

Product Data Sheet

Product Name: MLN8237 (Alisertib)

Cat. No.: GC12690

Chemical Properties

Cas. No. 1028486-01-2

Chemical Name 4-[[9-chloro-7-(2-fluoro-6-methoxyphenyl)-5H-pyrimido[5,4-d][2]benzazepin-2-yl]amino]-2-methoxybenzoic acid

SMILES COC1=C(C(=CC=C1)F)C2=NCC3=CN=C(N=C3C4=C2C=C(C=C4)Cl)NC5=CC(=C(C=C5)C(=O)O)OC

Formula $C_{27}H_{20}ClFN_4O_4$

M.Wt 518.92

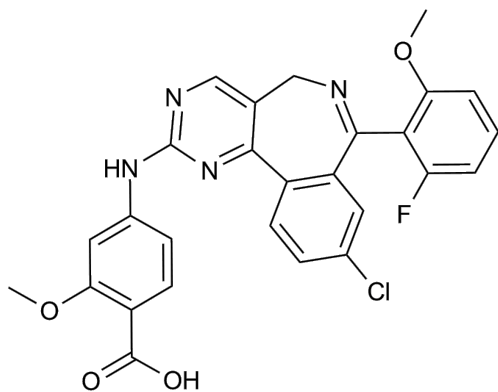
Solubility ≥ 25.9 mg/mL in DMSO

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

Cell experiment [1]:

Cell lines HepG2 and Hep3B cells

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

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Preparation Method Treated HepG2 and Hep3B cells with various concentrations of MLN8237 (7-5000nM) for 48 hours and concentration-survival curves were plotted.

Reaction Conditions 7-5000nM; 48 hours

Applications The results clearly showed that MLN8237 inhibited cell growth in a concentration-dependent manner and cotreated with alisertib significantly enhanced the cytotoxicity of lenvatinib.

Animal experiment [2]:

Animal models MCL SCID mouse xenograft model

Preparation Method There were 6 cohorts of 12 mice: vehicle control, MLN8237 at 10mg/kg and 30mg/kg PO once a day for 3 weeks, docetaxol at 10mg/kg IP once/week×4, MLN8237 at 10mg/kg or 30mg/kg for 3 weeks + docetaxel 10mg/kg once/week×4. MLN8237 doses were chosen based on prior dose finding studies provided by Millennium Pharmaceuticals, while docetaxel dose was based on a clinically relevant dose in mouse xenograft tumor model.

Dosage form 10mg/kg and 30mg/kg; p.o.; 3 weeks

Applications Both combination treatments with docetaxel significantly increased survival over single agent treatments using MLN8237 (10mg/kg and 30mg/kg), and high MLN8237 + docetaxel combination treatment increased survival over single agent treatment with docetaxel.

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References:

[1] Hao J, et al. Antitumor Effect of Lenvatinib Combined with Alisertib in Hepatocellular Carcinoma by Targeting the DNA Damage Pathway. Biomed Res Int. 2021 Jul 22;2021:6613439.

[2] Qi W, et al. Aurora inhibitor MLN8237 in combination with docetaxel enhances apoptosis and anti-tumor activity in mantle cell lymphoma. Biochem Pharmacol. 2011 Apr 1;81(7):881-90.

Background

MLN8237 (Alisertib), as an investigational, orally available, selective aurora A kinase inhibitor, is usually used for the treatment of solid tumors and hematologic malignancies^[1].

In vitro, MLN8237 (0.001-10 μ M; 72h) dose-dependently inhibited the proliferation of leukemia MOLT-4, neuroblastoma IMR-32, and medulloblastoma Daoy cell lines, with IC₅₀ values of 0.02, 0.03, and 0.04 μ M, respectively^[2]. MLN8237 was effective against both Ewing sarcoma and neuroblastoma cell lines with IC₅₀ values of 32nM and 37nM, respectively^[4]. MLN8237 (0.01-50 μ M; 24h) dose-dependently inhibited the proliferation of U-2 OS cells and MG-63 cells with IC₅₀ of 16.6 μ M and 9.5 μ M, respectively^[5]. MLN8237 had aggressive inhibition against B-NHL cell proliferation with an IC₅₀ of 10-50nM and induced apoptosis with a dose- and time-dependent manner^[6].

In vivo, MLN8237 (30mg/kg; i.p.; every 3 days for 4 consecutive weeks) significantly inhibited tumor growth in nude mice bearing Hep3B xenografts^[3]. MLN8237 (30mg/kg/d; p.o.; 21d) markedly reduced tumor burden and increased overall survival in MM.1S cell xenograft-bearing mice^[7].

References:

[1] Pusalkar S, et al. Biotransformation Pathways and Metabolite Profiles of Oral [14C]Alisertib (MLN8237), an Investigational Aurora A Kinase Inhibitor, in Patients with Advanced Solid Tumors. Drug Metab Dispos. 2020 Mar;48(3):217-229.

[2] Muscal JA, et al. Additive effects of vorinostat and MLN8237 in pediatric leukemia,

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medulloblastoma, and neuroblastoma cell lines. Invest New Drugs. 2013 Feb;31(1):39-45.

[3] Hao J, et al. Antitumor Effect of Lenvatinib Combined with Alistertib in Hepatocellular Carcinoma by Targeting the DNA Damage Pathway. Biomed Res Int. 2021 Jul 22;2021:6613439.

[4] Carol H, et al. Efficacy and pharmacokinetic/pharmacodynamic evaluation of the Aurora kinase A inhibitor MLN8237 against preclinical models of pediatric cancer. Cancer Chemother Pharmacol. 2011 Nov;68(5):1291-304.

[5] Niu NK, et al. Pro-apoptotic and pro-autophagic effects of the Aurora kinase A inhibitor alisertib (MLN8237) on human osteosarcoma U-2 OS and MG-63 cells through the activation of mitochondria-mediated pathway and inhibition of p38 MAPK/PI3K/Akt/mTOR signaling pathway. Drug Des Devel Ther. 2015 Mar 12;9:1555-84.

[6] Qi W, et al. Aurora inhibitor MLN8237 in combination with docetaxel enhances apoptosis and anti-tumor activity in mantle cell lymphoma. Biochem Pharmacol. 2011 Apr 1;81(7):881-90.

[7] Görgün G, Calabrese E, Hideshima T, et al. A novel Aurora-A kinase inhibitor MLN8237 induces cytotoxicity and cell-cycle arrest in multiple myeloma. *Blood*. 2010;115(25):5202-5213.

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