

产品名称: **Lonafarnib**

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| 生物活性: | | | | |
| Description | Lonafarnib is an orally bioavailable farnesyl protein transferase (FPTase) inhibitor for H-ras, K-ras and N-ras with IC₅₀ of 1.9 nM, 5.2 nM and 2.8 nM, respectively. | | | |
| IC ₅₀ & Target | IC50: 1.9 nM (H-ras), 5.2 nM (K-ras), 2.8 nM (N-ras)[1] | | | |
| In Vitro | Lonafarnib (Sch66336) potently inhibits Ha-Ras processing in whole cells and blocks the trans formed growth properties of fibroblasts and human tumor cell lines expressing activated Ki-Ras proteins[1]. All treatment groups containing Lonafarnib (10 μM) show a significantly higher level of unfarnesylated H-Ras (116-137%) compared to control treatment[2]. | | | |
| In Vivo | In mouse, rat, and monkey systems, Lonafarnib (Sch66336) has excellent oral bioavailability and pharmacokinetic properties. In the nude mouse, Lonafarnib demonstrates potent oral activity in a wide array of human tumor xenograft models including tumors of colon, lung, pancreas, prostate, and urinary bladder origin[1]. Lonafarnib alone (80 mg/kg by oral gavage, once daily) has limited ability to inhibit orthotopic U87 tumors compared to vehicle treated control animals (T/C of 0.67). The combination of XRT/Tem (2.5Gy/day for 2 days; 5 mg/kg by oral gavage 90 min prior to XRT) is designed to produce modest tumor growth inhibition in vivo(T/C of 0.42). Concurrent Lonafarnib/XRT/Tem (Lonafarnib 80 mg/kg by oral gavage, once daily, XRT 2.5Gy/day for 2 days, and Tem 5 mg/kg by oral gavage 90 min prior to XRT) provides the strongest growth reduction (T/C of 0.02) and is significantly more effective than XRT/Tem (p<0.04), with the majority of animals demonstrating a decrease in tumor volume (p<0.05) after two weeks and persisting after 4 weeks (p<0.05)[2]. | | | |
| Solvent&Solubility | In Vitro: DMSO : ≥ 100 mg/mL (156.54 mM) * "≥" means soluble, but saturation unknown. | | | |
| | | <div><div>Solvent</div><div>Mass</div><div>Concentration</div></div> | 1 mg | 5 mg |
| | Preparing | 1 mM | 1.5654 mL | 7.8269 mL |
| | Stock Solutions | 5 mM | 0.3131 mL | 1.5654 mL |
| | | 10 mM | 0.1565 mL | 0.7827 mL |
| *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。 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。 In Vivo: 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 In Vitro 方式配制澄清的储备液，再依次添加助溶剂： ——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 <div>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</div> <div>Solubility: ≥ 2.5 mg/mL (3.91 mM); Clear solution</div> <div>此方案可获得 ≥ 2.5 mg/mL (3.91 mM, 饱和度未知) 的澄清溶液。</div> | | | | |

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| | <p>以 1 mL 工作液为例，取 100 μL 25.0 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% (20% SBE-β-CD in saline) Solubility: \geq 2.5 mg/mL (3.91 mM); Clear solution 此方案可获得 \geq 2.5 mg/mL (3.91 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: \geq 2.5 mg/mL (3.91 mM); Clear solution 此方案可获得 \geq 2.5 mg/mL (3.91 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。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</p> |
| References | <p>[1]. Liu M, et al. Antitumor activity of SCH 66336, an orally bioavailable tricyclic inhibitor of farnesyl protein transferase, in human tumor xenograft models and wap-ras transgenic mice. <i>Cancer Res.</i> 1998 Nov 1;58(21):4947-56.</p> <p>[2]. Chaponis D, et al. Lonafarnib (SCH66336) improves the activity of temozolomide and radiation for orthotopic malignant gliomas. <i>J Neurooncol.</i> 2011 Aug;104(1):179-89.</p> |
| 实验参考： | |
| Cell Assay | <p>CellTiter96 Aqueous Assay kit is used. Assays are performed with 5000 cells/well in a 96-well tissue culture plate. Plates are irradiated 24 h after drug exposure and assayed 96 h after XRT, with fresh drug treatments applied each day. For quantification, dye is added directly to each well, plates are washed as per the manufactures recommendation and cell viability determined by optical density. Significance is analyzed using the Student's T-test. 12-well plates are seeded with 100,000 cells/well. Drug treatments are initiated 24 h after plating, and media is replaced every 24 h for a total of 96 h of drug exposure. Plates are irradiated after 24 h of drug exposure. Cells from triplicate sets of treatments are trypsonized and counted 48 h after irradiation using a Z1 series coulter counter, and compared to cell numbers from wells counted on Day 1 (the day drug treatment is initiated). Proliferation after drug treatments are normalized to the control wells and expressed as % of the control treatment. Significance is analyzed using the Student's T-test[2].</p> |
| Animal Administration | <p>Mice[2] Lonafarnib is given once daily at 80mg/kg with twice weekly weightings to ensure accurate dosing. Temozolomide (Tem) is given by gavage at 5 mg/kg 90 min prior to XRT. For irradiation, anesthetized mice are placed in a lead shielding apparatus which limited radiation exposure to the head only. Treatment (2.5Gy/day for two days) is delivered using a Gammacell 40 irradiator delivering 100 rads/min. For in vivo combination experiments, suboptimal doses of XRT/Tem are selected to permit identification of synergistic effects of Lonafarnib.</p> |
| Kinase Assay | <p>FPTactivity is determined by measuring the transfer of [3H]farnesyl from [3H]farnesyl PPI to trichloroacetic acid-precipitable Ha-Ras-CVLS. GGPT-1 activity is similarly determined using [3H]geranylgeranyl diphosphate and Ha-Ras-CVLL as substrates[1].</p> |
| | <p>[1]. Liu M, et al. Antitumor activity of SCH 66336, an orally bioavailable tricyclic inhibitor of farnesyl protein transferase, in human tumor xenograft models and wap-ras transgenic mice. <i>Cancer Res.</i></p> |

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| References | <p><u>1998 Nov 1;58(21):4947-56.</u></p> <p>[2]. <u>Chaponis D, et al. Lonafarnib (SCH66336) improves the activity of temozolomide and radiation for orthotopic malignant gliomas. J Neurooncol. 2011 Aug;104(1):179-89.</u></p> |
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源叶生物