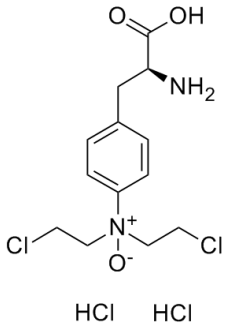
Data Sheet

Product Name:	PX-478
Cat. No.:	HY-10231
CAS No.:	685898-44-6
Molecular Formula:	$C_{13}H_{20}Cl_4N_2O_3$
Molecular Weight:	394.12
Target:	Autophagy; HIF/HIF Prolyl-Hydroxylase
Pathway:	Autophagy; Metabolic Enzyme/Protease
Solubility:	H_2O: ≥ 35 mg/mL



BIOLOGICAL ACTIVITY:

PX-478 is an inhibitor of hypoxia-inducible factor-1α (**HIF-1α**), and is cytotoxic to a variety of cancer cell lines under normoxia and hypoxia in vitro with **IC50** of 20-30 μM.

IC50 & Target: HIF-1α[1]

In Vitro: PC3 and DU 145 cells express HIF-1α protein are treated with PX-478 for 20 hr under normoxia. PC3 cells are more sensitive to PX-478 as compared with DU 145 cells. Densitometric analysis shows that the IC_{50} for HIF-1α inhibition for PC3 cells under normoxic condition is 20-25 μM, whereas the IC_{50} for HIF-1α inhibition for the DU 145 cells is 40-50 μM. PC3 and DU 145 cells are treated with different concentrations of PX-478 (10, 20, 30, 40, 50, and 60 μM) for 18-20 hr under normoxia or hypoxia. Under normoxia, PC3 cells are more sensitive to PX-478 than DU 145 cells. IC_{50} for clonogenic survival (n=3) is 17 μM for PC3 cells and 35 μM for DU 145 cells. When cells are treated with the drug under hypoxic condition for 18 hr, the IC_{50} is 16 μM for PC3 cells and 22 μM for DU 145 cells. Thus DU 145 cells are more sensitive to PX-478 under hypoxic condition[1].

In Vivo: PX-478 is administered to mice with congenital HO (*Nfatc1-Cre/caACVR1$^{fl/fl}$*) every other day starting from birth for 2 wk. Treated mice have significantly less ectopic bone at the ankle joints compared with mutant mice treated with vehicle (6.8 mm^3 vs. 2.2 mm^3, $P<0.01$)[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: PX-478 is prepared as a 10 mM stock in distilled water and used immediately[1].[1]To determine the effect of PX-478 in combination with radiation, cells are treated with PX-478 for 24 hr under normoxic condition, irradiated and plated after 1 hr. Colonies are stained with crystal violet after 12 days and the colonies of >50 cells are counted. For combination treatments, net survival is calculated by correcting the toxicity of PX-478 alone. Enhancement factor (EF) is calculated by dividing the dose of radiation required to reduce plating efficiency to 10% when cells are treated with radiation alone by the dose of radiation required to reduce plating efficiency to 10% when cells are treated with PX-478 and radiation[1]. **Animal Administration:** PX-478 is prepared in PBS solution[2].[2]

Mice[2]

Burn/tenotomy or hybrid HO mice are administered PX-478 (100 mg/kg) or Rapamycin (5 mg/kg) in PBS solution via intraperitoneal injection. Mice receive injections every other day for the duration of the study. *Nfatc1-Cre/caACVR1$^{fl/wt}$* mice are administered PX-478 (100 mg/kg) every other day for a total of 2 wk.

References:

[1]. Palayoor ST, et al. PX-478, an inhibitor of hypoxia-inducible factor-1alpha, enhances radiosensitivity of prostate carcinoma cells. Int J Cancer. 2008 Nov 15;123(10):2430-2437.

[2]. Agarwal S, et al. Inhibition of Hif1α prevents both trauma-induced and genetic heterotopic ossification. Proc Natl Acad Sci U S A. 2016 Jan 19;

113(3):E338-47.

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