LY2409881 trihydrochloride

Cat. No.: HY-B0788A

CAS No.: 946518-60-1

Molecular Formula: $C_{24}H_{32}Cl_4N_6OS$

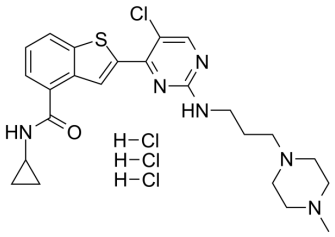
Molecular Weight: 594.43

Target: IKK; Apoptosis

Pathway: NF-κB; Apoptosis

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 14.29 mg/mL (24.04 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6823 mL	8.4114 mL	16.8228 mL
5 mM	0.3365 mL	1.6823 mL	3.3646 mL
10 mM	0.1682 mL	0.8411 mL	1.6823 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 20% SBE-β-CD in saline
   Solubility: 35 mg/mL (58.88 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.43 mg/mL (2.41 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.43 mg/mL (2.41 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.43 mg/mL (2.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LY2409881 trihydrochloride is a selective IκB kinase β (IKK2) inhibitor with an IC_{50} of 30 nM.

IC_{50} & Target

IKK2

30 nM (IC_{50})

In Vitro

LY2409881 is an IKK2 inhibitor that inhibits TNFα-induced activation of NF-κB. By in vitro kinase assay, LY2409881 potently

	inhibits IKK2, with an IC_{50} of 30 nM. In contrast, the IC_{50} for IKK1 and other common kinases is at least one log higher. The specificity of LY2409881 for NF-κB signaling is further studied in a cell-based assay, by examining the effect of LY2409881 in the TNFα-dependent antiapoptosis function. TNFα is a well-characterized upstream stimulus of NF-κB. In the ovarian cancer cell line SKOV3, LY2409881 demonstrates moderate cytotoxicity, whereas TNFα at 10 ng/mL does not cause any cytotoxicity. In contrast, coadministration of LY2409881 and TNFα results in markedly higher cell killing compared with LY2409881. This is because TNFα-dependent activation of antiapoptotic signals mediated by NF-κB is blocked by LY2409881, while the proapoptotic TNF receptor-associated death domain (TRADD) and FAS-associated death domain (FADD) cascade pathways activated by TNFα are not affected by LY2409881[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	A well-established xenograft model of DLBCL is used to confirm the activity of LY2409881 in vivo. SCID-beige mice implanted with LY10 cell-derived tumors are given intraperitoneal injections of LY2409881 twice weekly at three different doses: 50, 100, and 200 mg/kg. The treatments are well tolerated, resulting in no death or severe morbidity of the mice. The average tumor volume is graphed as a function of time for each treatment group. The rates of tumor volume growth of the treatment groups are all significantly slower than the untreated control group ($P \leq 0.01$)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	OCI-Ly1, OCI-Ly7, and Su-DHL4 are GCB DLBCL cell lines; OCI-Ly3, OCI-Ly10, HBL1, and Su-DHL2 are ABC DLBCL lines. These cell lines are grown in Iscove Modified Dulbecco Medium with 10% FCS. Fresh medium is added every 2 to 3 days, and the cells are kept at a cell concentration of 0.1 to 1×10^6/mL. Cytotoxicity is evaluated using the CellTiter-Glo Reagent. Experiments are carried out in 96-well plates, with each treatment in triplicate. Samples are taken at typically 24, 48, and 72 hours after treatment. Cytotoxicity is expressed by the decreasing percentage of live cells in each treatment (LY2409881; 0.01, 0.1, 1 and 10 μM) relative to the untreated control from the same experiment, as a function of time. IC_{50} for each cell line is calculated using the CalcuSyn Version 2.0 software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Mouse experiments are carried out. Five- to 7-week-old SCID beige mice are injected with 107 Ly10 cells mixed in Matrigel in the posterior flank subcutaneously. When the tumors approach 150 mm^3, the mice are divided into four groups of 8 mice: (i) control group, which receive 5% dextrose in water; (ii) LY2409881 at 50 mg/kg in D5W; (iii) LY2409881 at 100 mg/kg in D5W; and (iv) LY2409881 at 200 mg/kg in D5W. LY2409881 or D5W is administered intraperitoneally on day 1 and 4 of every week for 4 weeks. The data are expressed as average tumor volume (mm3) per group as a function of time. Tumor volume is calculated. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Clin Transl Med. 2022 Jun;12(6):e850.
- Int J Mol Sci. 2023, 24(1), 320.

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REFERENCES

[1]. Deng C, et al. The novel IKK2 inhibitor LY2409881 potently synergizes with histone deacetylase inhibitors in preclinical models of lymphoma through the downregulation of NF-κB. Clin Cancer Res. 2015 Jan 1;21(1):134-45.

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

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