



EPZ-6438

货号: E3909

储存条件: 粉末-20°C可保存3年; 液体-80°C可保存12月。

产品描述

EZH2 is the enzymatically active core subunit of the PRC2 complex, which methylates H3K27 and facilitates chromatin compaction and gene silencing. EPZ-6438 is a potent and selective inhibitor of EZH2 with K_i value of 2.5 ± 0.5 nM (measured by competition with SAM), with selectivity >4,500-fold over 14 other HMTs, 35-fold over EZH1. Similar potency can be observed for EZH2 proteins bearing all known lymphoma change-of-function mutations. Treatment with EPZ-6438 (6 - 1100 nM) for 4 days caused specific concentration-dependent reductions in global H3K27Me3 levels in a panel of SMARCB1-deficient MRT cells and SMARCB1 wild-type control cells. And this specific inhibition on cellular H3K27 methylation led to selective apoptotic killing of SMARCB1 mutant MRT cells with IC50 values in the nanomolar range. EPZ-6438 (1 μ M) treatment of G401 SMARCB1-deleted cells for up to 7 days strongly induced expression of CD133, DOCK4 and PTPRK (genes important for neuronal differentiation) and up-regulated cell cycle inhibitors CDKN1A, CDKN2A and tumor suppressor BIN1, all in a time-dependent manner, as well as down-regulated the expression of hedgehog pathway genes MYC and EZH2. Oral treatment of EPZ-6438 on dose of 125, 250 and 500 mg/kg, twice daily, for 21 days induced tumor regressions in SCID mice bearing s.c. G401 xenografts. Correlating with the antitumor activity, tumors that were harvested from subsets of mice from each group on day 21 showed strong inhibition of H3K27Me3. Up to now, phase 2 studies of EPZ-6438 on treatment for Diffuse Large B-cell Lymphoma, Rhabdoid Tumors, Relapsed or Refractory B-cell Non-Hodgkin's Lymphoma, Advanced Malignant Solid Neoplasm, etc., are recruiting (see <https://clinicaltrials.gov/>).

作用机制

EPZ-6438 inhibits EZH2 in a manner competitive with the substrate S-adenosylmethionine (SAM) binding to EZH2.

产品信息

CAS号	1403254-99-8	
分子式	Ca4H44N4O4	
分子量	572.74	
别名	E 7438;Tazemetostat	
溶解度	DMSO	4.25 mg/mL (7.4 mM)
	Water	insoluble

