PI-103

Inhibitor of PI3K & mTOR; Autophagy inducer

Catalog # inh-pi10

For research use only

Version # 15D03-MM

PRODUCT INFORMATION

Contents:

•5 mg PI-103

Storage and stability:

- PI-103 is provided lyophilized and shipped at room temperature. Store at -20 °C. Lyophilized PI-103 is stable for 3 years when properly stored.
- Upon resuspension, prepare aliquots of PI-103 and store at -20 °C. Resuspended PI-103 is stable for 6 months when properly stored.

Quality control:

- Purity: ≥97% (UHPLC)
- The absence of bacterial contamination (e.g. lipoproteins and endotoxins) is confirmed using HEK-Blue™ TLR2 and HEK-Blue™ TLR4 cells.

DESCRIPTION

PI-103 is a potent ATP-competitive dual inhibitor of phosphatidylinositol 3-kinase (PI3K) and mTOR (mammalian target of rapamycin). PI3K, an important intracellular mediator, regulates multiple cellular functions including cell growth and survival. PI3K activates a number of downstream targets including the serine/threonine kinase Akt that activates mTOR, the master negative regulator of autophagy. By inhibiting mTOR activity, PI-103 induces autophagy and promotes cell survival[1, 2]. Conversely, combining PI-103 with inhibitors of autophagy, such as 3-methyladenine or bafilomycin A1, leads to apoptosis[1].

1. Fan QW. & Weiss W., 2011. Autophagy and Akt promote survival in glioma. Autophagy7(5): 536-8. **2. Park S. et al., 2008.** PI-103, a dual inhibitor of Class IA phosphatidylinositide 3-kinase and mTOR, has antileukemic activity in AML.Leukemia. 22(9):1698-706. **3. Aronson LI. et al., 2013.** Understanding the interplay between the proteasome pathway and autophagy in response to dual PI3K/mTOR inhibition in myeloma cells is essential for their effective clinical application. Leukemia. 27(12):2397-403. **5. López-Fauqued M. et al., 2010.** The dual PI3K/mTOR inhibitor PI-103 promotes immunosuppression, in vivo tumor growth and increases survival of sorafenib-treated melanoma cells. Int J Cancer. 126(7):1549-61.

CHEMICAL PROPERTIES

Solubility: 10 mg/ml (28.7 mM) in DMSO

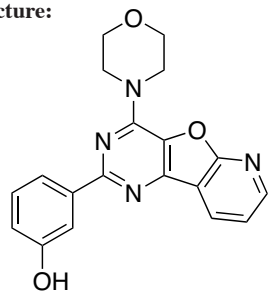
Synonym: 3-[4-(4-Morpholinylpyrido[3',2':4,5]furo[3,2-d]pyrimidin-2-yl]phenol hydrochloride

CAS number: 371935-74-9

Formula: $C_{19}H_{16}N_4O_3$

Molecular weight: 348.4

Structure:



METHODS

Preparation of 10 mg/ml (28.7 mM) stock solution

- Add 1 ml of DMSO to 10 mg of PI-103. Mix by vortexing.
- Prepare further dilutions by adding the appropriate amount of endotoxin-free water.

Working concentration: 0.1-10 µM (35 ng/ml -3.5 µg/ml) for cell culture assays

PROTOCOLS

For reference only; as described in the indicated publications.

Cell Culture Assay[2]

Cells: Human leukemic cell lines; MOLM14, OCI-AML3 and MV4-11
Working concentration: 0.1-1 µM
Treatment time: 48 hours
Method: MTS assay (colorimetric assay for assessing cell viability)

Cell Culture Assay[3]

Cells: Multiple myeloma cell lines; NCI- H929, MM.1S and U266 cells
Working concentration: 1–10 µmol/L
Treatment time: 24 hours
Method: Acridine orange staining for autophagy detection using confocal microscopy and flow cytometry. Western blotting to detect the autophagosome markers, LC3II.

Animal Study[5]

Animal model: Myeloma xenograft model in FVB/N mice
Dose: 10 mg/kg
Administration: Daily intraperitoneal injection for 8 days.

RELATED PRODUCTS

Product	Description	Catalog Code
Bafilomycin A1	Autophagy inhibitor	tlrl-baf1
Everolimus	Autophagy inducer	tlrl-eve
3-Methyladenine	Autophagy inhibitor	tlrl-3ma
Rapamycin	Autophagy inducer	tlrl-rap
Resveratrol	Autophagy inducer	tlrl-resv
Temsirolimus	Autophagy inducer	tlrl-tems

TECHNICAL SUPPORT
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