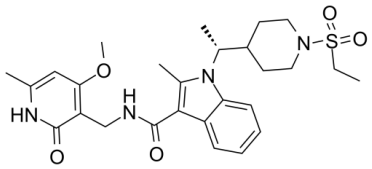
Data Sheet

Product Name:	CPI-169
Cat. No.:	CS-3174
CAS No.:	1802175-07-0
Molecular Formula:	C27H36N4O5S
Molecular Weight:	528.66
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Solubility:	DMSO : ≥ 59 mg/mL (111.60 mM)



BIOLOGICAL ACTIVITY:

CPI-169 (CPI 169 R-enantiomer) is a novel and potent **EZH2** inhibitor, with **IC_{50}**s of 0.24 nM, 0.51 nM, and 6.1 nM for EZH2 WT, EZH2 Y641N, and EZH1, respectively. IC50 & Target: IC50: 0.24 nM (EZH2 WT), 0.51 nM (EZH2 Y641N), 6.1 nM (EZH1) **In Vitro:** CPI-169 (CPI 169 R-enantiomer) inhibits the catalytic activity of PRC2 with an IC_{50} of < 1nM, decreases cellular levels of H3K27me3 with an EC_{50} of 70 nM, and triggers cell cycle arrest and apoptosis in a variety of cell lines[1]. In KARPAS-422 cells, CPI-169 shows a dose-dependent inhibitory effect on cell viability, and produces synergy anti-proliferative activity when used in combination with ABT-199. In 16 out of 25 NHL cell lines, CPI-169 also suppresses cell growth with GI_{50} of <5 μM[2]. **In Vivo:** CPI-169 (CPI 169 R-enantiomer) (200 mpk, s.c. BID) is well tolerated in mice with no observed toxic effect or body weight loss. CPI-169 treatment leads to tumor growth inhibition (TGI) of an EZH2 mutant KARPAS-422 DLBCL xenograft. CPI-169 (100 mpk, BID) with a single dose of CHOP leads tumors to rapidly regress and become unpalpable[1]. In mice bearing KARPAS-422 xenografts, CPI-169 (200 mg/kg, s.c.) effectively suppresses H3K27me3 levels and results in lymphoma tumor regression without affecting body weight or causing any overt adverse effects[2].

PROTOCOL (Extracted from published papers and Only for reference)

Animal administration [2] Administered subcutaneously at 200 mpk twice daily (BID), CPI-169 is well tolerated in mice with no observed toxic effect or body weight loss. In the present study we show that CPI-169 treatment led to tumor growth inhibition (TGI) of an EZH2 mutant KARPAS-422 DLBCL xenograft. The TGI is proportional to the dose administered and to the reduction of the pharmacodynamic marker H3K27me3. The highest dose, 200 mpk, BID led to complete tumor regression.

References:

[1]. Vidya Balasubramanian, et al. CPI-169, a novel and potent EZH2 inhibitor, synergizes with CHOP in vivoand achieves complete regression in lymphoma xenograft models. Cancer Res October 1, 2014 74; 1697

[2]. Bradley WD, et al. EZH2 inhibitor efficacy in non-Hodgkin's lymphoma does not require suppression of H3K27 monomethylation. Chem Biol. 2014 Nov 20;21(11):1463-75

CAIndexNames:

(R)-1-(1-(1-(ethylsulfonyl)piperidin-4-yl)ethyl)-N-((4-methoxy-6-methyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-methyl-1H-indole-3-carboxamide

SMILES:

CC(N1)=CC(OC)=C(CNC(C2=C(C)N([C@H](C)C3CCN(S(=O)(CC)=O)CC3)C4=CC=CC=C24)=O)C1=O

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

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