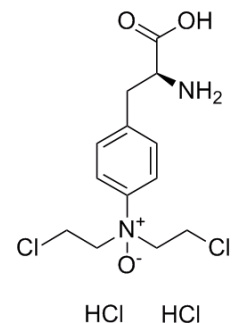


Data Sheet

Product Name:	PX-478
Cat. No.:	HY-10231
CAS No.:	685898-44-6
Molecular Formula:	C ₁₃ H ₂₀ Cl ₄ N ₂ O ₃
Molecular Weight:	394.12
Target:	Autophagy; HIF/HIF Prolyl-Hydroxylase
Pathway:	Autophagy; Metabolic Enzyme/Protease
Solubility:	H ₂ O: ≥ 35 mg/mL



BIOLOGICAL ACTIVITY:

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

IC₅₀ & Target: HIF-1 α ^[1]

In Vitro: PC3 and DU 145 cells express HIF-1 α 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 IC₅₀ for HIF-1 α inhibition for PC3 cells under normoxic condition is 20-25 μ M, whereas the IC₅₀ for HIF-1 α inhibition for the DU 145 cells is 40-50 μ M. PC3 and DU 145 cells are treated with different concentrations of PX-478 (10, 20, 30, 40, 50, and 60 μ M) for 18-20 hr under normoxia or hypoxia. Under normoxia, PC3 cells are more sensitive to PX-478 than DU 145 cells. IC₅₀ for clonogenic survival (n=3) is 17 μ M for PC3 cells and 35 μ M for DU 145 cells. When cells are treated with the drug under hypoxic condition for 18 hr, the IC₅₀ is 16 μ M for PC3 cells and 22 μ M 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 mm³ vs. 2.2 mm³, 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-1 α , enhances radiosensitivity of prostate carcinoma cells. *Int J Cancer*. 2008 Nov 15;123(10):2430-2437.

[2]. Agarwal S, et al. Inhibition of Hif1 α prevents both trauma-induced and genetic heterotopic ossification. *Proc Natl Acad Sci U S A*. 2016 Jan 19;

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

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