Ribociclib succinate hydrate

Cat. No.: HY-15777C

CAS No.: 1374639-79-8

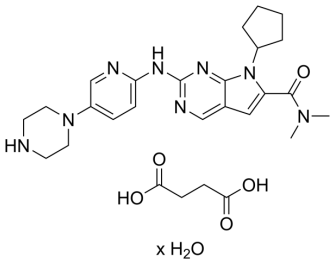
Molecular Formula: $C_{23}H_{30}N_8O.C_4H_6O_4.xH_2O$

Target: CDK

Pathway: Cell Cycle/DNA Damage

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro	DMSO : ≥ 20 mg/mL H_2O : 4 mg/mL (Need ultrasonic) * "≥" means soluble, but saturation unknown.
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.5 mg/mL (Infinity mM); Clear solution 2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (Infinity mM); Clear solution 3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (Infinity mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Ribociclib succinate hydrate (LEE011 succinate hydrate) is a highly specific CDK4/6 inhibitor with IC_{50} values of 10 nM and 39 nM, respectively, and is over 1,000-fold less potent against the cyclin B/CDK1 complex.	
IC_{50} & Target	CDK4 10 nM (IC_{50})	CDK6 39 nM (IC_{50})
In Vitro	Treating a panel of 17 neuroblastoma cell lines with Ribociclib (LEE011) across a four-log dose range (10 to 10,000 nM). Treatment with Ribociclib significantly inhibits substrate adherent growth relative to the control in 12 of the 17 neuroblastoma cell lines examined (mean IC_{50}=306±68 nM, considering sensitive lines only, where sensitivity is defined as an IC_{50} of less than 1 μM. Ribociclib treatment of two neuroblastoma cell lines (BE2C and IMR5) with demonstrated sensitivity to CDK4/6 inhibition results in a dose-dependent accumulation of cells in the G_0/G_1 phase of the cell cycle. This G_0/G_1 arrest becomes significant at Ribociclib concentrations of 100 nM (p=0.007) and 250 nM (p=0.01), respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	
In Vivo	CB17 immunodeficient mice bearing BE2C, NB-1643 (MYCN amplified, sensitive in vitro), or EBC1 (non-amplified, resistant in vitro) xenografts are treated once daily for 21 days with Ribociclib (LEE011; 200 mg/kg) or with a vehicle control. This dosing strategy is well tolerated, as no weight loss or other signs of toxicity are observed in any of the xenograft models. Tumor	

	growth is significantly delayed throughout the 21 days of treatment in mice harboring the BE2C or 1643 xenografts (both, $p<0.0001$), although growth resumed post-treatment[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Cells are grown for 24 hours in 35 mm plates, treated with 500 nM Ribociclib for 6 days, and then fixed and stained overnight. Cells are then imaged for SA-β-gal using an Axio Observer D.1 phase contrast microscope. The percentage of SA-β-gal positive cells is determined by counting the number of positive cells present in three separate microscope frames, and then normalizing to the control. To assess apoptotic activity, cells are plated in triplicate in 96 well plates, treated with Ribociclib, and assayed for caspase 3/7 activation 16 hours after treatment with Caspase-Glo 3/7. Cells treated with SN-38 are used as a positive control[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] The BE2C, NB-1643, or EBC1 cell line-derived xenografts are implanted subcutaneously into the right flank of CB17 $SCID^{-/-}$ mice. Animals bearing engrafted tumors of 200-600 mm^3 are then randomized to oral treatment with 200 mg/kg Ribociclib in 0.5 % methylcellulose (n=10) or vehicle (n=10) daily for a total of 21 days. Tumor burden is determined periodically throughout treatment according to the formula $(\pi/6)\times d^2$, where d represents the mean tumor diameter obtained by caliper measurement. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2023 Jun 8;186(12):2628-2643.e21.
- Cancer Discov. 2023 Dec 4.
- Nature Cancer. 2021 Apr;2(4):429-443.
- Mil Med Res. 2022 Dec 19;9(1):71.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.

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REFERENCES

[1]. VanArsdale T, et al. Molecular Pathways: Targeting the Cyclin D-CDK4/6 Axis for Cancer Treatment. Clin Cancer Res. 2015 Jul 1;21(13):2905-10.

[2]. Rader J, et al. Dual CDK4/CDK6 Inhibition Induces Cell-Cycle Arrest and Senescence in Neuroblastoma. Clin Cancer Res. 2013 Nov 15;19(22):6173-82.

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