

Product Data Sheet

Product Name: LY2801653 (Merestinib)

Cat. No.: GC11057

Chemical Properties

Cas. No. 1206799-15-6

Chemical Name N-[3-fluoro-4-[1-methyl-6-(1H-pyrazol-4-yl)indazol-5-yl]oxyphenyl]-1-(4-fluorophenyl)-6-methyl-2-oxopyridine-3-carboxamide

SMILES CC1=CC=C(C(=O)N1C2=CC=C(C=C2)F)C(=O)NC3=CC(=C(C=C3)OC4=C(C=C5C(=C4)C=NN5C)C6=CN=C6)F

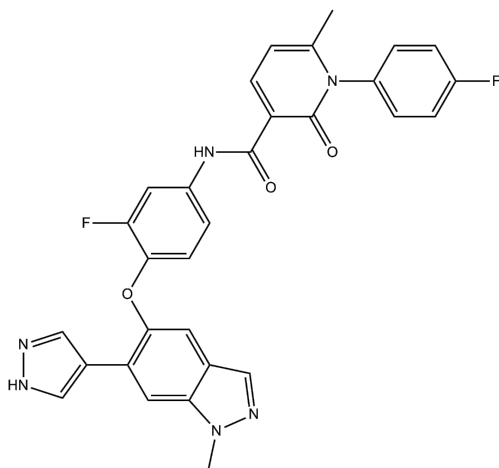
Formula $C_{30}H_{22}F_2N_6O_3$ M.Wt 552.53

Solubility ≥ 27.65 mg/mL in DMSO, ≥ 5.02 mg/mL in EtOH with ultrasonic and warming 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]:

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Cell lines	MKN45 cells
Preparation Method	MKN45 cells were cultured in RPMI 1640 medium, supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin, at 37°C in an incubator with 5% CO ₂ . Cells were seeded in a 96-well plate at a density of 5000 cells/well. After seeding, cells were treated with vehicle or serial dilutions of LY2801653 (0, 10, 20, 50, 100, and 500nM) for 72h, cell viability was measured.
Reaction Conditions	0, 10, 20, 50, 100, and 500nM; 72h
Applications	LY2801653 treatment markedly decreased the cell viability of MKN45 cells in a dose-dependent manner.
Animal experiment [2]:	
Animal models	Female athymic nude mice
Preparation Method	Female athymic nude mice (8 weeks old; 22-25g) were housed under controlled conditions with a relative humidity of 55%±5%, room temperature maintained at 23°C-24°C, and a 12h light/dark cycle. Food and water were provided ad libitum. Hs746t cells were expanded in culture, harvested, and washed in HBSS. Approximately 5×10 ⁶ cells in HBSS were implanted subcutaneously into the hind flank of each mouse. LY2801653 was formulated as a solution in 10% PEG 400/90%, and was dosed once daily orally (12mg/kg) in mice when tumors were an average size of 150mm ³ . After 21 days, tumor burden was measured.
Dosage form	12mg/kg/day; 21 days; p.o.

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Applications	LY2801653 treatment inhibited tumor growth in mice with Hs746t xenografts.
References:[1] Zhu C, Shi H, Wu M, et al. A dual MET/AXL small-molecule inhibitor exerts efficacy against gastric carcinoma through killing cancer cells as well as modulating tumor microenvironment[J]. MedComm, 2020, 1(1): 103-118.[2] Yan S B, Um S L, Peek V L, et al. MET-targeting antibody (emibetuzumab) and kinase inhibitor (merestinib) as single agent or in combination in a cancer model bearing MET exon 14 skipping[J]. Investigational new drugs, 2018, 36(4): 536-544.	

Background

LY2801653 (Merestinib) is a potent, orally bioavailable c-Met inhibitor ($IC_{50}=4.7nM$; K_i value= $2nM$), with K_D values of $20nM$, $92nM$, and $54nM$ for NTRK1, NTRK2, and NTRK3, respectively [1].

LY2801653 inhibits MET activity by stabilizing the inactive DFG-out conformation, suppresses MET-dependent tumor cell proliferation and migration/dissemination, and induces vascular normalization in xenograft tumors[2]. LY2801653 has been widely used to block Mnk kinase activity in acute myeloid leukemia cells and restrain leukemic progenitors[3].

In vitro, LY2801653 treatment for 72 hours significantly inhibited the viability of A549, H1703, and H1993 cells, with IC_{50} values of $627.6nM$, $72.9nM$, and $9.28nM$, respectively[4]. Incubation of MET-overexpressing MKN45 cells with $50nM$ LY2801653 for 72 hours suppressed proliferation, accompanied by increased cleaved caspase-3 levels and decreased levels of Cyclin A2, Cyclin D1, and MCL-1[5]. $10\mu M$ of LY2801653 pretreatment for 1 hour effectively blocked the apoptosis induced by elesclomol- $CuCl_2$ (ES-Cu) in HT-22 cells and reduced the level of reactive oxygen species (ROS)[6].

In vivo, LY2801653 treatment via oral administration at a dose of $12mg/kg$ daily for 5 weeks significantly inhibited tumor growth in the A549 xenograft mouse model[7]. Oral administration of LY2801653 at a dose of $12mg/kg/day$ for 21 consecutive days induced tumor regression in the Hs746t xenograft tumor model[8].

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- [1] Konicek B W, Capen A R, Credille K M, et al. Merestinib (LY2801653) inhibits neurotrophic receptor kinase (NTRK) and suppresses growth of NTRK fusion bearing tumors[J]. *Oncotarget*, 2018, 9(17): 13796.
- [2] Yan S B, Peek V L, Ajamie R, et al. LY2801653 is an orally bioavailable multi-kinase inhibitor with potent activity against MET, MST1R, and other oncoproteins, and displays anti-tumor activities in mouse xenograft models[J]. *Investigational new drugs*, 2013, 31(4): 833-844.
- [3] Kosciuczuk E M, Saleiro D, Kroczyńska B, et al. Merestinib blocks Mnk kinase activity in acute myeloid leukemia progenitors and exhibits antileukemic effects in vitro and in vivo[J]. *Blood, The Journal of the American Society of Hematology*, 2016, 128(3): 410-414.
- [4] Kawada I, Hasina R, Arif Q, et al. Dramatic antitumor effects of the dual MET/RON small-molecule inhibitor LY2801653 in non-small cell lung cancer[J]. *Cancer research*, 2014, 74(3): 884-895.
- [5] Zhu C, Shi H, Wu M, et al. A dual MET/AXL small-molecule inhibitor exerts efficacy against gastric carcinoma through killing cancer cells as well as modulating tumor microenvironment[J]. *MedComm*, 2020, 1(1): 103-118.
- [6] Luo X, Linghu M, Zhou X, et al. Merestinib inhibits cuproptosis by targeting NRF2 to alleviate acute liver injury[J]. *Free Radical Biology and Medicine*, 2025, 229: 68-81.
- [7] Wu W, Bi C, Credille K M, et al. Inhibition of tumor growth and metastasis in non-small cell lung cancer by LY2801653, an inhibitor of several oncokinases, including MET[J]. *Clinical Cancer Research*, 2013, 19(20): 5699-5710.
- [8] Yan S B, Um S L, Peek V L, et al. MET-targeting antibody (emibetuzumab) and kinase inhibitor (merestinib) as single agent or in combination in a cancer model bearing MET exon 14 skipping[J]. *Investigational new drugs*, 2018, 36(4): 536-544.

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