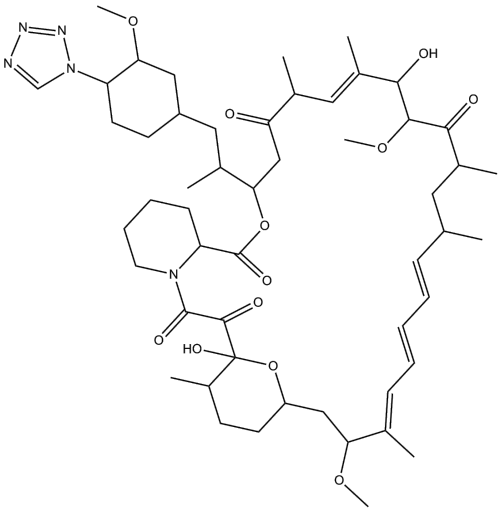
Product Data Sheet

Product Name: Zotarolimus(ABT-578)
Cat. No.: GC14224

Chemical Properties

Cas. No.	221877-54-9		
Formula	$C_{52}H_{79}N_5O_{12}$	M.Wt	966.21
Solubility	DMF: 15mg/mL,DMSO: 15mg/mL,Ethanol: 20mg/mL,Ethanol:PBS (pH 7.2) (1:3): 0.25mg/mL	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	Human coronary artery smooth muscle cell (HCASMC)
Preparation Method	HCASMCs were cultured in SmGM-2 growth media, containing fetal bovine serum (5%) and a specific cocktail of growth factors and antibiotics. All cells were cultured in a 37ºC and 5% CO_2 environment, and refed every 3–4 days or passed on reaching 80% confluence. HCASMCs were seeded at a density optimal for growth (1.5×10^4 cells per centimeter square) in black-walled 96-well plates. Proliferation of HCASMCs under constant exposure to Zotarolimus over a range of concentrations (0.00001, 0.0001, 0.001, 0.01, 0.1, and 1μM) and over a period of 48 hours was observed using the pico green dye assay used for evaluation.
Reaction Conditions	0.00001, 0.0001, 0.001, 0.01, 0.1, and 1μM; 48h
Applications	Zotarolimus treatment significantly reduced the viability of HCASMCs in a dose-dependent manner.

Animal experiment [2]:

Animal models	Male BALB/c nude mice

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Preparation Method	Six weeks old male BALB/c nude mice were maintained in a constant temperature (22±2°C) and constant humidity (55±5%) environment with a light/dark cycle of 12h/12h. After the mice were anesthetized by intraperitoneal injection of Zoletil, 100μl HCT-116 cell suspension containing 1×10^6 live HCT-116 cells was injected subcutaneously into the hind limbs. After 7 days of continuous feeding, the mice with tumors of 4-5mm in diameter were divided into 3 groups. Tumor growth was analyzed after three weeks of intraperitoneal injection of 5-fluorouracil (5-FU; 50mg/kg/week) and Zotarolimus (2mg/kg/day) in the second and third groups, respectively. After three weeks, tumor growth was analyzed.
Dosage form	2mg/kg/day for 3 weeks; i.p.
Applications	Zotarolimus treatment suppressed tumor growth in HCT-116 cell xenograft tumor mouse model.

References:

[1] Steinfeld D S, Liu A P, Hsu S H, et al. Comparative assessment of transient exposure of paclitaxel or zotarolimus on in vitro vascular cell death, proliferation, migration, and proinflammatory biomarker expression[J]. Journal of Cardiovascular Pharmacology, 2012, 60(2): 179-186.
[2] Chang G R, Kuo C Y, Tsai M Y, et al. Anti-cancer effects of zotarolimus combined with 5-fluorouracil treatment in HCT-116 colorectal cancer-bearing BALB/c nude mice[J]. Molecules, 2021, 26(15): 4683.

Background

Zotarolimus(ABT-578) is an immunosuppressant that inhibits immunophilin FKBP12 binding with an IC_{50} of 2.8±0.16nM[1]. Zotarolimus binds to the immunoaffinity protein FKBP12 to form the Zotarolimus-FKBP12 complex, which inhibits mammalian target of rapamycin (mTOR) to regulate intracellular metabolism[2]. Zotarolimus has been widely used in the development of novel drug-eluting stents to prevent coronary restenosis[3].

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In vitro, Zotarolimus treatment for 48h inhibited human coronary artery smooth muscle cell (HCASMC) proliferation, with an IC_{50} value of 0.8nM[4]. Treatment with 1μM Zotarolimus for 48 hours significantly inhibited the migration of human coronary artery endothelial cells (HCAECs) and reduced the expression of pro-inflammatory cytokines[5].

In vivo, Zotarolimus treatment via intraperitoneal injection at a dose of 2mg/kg/day for 3 weeks suppressed tumor growth in the HCT-116 cell xenograft tumor mouse model[6]. Combined administration of Zotarolimus (2mg/kg/day) and 5-fluorouracil (100mg/kg/week) by intraperitoneal injection for 3 weeks significantly inhibited the progression of lung adenocarcinoma in the A549 cell xenograft mouse model and suppressed the expression of IL-1β and TNF-α[7].

References:

[1] Garcia-Touchard A, Burke S E, Toner J L, et al. Zotarolimus-eluting stents reduce experimental coronary artery neointimal hyperplasia after 4 weeks[J]. European heart journal, 2006, 27(8): 988-993.
[2] Shokati T, Drake S H, Zhao W, et al. Structural Identification of Zotarolimus (ABT-578) Metabolites Generated by Human Liver Microsomes Using Ion-Trap and High-Resolution Time-of-Flight Mass Spectrometry in Combination with the Analysis of Fragmentation Patterns[J]. Metabolites, 2023, 13(10): 1093.
[3] Burke S E, Kuntz R E, Schwartz L B. Zotarolimus (ABT-578) eluting stents[J]. Advanced drug delivery reviews, 2006, 58(3): 437-446.
[4] Chen Y W, Smith M L, Sheets M, et al. Zotarolimus, a novel sirolimus analogue with potent anti-proliferative activity on coronary smooth muscle cells and reduced potential for systemic immunosuppression[J]. Journal of cardiovascular pharmacology, 2007, 49(4): 228-235.
[5] Steinfeld D S, Liu A P, Hsu S H, et al. Comparative assessment of transient exposure of paclitaxel or zotarolimus on in vitro vascular cell death, proliferation, migration, and proinflammatory biomarker expression[J]. Journal of Cardiovascular Pharmacology, 2012, 60(2): 179-186.
[6] Chang G R, Kuo C Y, Tsai M Y, et al. Anti-cancer effects of zotarolimus combined with 5-fluorouracil treatment in HCT-116 colorectal cancer-bearing BALB/c nude mice[J]. Molecules, 2021, 26(15): 4683.
[7] Wu C F, Wu C Y, Chiou R Y Y, et al. The anti-cancer effects of a zotarolimus and 5-fluorouracil combination treatment on A549 cell-derived tumors in Balb/c nude mice[J]. International Journal of Molecular Sciences, 2021, 22(9): 4562.

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