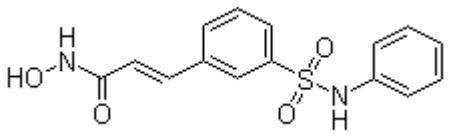
Product Introduction

Belinostat (PXD101)

Belinostat (PXD101) is a novel **HDAC** inhibitor with **IC50** of 27 nM, with activity demonstrated in cisplatin-resistant tumors. Phase 1/2.

Technical Data:

Molecular Weight (MW):	318.35	
Formula:	$C_{15}H_{14}N_2O_4S$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 64 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	414864-00-9	

Biological Activity

Belinostat inhibits the growth of tumor cells (A2780, HCT116, HT29, WIL, CALU-3, MCF7, PC3 and HS852) with IC50 from 0.2-0.66 μM. PD101 shows low activity in A2780/cp70 and 2780AD cells, which are cisplatin and doxorubicin-resistant derivatives of A2780 cells. Belinostat could induce apoptosis through PARP cleavage and acetylation of histones H3/H4. [1] Belinostat inhibits bladder cancer cell growth, especially in 5637 cells, which shows accumulation of G0-G1 phase, decrease in S phase and increase in G2-M phase. [2] The growth inhibitory activity of belinostat on cell lines is not strongly influenced by the

multidrug-resistant phenotype, whereas the activity of docetaxel is clearly affected. Belinostat could enhance the growth inhibitory activity of docetaxel or carboplatin in OVCAR-3 and A2780 cells. Belinostat also shows enhanced tubulin acetylation in ovarian cancer cell lines. [3] A recent study shows that Belinostat activates protein kinase A in a TGF-β signaling-dependent mechanism and decreases survivin mRNA. [4]

Belinostat indicates significant tumor growth delay in A2780 and A2780/cp70 xenograft at a dose of 10mg/kg with no effects on the body weight. [1] Belinostat also induces p21WAF1, HDAC core and cell communication genes in mouse bladder tumors. [2] Belinostat monotherapy induces dose-proportional antitumor effects with TGI of 47% at a dose of 100mg/kg in A2780 xenograft. The combination of Belinostat (100 mg/kg) with carboplatin (40 mg/kg) could delay tumor growth from 18.6 days to 22.5 days. [3] Combining with bortezomib, Belinostat results in great tumor inhibition and gastrointestinal toxicity in mice with bortezomib-resistant UMSCC-11A xenograft. [5]

Lead compound of Topotarget.

References

[1] Plumb JA, et al. Mol Cancer Ther, 2003, 2(8), 721-728.

[2] Buckley MT, et al. J Transl Med, 2007, 5:49.

[3] Qian X, et al. Mol Cancer Ther, 2006, 5(8), 2086-2095.

[4] Chowdhury S, et al. J Biol Chem, 2011, 286(35), 30937-30948.

[5] Duan J, et al. Mol Cancer Ther, 2007, 6(1), 37-50.

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