

产品名称: LEE011  
产品别名: Ribociclib; 瑞博西尼

| 生物活性:              |   |                                  |           |            |            |
|--------------------|---|----------------------------------|-----------|------------|------------|
| Description        | Ribociclib (LEE01) is a highly specific <b>CDK4/6</b> inhibitor with <b>IC<sub>50</sub></b> values of 10 nM and 39 nM, respectively, and is over 1,000-fold less potent against the cyclin B/CDK1 complex.  |                                  |           |            |            |
|                    | CDK4  | CDK6                             |           |            |            |
|                    | 10 nM (IC <sub>50</sub> )   | 39 nM (IC <sub>50</sub> )        |           |            |            |
| 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 IC50=306±68 nM, considering sensitive lines only, where sensitivity is defined as an IC50 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 G0/G1 phase of the cell cycle. This G0/G1 arrest becomes significant at Ribociclib concentrations of 100 nM (p=0.007) and 250 nM (p=0.01), respectively[2]. |                                  |           |            |            |
| 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].   |                                  |           |            |            |
| Solvent&Solubility | <b>In Vitro:</b><br><b>DMSO : 5.4 mg/mL (12.43 mM; Need ultrasonic)</b>   |                                  |           |            |            |
|                    | Preparing Stock Solutions   | Solvent<br>Mass<br>Concentration | 1 mg      | 5 mg       | 10 mg      |
|                    |   | 1 mM                             | 2.3013 mL | 11.5064 mL | 23.0128 mL |
|                    |   | 5 mM                             | 0.4603 mL | 2.3013 mL  | 4.6026 mL  |
|                    |   | 10 mM                            | 0.2301 mL | 1.1506 mL  | 2.3013 mL  |
|                    | <p>*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液。一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。</p> <p>储备液的保存方式和期限: -80℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。</p> <p><b>In Vivo:</b></p> <p>请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 <b>In Vitro</b> 方式配制澄清的储备液，再依次添加助溶剂：</p> <p>——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶</p> <p>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: ≥ 1.5 mg/mL (3.45 mM); Clear solution</p> <p>此方案可获得 ≥ 1.5 mg/mL (3.45 mM，饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例，取 100 μL 15.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。</p>                           |                                  |           |            |            |

|                       |  |
|-----------------------|--|
|                       | <p>2.请依序添加每种溶剂： 10% DMSO →90% corn oil</p> <p>Solubility: <math>\geq 1.5</math> mg/mL (3.45 mM); Clear solution</p> <p>此方案可获得 <math>\geq 1.5</math> mg/mL (3.45 mM, 饱和度未知) 的澄清溶液, 此方案不适用于实验周期在半个月以上的实验。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 15.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中, 混合均匀。</p>   |
| References            | <p>[1]. <a href="#">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.</a></p> <p>[2]. <a href="#">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.</a></p>  |
| 实验参考:                 |  |
| Cell Assay            | <p>Cells are grown for 24 hours in 35 mm plates, treated with 500 nM Ribociclib (LEE011) for 6 days, and then fixed and stained overnight. Cells are then imaged for SA-<math>\beta</math>-gal using an Axio Observer D.1 phase contrast microscope. The percentage of SA-<math>\beta</math>-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 (LEE011), 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].</p> |
| Animal Administration | <p>Mice[2]</p> <p>The BE2C, NB-1643, or EBC1 cell line-derived xenografts are implanted subcutaneously into the right flank of CB17 SCID<sup>-/-</sup> mice. Animals bearing engrafted tumors of 200-600 mm<sup>3</sup> are then randomized to oral treatment with 200 mg/kg Ribociclib (LEE011) 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 <math>(\pi/6) \times d^2</math>, where d represents the mean tumor diameter obtained by caliper measurement.</p>  |
| References            | <p>[1]. <a href="#">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.</a></p> <p>[2]. <a href="#">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.</a></p>  |