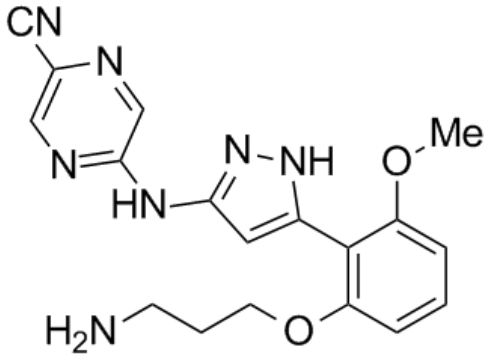
Product Data Sheet

Product Name: LY2606368
Cat. No.: GC15663

Chemical Properties

Cas. No.	1234015-52-1		
Chemical Name	(Z)-5-((5-(2-(3-aminopropoxy)-6-methoxyphenyl)-1H-pyrazol-3(2H)-ylidene)amino)pyrazine-2-carbonitrile		
Formula	C18H19N7O2	M.Wt	365.39
Solubility	<0.73mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Kinase experiment [1]:

Preparation Method Purified CHK1 was incubated with LY2606368 and substrate was added to detect whether LY2606368 was inhibited.

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Reaction Conditions	10^{-6}-10nM LY2606368
Applications	LY2606368 is an ATP-competitive protein kinase inhibitor with a Ki of 0.9 nmol/L against purified CHK1.

Cell experiment [2]:

Cell lines	HeLa cells
Preparation Method	Cells were treated with LY2606368 for 7 hours and stained for evidence of DNA DSB using both TUNEL and an antibody for H2AX phosphorylated on serine 139.
Reaction Conditions	33 nmol/L LY2606368 for 7 hours
Applications	LY2606368 triggered S-phase DNA damage, such as pH2AX (S139) and TUNEL positive staining cells significantly increased in S-phase cells. LY2606368 also requires CDC25A and CDK2 to trigger DNA damage. In addition, LY2606368 causes replication catastrophe.

Animal experiment [3]:

Animal models	Female CD-1nu-/nu mice carrying CALU-6 tumors (26-28 g)
Preparation Method	Vehicle consisting of 20% Captisol (CyDex Inc) pH4 or LY2606368 was administered by subcutaneous injection in a volume of 200 ml(10 mmol/L). 4,8, 12, 24, and 48 hours after drug administration, blood for plasma drug exposure was extracted

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Dosage form	1, 3.3, or 10 mg/kg LY2606368 twice daily for 2 days
Applications	Up to 72.3% inhibition of tumor growth was observed in the three doses of LY2606368 tested, and mice lost no more than 3% of their body weight, indicating that LY2606368 was well tolerated in any treatment group. In addition, tumor regrowth was slow in the highest dose group during the 28-day recovery period, indicating a durable tumor response to LY2606368.

References:

[1]. King C, Diaz HB, et,al. LY2606368 Causes Replication Catastrophe and Antitumor Effects through CHK1-Dependent Mechanisms. Mol Cancer Ther. 2015 Sep;14(9):2004-13. doi: 10.1158/1535-7163.MCT-14-1037. Epub 2015 Jul 3. PMID: 26141948.

Background

LY2606368 is a novel selective ATP-competitive second-generation cell cycle checkpoint kinase 1 (CHK1) inhibitor (Ki=0.9nM; IC_{50}≤1nM). LY2606368 inhibits CHK1 activity to release the protective effect of DNA damage checkpoints. LY2606368 reduces the stability of the CDC25A-CDK2 pathway, leading to double-strand DNA breaks and replication catastrophe, thereby causing tumor cell death. LY2606368 enhances the cytotoxicity of DNA-damaging agents and reverses chemotherapy resistance. LY2606368 can be used in research related to solid tumors such as small cell lung cancer, ovarian cancer, breast cancer, and prostate cancer[1-4].

In vitro, LY2606368 (1.7–100nM) was used to treat KHOS-240S, SAOS-2, OSRH-2011/5, and OSKG osteosarcoma cells for 24–48h. LY2606368 significantly reduced clonogenic survival, induced apoptosis, and upregulated γH2AX, indicating double-strand DNA breaks[5]. LY2606368 (1–1000nM) was applied to treat various tumor cells including AsPC-1, SW620, MDA-MB-231, and H322M for 6–48h. LY2606368 caused growth inhibition and cell death[6].

In vivo, LY2606368 (10mg/kg; every 12h) was injected subcutaneously into NSG mice bearing B-ALL patient-derived xenograft (PDX) models. The treatment lasted for 3 consecutive days followed by 4

days off, and this cycle was repeated for 4–5 weeks. LY2606368 significantly prolonged the median survival of B-ALL PDX mice[7]. LY2606368 (single dose of 15mg/kg, or 1-10mg/kg; 3 days on/4 days off; 3 cycles) was injected subcutaneously into CD-1 nu/nu mice bearing Calu-6 xenografts. LY2606368 significantly inhibited CHK1(S296) autophosphorylation in tumor tissues and induced DNA damage. In the multiple-dose regimen, LY2606368 significantly suppressed tumor growth[8].

References:

[1] Konstantinopoulos PA, Lee JM, Gao B, et al. A Phase 2 study of prexasertib (LY2606368) in platinum resistant or refractory recurrent ovarian cancer. Gynecol Oncol. 2022 Nov;167(2):213-225.
[2] Yin Y, Shen Q, Zhang P, et al. Chk1 inhibition potentiates the therapeutic efficacy of PARP inhibitor BMN673 in gastric cancer. Am J Cancer Res. 2017 Mar 1;7(3):473-483.
[3] Sarchi M, Clough CA, Crosse EI, et al. Mis-splicing of Mitotic Regulators Sensitizes SF3B1-Mutated Human HSCs to CHK1 Inhibition. Blood Cancer Discov. 2024 Sep 3;5(5):353-370.
[4] Fu Y, Kang X, Li W, et al. The low-dose CHK1 inhibitor prexasertib triggers VDAC1 dephosphorylation to activate mtDNA-STING signaling and synergize immunotherapy. Cell Rep. 2025 May 27;44(5):115605.
[5] Heidler CL, Roth EK, Thiemann M, et al. Prexasertib (LY2606368) reduces clonogenic survival by inducing apoptosis in primary patient-derived osteosarcoma cells and synergizes with cisplatin and talazoparib. Int J Cancer. 2020 Aug 15;147(4):1059-1070.
[6] Ditano JP, Eastman A. Comparative Activity and Off-Target Effects in Cells of the CHK1 Inhibitors MK-8776, SRA737, and LY2606368. ACS Pharmacol Transl Sci. 2021 Feb 12;4(2):730-743.
[7] Ostergaard J, Jonart LM, Ebadi M, et al. Preclinical efficacy of prexasertib in acute lymphoblastic leukemia. Br J Haematol. 2021 Sep;194(6):1094-1098.
[8] King C, Diaz HB, McNeely S, et al. LY2606368 Causes Replication Catastrophe and Antitumor Effects through CHK1-Dependent Mechanisms. Mol Cancer Ther. 2015 Sep;14(9):2004-13.

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