Galunisertib

Cat. No.: HY-13226

CAS No.: 700874-72-2

Molecular Formula: $C_{22}H_{19}N_5O$

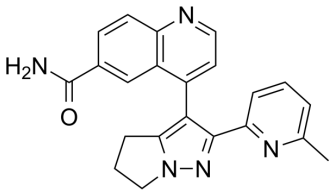
Molecular Weight: 369.42

Target: TGF-β Receptor

Pathway: TGF-beta/Smad

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (270.69 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7069 mL	13.5347 mL	27.0695 mL
5 mM	0.5414 mL	2.7069 mL	5.4139 mL
10 mM	0.2707 mL	1.3535 mL	2.7069 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 5.75 mg/mL (15.56 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.63 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.63 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.63 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Galunisertib (LY2157299) is an oral and selective TGF-β receptor type I (TGF-βRI) kinase inhibitor with an IC_{50} of 56 nM.

IC_{50} & Target

IC50: 56 nM (TGF-βRI)[4]

In Vitro

Galunisertib (LY2157299) (0.1, 1, 10, and 100 μM) displays a slight dose-dependent potentiation of Bay 43-9006 in SK-Sora,

	HepG2, and Hep3B cell lines but not in JHH6, SK-HEP1, and HuH7 cell lines[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Human xenografts Calu6 (non-small cell lung cancer) and MX1 (breast cancer) are implanted subcutaneously in nude mice. After oral administration of 75 mg/kg, Galunisertib (LY2157299) induces a 70% decrease in pSmad for both types of cell lines. The time at which pSmad recovered 80% of baseline is approximately 6 h after administration[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Cell survival is determined using the MTT assay. The conversion of yellow water-soluble tetrazolium MTT into purple insoluble formazan is catalyzed by mitochondrial dehydrogenases and used to estimate the number of viable cells. In brief, cells are seeded in 96-well tissue culture plates at a density of 2×10^3 cells/well. After drug exposure, cells are incubated with 0.4 mg/mL MTT for 4 hours at 37°C. After incubation, the supernatant is discarded, insoluble formazan precipitates are dissolved in 0.1 mL of DMSO, and the absorbance is measured at 560 nm by use of a microplate reader. Wells with untreated cells or with drug-containing medium without cells are used as positive and negative controls respectively. For proliferation assay, MTT assay is done daily to determine the number of viable cells in untreated control andGalunisertib (LY2157299) (0.1, 1, 10, and 10 μM)-treated group[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] Charles River nude mice (weight 25 mg) are used. Galunisertib (LY2157299) is given orally as a single dose or in a multiple dosing design. The value of the dose levels given in a single dose manner is 10 (n=3), 30 (n=8), 50 (n=26), 75 (n=69), 100 (n=3), 150 (n=21) and 300 (n=3) mg/kg. Animals are sacrificed at the following times: 0.5, 1, 1.5, 2, 4, 8 and 16 h after administration, then the tumor is removed and blood is recovered. In the multiple dosing study, Galunisertib (LY2157299) is administered twice a day (bid) at the dose of 75 mg/kg every 12 h for 20 consecutive days to 31 mice. Animals are sacrificed at 2 h after the last administration at days 10, 15, 20 and 25, and the tumor is removed for pSmad determination and the blood is recovered for determination of drug levels in plasma. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Nat Commun. 2024 Feb 14;15(1):1348.
- J Exp Clin Cancer Res. 2023 Oct 3;42(1):258.
- J Exp Clin Cancer Res. 2023 Aug 9;42(1):200.
- Cancer Lett. 2023 Jul 29;216330.

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REFERENCES

[1]. Cong L, et al. Targeting the TGF-β receptor with kinase inhibitors for scleroderma therapy. Arch Pharm (Weinheim). 2014 Sep;347(9):609-15.

[2]. Serova M, et al. Effects of TGF-beta signalling inhibition with galunisertib (LY2157299) in hepatocellular carcinoma models and in ex vivo whole tumor tissue samples from patients. Oncotarget. 2015 Aug 28;6(25):21614-27

[3]. Bueno L, et al. Semi-mechanistic modelling of the tumour growth inhibitory effects of LY2157299, a new type I receptor TGF-beta kinase antagonist, in mice. Eur J

Cancer. 2008 Jan;44(1):142-50.

[4]. Herbertz S, et al. Clinical development of galunisertib (LY2157299 monohydrate), a small molecule inhibitor of transforming growth factor-beta signaling pathway. Drug Des Devel Ther. 2015 Aug 10;9:4479-99.

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