Product Data Sheet

Product Name: PTC209 HBr
Cat. No.: GC12147

Chemical Properties

Cas. No.	1217022-63-3		
Chemical Name	N-(2,6-dibromo-4-methoxyphenyl)-4-(2-methylimidazo[1,2-a]pyrimidin-3-yl)thiazol-2-amine hydrobromide		
SMILES	BrC1=CC(OC)=CC(Br)=C1NC2=NC(C3=C(C)N=C4N3C=CC=N4)=CS2.Br		
Formula	$C_{17}H_{13}Br_2N_5OS.HBr$	M.Wt	576.10
Solubility	≥ 22.9mg/mL in DMSO with gentle warming	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	PTC209 HBr		

Protocol

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Cell experiment:

MTT assays are used to assess proliferation of Abrams, D17, and Moresco canine OSA cells following treatment of PTC-209 alone and in combination with Dox or Carbo. 500 cells are seeded in 96 well plates with DMEM/10%FBS and allowed to adhere overnight (16-18 hrs). For single treatment PTC-209 experiments, cells are incubated with drug for 72hrs at final concentrations of 0, 200, 300, 400, 500, and 600nM. For combination treatment experiments, cells are incubated with drug(s) for 72hrs at the following final concentrations: PTC-209 (0, 100, 200, and 500 nM), Dox (0, 3, and 30 nM), Carbo (0, 3, and 30 μM). Vehicle controls include DMSO (PTC-209), 0.9% saline (Dox), and water (Carbo). Additional controls included untreated (UT) cells (no veh or drug) and wells containing media (DMEM/10%FBS) alone (to assess background absorbance). Briefly, MTT solution is added to each well at a final conc. of 0.5mg/mL and incubated at 37°C for 4hrs. 200uL of DMSO is added to dissolve formazin crystals and absorbance is measured at 570nM and 630nM (reference wavelength) using a spectrophotometer (Spectramax 190). 6 wells per group are used for PTC-209 single treatment experiments, and 4 wells per group are used for combination treatment experiments, and all experiments are repeated twice. Statistical analysis is performed using 2-way ANOVA with Tukey’s multiple comparisons test.

Animal experiment:

Mice[1] For the experiments where mice are dosed with the drug in vivo, tumor cells are injected subcutaneously into nude mice (male, aged 8-10 weeks), and when the tumors reach an approximate 0.2 cm3 volume, PTC-209 is administered subcutaneously once a day at a dose of 60 mg per kg body weight (control animals received equal volumes of vehicle, 14% DMSO, 36% polyethylene glycol 400 and 50% polypropylene glycol). Tumor volume measurements are recorded every 3-7 d until the endpoint is reached.

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References:

[1]. Kreso A, et al. Self-renewal as a therapeutic target in human colorectal cancer. Nat Med. 2014 Jan;20(1):29-36.
[2]. Christian Mayr, et al. The BMI1 inhibitor PTC-209 is a potential compound to halt cellular growth in biliary tract cancer cells. Oncotarget. 2016 Jan 5; 7(1): 745-758.
[3]. Shahi MH, et al. BMI1 is expressed in canine osteosarcoma and contributes to cell growth and chemotherapy resistance. PLoS One. 2015 Jun 25;10(6):e0131006.

Background

PTC-209 HBr is the hydrobromide salt of PTC-209, a potent and selective BMI-1 inhibitor (IC50 = 0.5μM). It irreversibly impairs the colorectal tumor growth. [1]
BMI-1 is a component of polycomb repressive complex 1 (PRC1) and act as an epigenetic

chromatin modifier for a variety of genes. [1]
PTC-209 inhibited both UTR-mediated reporter expression and endogenous BMI-1 expression in HCT116 (human colorectal cell) and HT1080 (human fibrosarcoma tumor cell) in a dose dependent manner. In addition, the inhibitory effect of PTC-209 was not from its cytotoxicity. PTC-209 also specifically reduced PRC1 activity. [1]
Viable colorectal cancer cell samples treated with PTC-209 ex vivo were injected back to the recipient mice in vivo, the mice exhibited reduced or no tumor growth comparing with the control groups. Thus PTC-209 irreversibly impaired colorectal cancer-initiating cells. Furthermore, in contrast with the control groups, tumor volume was significantly reduced in the colorectal tumor cell transplanted mice following PTC-209 administration. [1]

References:

[1] Kreso A, van Galen P, Pedley NM, Lima-Fernandes E, Frelin C, Davis T, Cao L,Baiazitov R, Du W, Sydorenko N, Moon YC, Gibson L, Wang Y, Leung C, Iscove NN,Arrowsmith CH, Szentgyorgyi E, Gallinger S, Dick JE, O'Brien CA. Self-renewal as a therapeutic target in human colorectal cancer. Nat Med. 2014 Jan;20(1):29-36.

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