Abemaciclib

Cat. No.: HY-16297A

CAS No.: 1231929-97-7

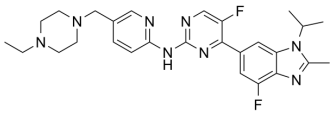
Molecular Formula: $C_{27}H_{32}F_2N_8$

Molecular Weight: 506.59

Target: CDK

Pathway: Cell Cycle/DNA Damage

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 5 mg/mL (9.87 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9740 mL	9.8699 mL	19.7398 mL
	5 mM	0.3948 mL	1.9740 mL	3.9480 mL
	10 mM	---	---	---

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

In Vivo

1. Add each solvent one by one: 0.5% HEC
   Solubility: 3.33 mg/mL (6.57 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.5 mg/mL (0.99 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.5 mg/mL (0.99 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.5 mg/mL (0.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Abemaciclib (LY2835219) is a selective CDK4/6 inhibitor with IC_{50} values of 2 nM and 10 nM for CDK4 and CDK6, respectively.

IC_{50} & Target				
	Cdk4/cyclin D1 2 nM (IC_{50})	CDK6/cyclinD1 10 nM (IC_{50})	CDK9/cyclinT1 57 nM (IC_{50})	CDK5/p35 287 nM (IC_{50})
	Cdk5/p25 355 nM (IC_{50})	CDK2/cyclinE 504 nM (IC_{50})	CDK1/cyclinB1 1627 nM (IC_{50})	CDK7/Mat1/cyclinH1 3910 nM (IC_{50})

	PIM1 50 nM (IC_{50})	PIM2 3400 nM (IC_{50})	HIPK2 31 nM (IC_{50})	DYRK2 61 nM (IC_{50})
	CK2 117 nM (IC_{50})	GSK3b 192 nM (IC_{50})	JNK3 389 nM (IC_{50})	FLT3 (D835Y) 403 nM (IC_{50})
	DRAK1 659 nM (IC_{50})	FLT3 3960 nM (IC_{50})		

In Vitro

Abemaciclib reduces cell viability with the IC_{50} values ranging from 0.5 μM to 0.7 μM, inhibits Akt and ERK signaling but not mTOR activation at head and neck squamous cell carcinoma (HNSCC) cells[1]. Abemaciclib shows inhibition on A375R1-4, M14R, and SH4R with EC_{50} values ranging from 0.3 to 0.6 μM; Abemaciclib inhibits the proliferation of the parental A375 and resistant A375RV1 and A375RV2 cells with similar potencies with IC_{50} values of 395, 260, and 463 nM, respectively[2]. Abemaciclib inhibits CDK4 and CDK6 with low nanomolar potency, inhibits Rb phosphorylation resulting in a G1 arrest and inhibition of proliferation, and its activity is specific for Rb-proficient cells[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Abemaciclib (45 mg/kg, p.o.) in combination with RAD001 causes a cooperative antitumor effect in HNSCC xenograft tumor[1]. Abemaciclib (45 or 90 mg/kg, p.o.) shows significant tumor growth inhibition in an A375 xenograft model[2].

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PROTOCOL

Cell Assay [1]

Cells are seeded in a 96-well plate, allowed to adhere overnight, and treated with DMSO control (0.1% v/v) or the indicated compounds for 72 h. Cell viability and proliferation are determined using a Cell Counting Kit according to the manufacturer's instructions. The interaction between Abemaciclib and mTOR inhibitor is determined using CompuSyn. Combination index (CI) values of 1 indicates and additive drug interaction, whereas a CI of <1 is synergistic and a CI of >1 is antagonistic.

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Animal Administration [1]

Six-week-old BALB/c female nude mice are injected subcutaneously with OSC-19 (1×10^6) cells. When tumor sizes reach approximately 100 mm^3, mice are randomized by tumor size and subjected to each treatment. At least 5 mice per treatment group are included. Each group of mice is dosed via daily oral gavage with vehicle, Abemaciclib (45 mg/kg/d or 90 mg/kg/d), RAD001 (5 mg/kg/d), or a combination of both. The Abemaciclib is dissolved in 1% HEC in 20 mM phosphate buffer (pH2.0). Tumor size and body weight are measured twice weekly. Tumor volumes are calculated using the following formula: $V=(L\times W^2)/2$. Mice are gavaged a final time on day 14 and sacrificed the following day. The tumors are removed for Western blot and immunohistochemistry.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2017 Aug 24;548(7668):471-475.
- Cell. 2018 Nov 1;175(4):984-997.e24.
- Adv Funct Mater. 2021 Apr 30.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Adv Sci (Weinh). 2020 Aug 4;7(18):2000906.

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REFERENCES

[1]. Ku BM, et al. The CDK4/6 inhibitor LY2835219 has potent activity in combination with mTOR inhibitor in head and neck squamous cell carcinoma. Oncotarget.?2016 Mar 22;7(12):14803-13.

[2]. Yadav V, et al. The CDK4/6 inhibitor LY2835219 overcomes PLX4032 resistance resulting from MAPK reactivation and cyclin D1 upregulation. Mol Cancer Ther. 2014 Oct;13(10):2253-63.

[3]. Gelbert LM, et al. Preclinical characterization of the CDK4/6 inhibitor LY2835219: in-vivo cell cycle-dependent/independent anti-tumor activities alone/in combination with NSC 613327. Invest New Drugs. 2014 Oct;32(5):825-37.

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