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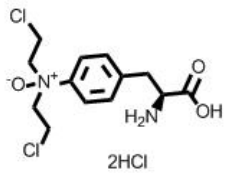
Hypoxia-inducible Factor-1α (HIF-1α) Inhibitor PX-478

Chemical Name: 4-[bis(2-chloroethyl)oxidoamino]-L-phenylalanine hydrochloride



Molecular Weight:	394.12
Formula:	$C_{13}H_{20}Cl_4N_2O_3$
Purity:	≥98%
CAS#:	685898-44-6
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

PX-478 is a highly potent and selective Hypoxia-inducible Factor-1α (HIF-1α) inhibitor. It lowers HIF-1α protein levels and HIF-1 transactivation in hypoxia and in normoxia in a variety of cancer cell lines, but has a more pronounced effect on translation of proteins, such as HIF-1α in hypoxia. PX-478 also enhances the radiosensitivity of prostate carcinoma PC3 cells. Its inhibition is independent of the tumor suppressor genes VHL and p53, and may be related to derangements in glucose uptake and metabolism due to inhibition of glucose transporter-1 (Glut-1). PX-478 has excellent activity against established human tumor xenografts, inducing tumor regressions with prolonged growth delays which correlate positively with HIF-1 levels. In high-fat-diet mice, PX-478 causes reduced fibrosis and fewer inflammatory infiltrates in their adipose tissues. Currently it is in phase I clinical trials for cancer patients.

How to Use:

In vitro: PX-478 was used at 1-10 μM final concentration in various in vitro assays. It is found to be not stable at basic buffer, and stable in acidic buffer.

In vivo: PX-478 was dosed to mice bearing tumor via IP injection or oral gavage at 100-120 mg/kg once per day. Formulation is 0.9% NaCl. Xenografts models are MCF-7 human breast cancer, HT-29 colon cancer, PC-3 prostate cancer, DU-145 prostate cancer, OvCar-3 ovarian cancer, A-549 non-small cell lung cancer, SHP-77 small cell lung cancer, and Caki-1 renal cancer, Panc-1, MiaPaCa, or BxPC-3 pancreatic cancer.

Reference:

1. Welsh S, et al. Antitumor activity and pharmacodynamic properties of PX-478, an inhibitor of hypoxia-inducible factor-1alpha. (2004) Mol Cancer Ther. 3(3):233-44.
2. Koh MY, et al. Molecular mechanisms for the activity of PX-478, an antitumor inhibitor of the hypoxia-inducible factor-1alpha. (2008) Mol Cancer Ther. 7(1):90-100.
3. Palayoor ST, et al. PX-478, an inhibitor of hypoxia-inducible factor-1alpha, enhances radiosensitivity of prostate carcinoma cells. (2008) Int J Cancer. 123(10):2430-7.
4. Sun K, et al. Selective inhibition of hypoxia-inducible factor 1α ameliorates adipose tissue dysfunction. (2013) Mol Cell Biol. 33(5):904-17.