

产品名称: **3-(6-甲基-2-吡啶基)-N-苯基-4-(4-喹啉基)-1H-吡唑-1-硫代甲酰胺**  
 产品别名: **A 83-01**

生物活性:

|                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |           |            |            |
|------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|-----------|------------|------------|
| Description                                                                                                                  | A 83-01 is a potent inhibitor of TGF-β type I receptor ALK5 kinase, type I nodal receptor ALK4 and type I nodal receptor ALK7, with IC <sub>50</sub> s of 12, 45 and 7.5 nM against the transcription induced by ALK5, ALK4 and ALK7, respectively.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |           |            |            |
| IC <sub>50</sub> & Target                                                                                                    | IC <sub>50</sub> : 12 nM (ALK5, cell-based), 45 nM (ALK4 cell-based), 7.5 nM (ALK7 cell-based)[1]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                           |           |            |            |
| In Vitro                                                                                                                     | A 83-01 is a potent inhibitor of TGF-β type I receptor ALK5 kinase, ALK4 and ALK7, reduces the level of ALK-5-induced transcription with an IC <sub>50</sub> of 12 nM in Mv1Lu cells, also blocks the ALK4-TD and ALK7-TD induced transcription with IC <sub>50</sub> s of 45 nM and 7.5 nM in R4-2 cells, and weakly suppresses that induced by constitutively active ALK-6, ALK-2, ALK-3, and ALK-1. A 83-01 (0.03-10 μM) potently prevents the growth-inhibitory effects of TGF-β, and completely inhibits the effect at 3 μM. A 83-01 (1-10 μM) inhibits TGF-β-induced Smad activation in HaCaT cells[1]. A 83-01 (1 μM) decreases cell motility, adhesion and invasion increased by TGF-β1 in HM-1 cells, but does not change cell proliferation[2] |                                           |           |            |            |
| In Vivo                                                                                                                      | A 83-01 (50, 150 and 500 μg/mouse, i.p.) significantly improves survival of the mice without body weight or neurobehavioral appearances[2]. A 83-01 (0.5 mg/kg, i.p.) shows a significantly strong antitumor effect in mice bearing M109 cells[3].                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                           |           |            |            |
| Solvent&Solubility                                                                                                           | <b>In Vitro:</b><br><b>DMSO : 30 mg/mL (71.17 mM; Need ultrasonic)</b><br><b>H<sub>2</sub>O : &lt; 0.1 mg/mL (insoluble)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |           |            |            |
|                                                                                                                              | Preparing<br><br>Stock Solutions                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <div>Solvent / Mass / Concentration</div> | 1 mg      | 5 mg       | 10 mg      |
|                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 1 mM                                      | 2.3724 mL | 11.8618 mL | 23.7237 mL |
|                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 5 mM                                      | 0.4745 mL | 2.3724 mL  | 4.7447 mL  |
|                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 10 mM                                     | 0.2372 mL | 1.1862 mL  | 2.3724 mL  |
|                                                                                                                              | <b>*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。</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |           |            |            |
|                                                                                                                              | 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。                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |           |            |            |
|                                                                                                                              | <b>In Vivo:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |           |            |            |
|                                                                                                                              | 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：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                           |           |            |            |
|                                                                                                                              | ——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: ≥ 0.83 mg/mL (1.97 mM); Clear solution                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |           |            |            |
| 此方案可获得 ≥ 0.83 mg/mL (1.97 mM, 饱和度未知) 的澄清溶液。                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |           |            |            |
| 以 1 mL 工作液为例，取 100 μL 8.3 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: 0.83 mg/mL (1.97 mM); Suspended solution; Need ultrasonic                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |           |            |            |

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|                       | <p>此方案可获得 0.83 mg/mL (1.97 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。</p> <p>以 1 mL 工作液为例，取 100 <math>\mu</math>L 8.3 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-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 <math>\rightarrow</math>90% corn oil</p> <p>Solubility: <math>\geq</math> 0.83 mg/mL (1.97 mM); Clear solution</p> <p>此方案可获得 <math>\geq</math> 0.83 mg/mL (1.97 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 8.3 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="#">Tojo M, et al. The ALK-5 inhibitor A-83-01 inhibits Smad signaling and epithelial-to-mesenchymal transition by transforming growth factor-beta. Cancer Sci. 2005 Nov;96(11):791-800.</a></p> <p>[2]. <a href="#">Yamamura S, et al. The activated transforming growth factor-beta signaling pathway in peritoneal metastases is a potential therapeutic target in ovarian cancer. Int J Cancer. 2012 Jan 1;130(1):20-8.</a></p> <p>[3]. <a href="#">Taniguchi Y, et al. Enhanced antitumor efficacy of folate-linked liposomal Adriamycin with TGF-<math>\beta</math> type I receptor inhibitor. Cancer Sci. 2010 Oct;101(10):2207-13.</a></p> |
| 实验参考：                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Cell Assay            | <p>HM-1 cells are seeded into a 96-well plate and are incubated for 18 hr. A 83-01 (1 <math>\mu</math>M) or vehicle are then added for 12 hr followed by the addition of TGF-<math>\beta</math>1 (1 ng/mL) or vehicle for 60 hr. The number of viable cells in each well is examined using the WST-1 assay[2].</p>                                                                                                                                                                                                                                                                                                                                                 |
| Animal Administration | <p>Mice[2]</p> <p>Female B6C3F1 mice used for the in vivo studies are maintained under specific pathogen-free conditions. To evaluate the effect of A 83-01 on the survival of mice bearing peritoneal dissemination, HM-1 cells (<math>1 \times 10^6</math>) are injected into the abdominal cavity via the left flank of the mouse. Starting the next day, A 83-01 (150 <math>\mu</math>g/body) or vehicles (PBS with 0.5% DMSO) are injected into the abdominal cavity three times per week. Mice are euthanized before reaching the moribund state[2]</p>                                                                                                      |
| References            | <p>[1]. <a href="#">Tojo M, et al. The ALK-5 inhibitor A-83-01 inhibits Smad signaling and epithelial-to-mesenchymal transition by transforming growth factor-beta. Cancer Sci. 2005 Nov;96(11):791-800.</a></p> <p>[2]. <a href="#">Yamamura S, et al. The activated transforming growth factor-beta signaling pathway in peritoneal metastases is a potential therapeutic target in ovarian cancer. Int J Cancer. 2012 Jan 1;130(1):20-8.</a></p> <p>[3]. <a href="#">Taniguchi Y, et al. Enhanced antitumor efficacy of folate-linked liposomal Adriamycin with TGF-<math>\beta</math> type I receptor inhibitor. Cancer Sci. 2010 Oct;101(10):2207-13.</a></p> |