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产品名称: **JNJ-26854165 (Serdemetan)**
产品别名: **Serdemetan**

生物活性:

Description

Serdemetan(JNJ-26854165) acts as a HDM2 ubiquitin ligase antagonist and also induces early apoptosis in p53 wild-type cells, inhibits cellular proliferation followed by delayed apoptosis in the absence of functional p53. IC50 value: HDM2 ubiquitin ligase Target: in vitro: JNJ 26854165 is a novel tryptamine derivative which activates p53 and acts as a HDM2 ubiquitin ligase antagonist. JNJ 26854165 inhibits cell growth and induces apoptosis in leukemia cell lines with IC50 values of 0.24, 0.33, 0.32 and 0.44 μ M at 72 hours for OCI-AML-3, MOLM-13, NALM-6 and REH cells, respectively. In addition, JNJ 26854165 accelerates proteasome-mediated degradation of p21 and antagonizes the transcriptional induction of p21 by p53. It also induces S-phase delay and upregulates E2F1 expression in p53 mutant cells, resulting in preferential apoptosis of S-phase cells. JNJ 26854165 is an oral Mdm2 inhibitor which can inhibit the interaction of Mdm2-p53 complex with the proteasome and increase p53 levels by binding to RING domain of Mdm2. A recent study shows that JNJ 26854165 inhibits clonogenic survival in four human cancer cell lines: H460, A549, p53-WT-HCT116, and p53-null-HCT116. in vivo: JNJ 26854165 leads to significant differences in EFS distribution in 17 of the 36 (47%) evaluable solid tumor xenografts and in 5 of 7 (71%) of the evaluable ALL xenografts using a dose of 20 mg/kg administered via oral gavage daily for 5 days, repeated for 6 weeks.

In Vitro:

DMSO : 50 mg/mL (152.25 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg
	1 mM		3.0450 mL	15.2249 mL	30.4497 mL
	5 mM		0.6090 mL	3.0450 mL	6.0899 mL
	10 mM		0.3045 mL	1.5225 mL	3.0450 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: $\geq$ 2.5 mg/mL (7.61 mM); Clear solution

此方案可获得 $\geq$ 2.5 mg/mL (7.61 mM, 饱和度未知) 的澄清溶液。

以 1 mL 工作液为例, 取 100 μ L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μ L PEG300 中, 混合均匀; 向上述体系中加入 50 μ L Tween-80, 混合均匀; 然后继续加入 450 μ L 生理盐水定容至 1 mL。



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	2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (7.61 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.61 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 (7.61 mM); Suspended solution 此方案可获得 ≥ 2.5 mg/mL (7.61 mM, 饱和度未知) 的均匀悬浊液, 悬浊液可用于口服和腹腔注射。 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]. T. Stühmer et al. A first-in-class HDM2-inhibitor (JNJ-26854165) in phase I development shows potent activity against multiple myeloma (MM) cells in vitro and ex vivo Journal of Clinical Oncology, 2008 ASCO Annual Meeting Proceedings (Post-Meeting Edition).Vol 26, No 15S (May 20 Supplement), 2008: 14694 [2]. Chargari C, Leteur C, Angevin E, Bashir T, Schoentjes B, Arts J, Janicot M, Bourhis J, Deutsch E.Preclinical assessment of JNJ-26854165 (Serdemetan), a novel tryptamine compound with radiosensitizing activity in vitro and in tumor xenografts.Cancer Lett. 2011 Dec 22;312(2):209-18. [3]. Smith MA, Gorlick R, Kolb EA, Lock R, Carol H, Maris JM, Keir ST, Morton CL, Reynolds CP, Kang MH, Arts J, Bashir T, Janicot M, Kurmasheva RT, Houghton PJ.Initial testing of JNJ-26854165 (Serdemetan) by the pediatric preclinical testing program.Pediatr Blood Cancer. 2012 Aug;59(2):329-32. [4]. Tabernero J, Dirix L, Sch?ffski P, Cervantes A, Lopez-Martin JA, Capdevila J, van Beijsterveldt L, Platero S, Hall B, Yuan Z, Knoblauch R, Zhuang SH.A phase I first-in-human pharmacokinetic and pharmacodynamic study of serdemetan in patients with advanced solid tumors.Clin Cancer Res. 2011 Oct 1;17(19):6313-21. Epub 2011 Aug 10. [5]. Kojima K, Burks JK, Arts J, Andreeff M.The novel tryptamine derivative JNJ-26854165 induces wild-type p53- and E2F1-mediated apoptosis in acute myeloid and lymphoid leukemias.Mol Cancer Ther. 2010 Sep;9(9):2545-57. Epub 2010 Aug 24.