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产品名称：LY2334737
产品别名：LY2334737

生物活性：

Description

LY2334737 is an orally available prodrug of gemcitabine which is a nucleoside analog used as chemotherapy. IC50 Value: Target: Nucleoside analog in vitro: Five cell lines that express CES2 responded to LY2334737treatment. LY2334737 was less cytotoxic to a SK-OV-3 CES2 knockdown than parental cells. The drug response of CES2-transfected HCT-116 cells correlated with CES2 expression level. Bystander studies showed statistically greater PC-3-GFP growth inhibition by LY2334737 when cells were cocultured with CES2 and not mock transfectants [1]. in vivo: Oral treatment of xenograft models with 3.2 mg/kg LY2334737 once a day for 21 days showed greater tumor growth inhibition of CES2 transfectant than the mock transfectant (P ≤ 0.001) [1]. The MTD was 40 mg LY2334737. Fatigue was the most frequent DLT for LY2334737monotherapy (4 patients) followed by elevated transaminase levels (2 patients), both observed at the 40- to 50-mg dose levels. Among the 10 patients in the combination arm, 2 had DLTs at the 40-mg dose level. These were fatigue and elevated liver enzyme levels [2]. Metronomic LY2334737 administration caused increased blood flow in luciferase-tagged LM2-4 tumor xenografts, and this effect, readily measured using contrast micro-ultrasound, coincided with a relative increase in tumor bioluminescence [3].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (256.81 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5681 mL	12.8406 mL	25.6812 mL
	5 mM	0.5136 mL	2.5681 mL	5.1362 mL
	10 mM	0.2568 mL	1.2841 mL	2.5681 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°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 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

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (6.42 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.42 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 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。

	2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.42 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.42 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.42 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.42 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。
References	[1]. Pratt SE, et al. Human carboxylesterase-2 hydrolyzes the prodrug of gemcitabine (LY2334737) and confers prodrug sensitivity to cancer cells. Clin Cancer Res. 2013 Mar 1;19(5):1159-68. [2]. Koolen SL, et al. Phase I study of Oral gemcitabine prodrug (LY2334737) alone and in combination with erlotinib in patients with advanced solid tumors. Clin Cancer Res. 2011 Sep 15;17(18):6071-82. [3]. Francia G, et al. Low-dose metronomic oral dosing of a prodrug of gemcitabine (LY2334737) causes antitumor effects in the absence of inhibition of systemic vasculogenesis. Mol Cancer Ther. 2012 Mar;11(3):680-9.