Applications

Combined treatment with PI-103 Hydrochloride and Olaparib significantly reduced tumor volume compared to radiation alone, demonstrating enhanced radiosensitization in triple-negative breast cancer xenografts. PI-103 Hydrochloride alone showed synergistic effects with Olaparib in blocking tumor growth post-irradiation.

References:

- [1] Gedaly R, Angulo P, Hundley J, et al. PI-103 Hydrochloride and sorafenib inhibit hepatocellular carcinoma cell proliferation by blocking Ras/Raf/MAPK and PI3K/AKT/mTOR pathways. *Anticancer Res.* 2010 Dec;30(12):4951-8.
- [2] Jang NY, Kim DH, Cho BJ, et al. Radiosensitization with combined use of olaparib and PI-103 Hydrochloride in triple-negative breast cancer. *BMC Cancer.* 2015 Mar 3;15:89.

Background

PI-103 Hydrochloride is a potent cell-permeable multi-target inhibitor that primarily acts on the PI3K and mTOR signaling pathways^[1]. PI-103 Hydrochloride inhibits PI3K subtypes p110 α (8nM), p110 β (88nM), p110 δ (48nM), and p110 γ (158nM), as well as mTOR complexes mTORC1 (20nM) and mTORC2 (83nM), while simultaneously inhibiting DNA-PK activity (2nM)^[2]. PI-103 Hydrochloride can induce mitochondrial apoptosis and autophagy in cells^[3]. PI-103 Hydrochloride can restore the sensitivity of cancer cells to radiotherapy and chemotherapy^[4].

In vitro, pretreatment of Dalton's lymphoma ascites (DLA) cells with PI-103 Hydrochloride (10 μ M) for 24 hours, followed by stimulation with H₂O₂ (1mM) for 30 minutes, significantly inhibited the PI3K-AKT signaling pathway and induced apoptosis, while reducing the accumulation of reactive oxygen species (ROS)^[5]. Pretreatment of Huh7 hepatocellular carcinoma cells with PI-103 Hydrochloride (2 μ M) for 1 hour, followed by stimulation with EGF (2.5nM) for 15 minutes, significantly inhibited the phosphorylation of key proteins in the PI3K/AKT/mTOR signaling pathway and blocked EGF-stimulated cell proliferation^[6].

In vivo, intraperitoneal injection of PI-103 Hydrochloride (10mg/kg) combined with olaparib (10mg/kg)

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three times per week, used to treat mouse models implanted with MDA-MB-435S cells for 2 weeks followed by radiotherapy (3Gy per fraction), significantly enhanced the inhibitory effect of radiotherapy on triple-negative breast cancer xenografts^[7]. Daily intraperitoneal injection of PI-103 Hydrochloride (10mg/kg or 70mg/kg) in FVB/N mice for 8 days to several weeks significantly promoted the growth of melanoma xenografts, while inhibiting thymocyte count and inducing immunosuppression^[8].

References:

- [1] Park S, Chapuis N, Bardet V, et al. PI-103 Hydrochloride, a dual inhibitor of Class IA phosphatidylinositide 3-kinase and mTOR, has antileukemic activity in AML. *Leukemia*. 2008 Sep;22(9):1698-706.
- [2] Raynaud FI, Eccles SA, Patel S, et al. Biological properties of potent inhibitors of class I phosphatidylinositide 3-kinases: from PI-103 Hydrochloride through PI-540, PI-620 to the oral agent GDC-0941. *Mol Cancer Ther*. 2009 Jul;8(7):1725-38.
- [3] Djuzenova CS, Fischer T, Katzer A, et al. Opposite effects of the triple target (DNA-PK/PI3K/mTOR) inhibitor PI-103 Hydrochloride on the radiation sensitivity of glioblastoma cell lines proficient and deficient in DNA-PKcs. *BMC Cancer*. 2021 Nov 11;21(1):1201.
- [4] Toulany M, Iida M, Keinath S, et al. Dual targeting of PI3K and MEK enhances the radiation response of K-RAS mutated non-small cell lung cancer. *Oncotarget*. 2016 Jul 12;7(28):43746-43761.
- [5] Maurya AK, Vinayak M. PI-103 Hydrochloride attenuates PI3K-AKT signaling and induces apoptosis in murine T-cell lymphoma. *Leuk Lymphoma*. 2017 May;58(5):1153-1161.
- [6] Gedaly R, Angulo P, Hundley J, et al. PI-103 Hydrochloride and sorafenib inhibit hepatocellular carcinoma cell proliferation by blocking Ras/Raf/MAPK and PI3K/AKT/mTOR pathways. *Anticancer Res*. 2010 Dec;30(12):4951-8.
- [7] Jang NY, Kim DH, Cho BJ, et al. Radiosensitization with combined use of olaparib and PI-103 Hydrochloride in triple-negative breast cancer. *BMC Cancer*. 2015 Mar 3;15:89.
- [8] López-Fauqued M, Gil R, Grueso J, et al. The dual PI3K/mTOR inhibitor PI-103 Hydrochloride promotes immunosuppression, in vivo tumor growth and increases survival of sorafenib-treated melanoma cells. *Int J Cancer*. 2010 Apr 1;126(7):1549-61.

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