



SNS-032

货号: S2377

储存条件: 粉末避光 2-8°C; 液体 -20°C:3-6 月, -80°C:12 月

产品描述

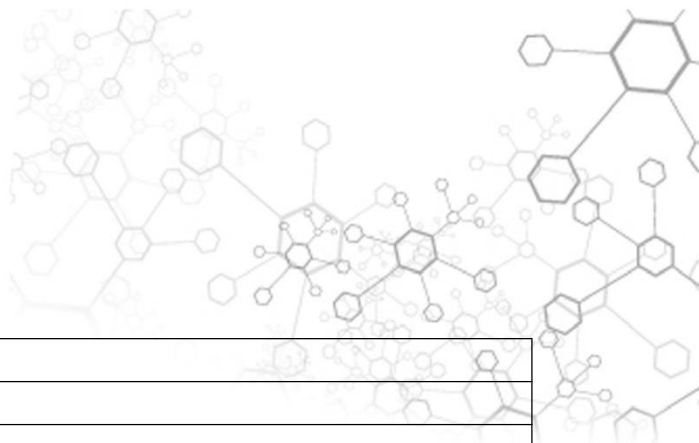
The CDKs (cyclin dependent kinases), as direct regulators of specific phases of the cell cycle, can control cellular proliferation and transcription with their activating cyclin partners and subunit inhibitors. Thus, the molecular events that distinguish the activities of CDKs can be leveraged as pharmacodynamics biomarkers for activity of the CDKs. For example, CDK2 inhibition can be assessed by increased level of cyclin E, decreased level of Cdc6 or phosphorylation of Rb. Decreased phosphorylation of pSer5 and pSer2 of RNA pol II CTD would indicate inhibition of CDKs 7 and 9, respectively. SNS-032 (BMS-387032) is a selective inhibitor of CDK2/Cyclin A, CDK2/Cyclin E, CDK7/Cyclin H and CDK9/Cyclin T with IC50 values of 38, 48, 62 and 4 nM (measured by enzymatic activity assay), respectively, with modest inhibitory activity against CDK5/p35, CDK1/Cyclin B and CDK4/Cyclin D with IC50 values of 340, 480 and 925 nM. After exposure to 0.03 - 3 μ M SNS-032, stabilization of cyclin E can be observed by 4h and persisted for at least 2h post-washout of SNS-032 in RPMI-8226 cells, accompanied with decrease in Cdc6 at 4h. Cellular IC50 values of 231 nM and 192 nM for SNS-032 for 16h were identified for inhibition of CDK7 and CDK9, which was read out by phosphorylation of Ser5 and Ser2 of RNA Pol II CTD, in RPMI-8226 MM cells. 300 nM SNS-032 for up to 6h showed both decrease of pSer2 RNA Pol II-CTD and increase in cleaved PARP. Treatment with 300 nM SNS-032 for 24h caused arrested cell cycle progression at G2/M in asynchronous HCT116 cells. Exposure with 0.3 μ M SNS-032 for 6 hours can significant decrease the mRNA and protein level of Mcl-1 and XIAP, the antiapoptotic proteins, in CLL cells from the same set of 6 patients. Treatment with 15 mg/kg SNS-032 intraperitoneally every 2 days for about 2 weeks can inhibit the growth of xenografts, BaF3-T674I FIP1L1-PDGFR α or KBM5-T315I cells, in nude mice. Up to now, a phase 1 study of SNS-032 treatment for B-lymphoid malignancies, chronic lymphocytic leukemia, mantle cell lymphoma and multiple myeloma has been completed (see in <https://www.clinicaltrials.gov/>).

作用机制

SNS-032 can compete with ATP-binding pocket to CDK7 and 9.

	质量	1 mg	5 mg	10 mg
储存液制备	1 mM	2.6279mL	13.1396 mL	26.2791 mL
	5 mM	0.5256 mL	2.6279 mL	5.2558 mL
	10 mM	0.2628 mL	1.3140 mL	2.6279 mL





产品性质

CAS 号	345627-80-7	
分子式	$C_{17}H_{24}N_4O_2S_2$	
分子量	380.53	
溶解度	DMSO	70.0 mg/mL (184.0 mM)
	Water/Ethanol	insoluble

