产品名称：维替泊芬
产品别名：Verteporfin

生物活性：

Description	Verteporfin is a photosensitizer for photodynamic therapy to eliminate the abnormal blood vessels in the eye associated with conditions such as age-related macular degeneration. Verteporfin is a **YAP** inhibitor which disrupts YAP-TEAD interactions.
In Vitro	Verteporfin is specifically selected by PDX-cell screening. The concentrations to cause 50% growth inhibition (GI50) for PhLO, PhLH, and PhLK are 228 nM, 395 nM, and 538 nM, respectively, whereas GI50 for ALL-1, TCC-Y/sr, and NPhA1 are 3.93 μM, 2.11 μM, and 5.61 μM, respectively. GSH significantly reduces the sensitivity of 2 out of 3 PDX cells to verteporfin. Verteporfin reduces the mitochondrial membrane potential in PDX cells[1]. Verteporfin reduces the PTX-resistance on HCT-8/T cells by inhibiting YAP expression and combination therapy with verteporfin and paclitaxel (PTX) shows synergism on inhibition of YAP and cytotoxicity to HCT-8/T[2].
In Vivo	Verteporfin (10 mg/kg, c.s.c.) and dasatinib significantly reduces the leukemia cell ratio, and combined therapy further reduced the number of leukemia cells in the spleen[1].
Solvent&Solubility	***In Vitro:*** **DMF : 100 mg/mL** (**139.12 mM;** Need ultrasonic) **DMSO : 8 mg/mL** (**11.13 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.3912 mL	6.9561 mL	13.9123 mL
5 mM	0.2782 mL	1.3912 mL	2.7825 mL
10 mM	0.1391 mL	0.6956 mL	1.3912 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% DMF →40% PEG300 →5% Tween-80 →45% saline
Solubility: ≥ 2.5 mg/mL (3.48 mM); Clear solution

2.请依序添加每种溶剂： 10% DMF →90% (20% SBE-β-CD in saline)
Solubility: 2.5 mg/mL (3.48 mM); Suspended solution; Need ultrasonic

3.请依序添加每种溶剂： 10% DMF →90% corn oil
Solubility: 2.5 mg/mL (3.48 mM); Clear solution; Need ultrasonic

4.请依序添加每种溶剂： 10% DMSO →40% PEG300 →5% Tween-80 →45% saline
Solubility: ≥ 0.8 mg/mL (1.11 mM); Clear solution

此方案可获得 ≥ 0.8 mg/mL (1.11 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 8.0 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。 5.请依序添加每种溶剂： 10% DMSO →90% (20% SBE-β-CD in saline) Solubility: 0.8 mg/mL (1.11 mM); Suspended solution; Need ultrasonic and warming 此方案可获得 0.8 mg/mL (1.11 mM)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 8.0 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。
References	[1]. Morishita T, et al. The photosensitizer verteporfin has light-independent anti-leukemic activity for Ph-positive acute lymphoblastic leukemia and synergistically works with dasatinib. Oncotarget. 2016 Aug 2. [2]. Pan W, et al. Verteporfin can Reverse the Paclitaxel Resistance Induced by YAP Over-Expression in HCT-8/T Cells without Photoactivation through Inhibiting YAP Expression. Cell Physiol Biochem. 2016;39(2):481-90.

实验参考：

Cell Assay	PDX cells co-cultured with S17 cells are treated with 16 combinations of verteporfin (60 nM, 120 nM, 180 nM, and 240 nM) and dasatinib (12 nM, 24 nM, 36 nM, and 48 nM). The viabilities of cells treated with each combination are measured after 48 h using FACS Aria flow cytometer. In order to estimate drug interaction between verteporfin and dasatinib, a normalized isobologram and fraction affectedcombination index (CI) plot are made using CompuSyn software. CI values greater than 1.0 indicated antagonistic effects, equal to 1.0 additive effects, and below 1.0 synergistic effects. [1]
Animal Administration	Mice: PhLO cells (1.0×10^7/mouse) are injected intravenously into 6-week-old male NOG mice, which are then treated with vehicle, verteporfin (140 mg/kg/day), dasatinib (20 mg/kg/day), and a combination of these drugs from days 22 to 28. Verteporfin is administered by continuous subcutaneous infusion (c.s.c.) using Alzet osmotic pumps. An intraperitoneal injection (i.p.) is performed for dasatinib. All mice are sacrificed on day 28 and the chimerism of leukemia cells is investigated by flow cytometer using an anti-human CD19 antibody and antimouse CD45 antibody. Blood concentrations of verteporfin are calculated by LCMS-2020. [1]
References	[1]. Morishita T, et al. The photosensitizer verteporfin has light-independent anti-leukemic activity for Ph-positive acute lymphoblastic leukemia and synergistically works with dasatinib. Oncotarget. 2016 Aug 2. [2]. Pan W, et al. Verteporfin can Reverse the Paclitaxel Resistance Induced by YAP Over-Expression in HCT-8/T Cells without Photoactivation through Inhibiting YAP Expression. Cell Physiol Biochem. 2016;39(2):481-90.