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产品名称：Marinopyrrole A
产品别名：Maritoclax

生物活性：

Description	Maritoclax (Marinopyrrole A) is a novel and specific Mcl-1 inhibitor with an IC50 value of 10.1 μM, and shows >8 fold selectivity than BCL-xl (IC50 > 80 μM).
IC_{50} & Target	Mcl-1
	10.1 μM (IC_{50})
In Vitro	Maritoclax (Marinopyrrole A) blocks the binding of Bim BH3 α-helix to Mcl-1 but not Bcl-XL. Maritoclax (Marinopyrrole A) markedly inhibits the viability of Mcl-1-IRES-BimEL cells (EC50=1.6 μM) with a selectivity greater than 40-fold over Bcl-2-IRES-BimEL (EC50=65.1 μM) and Bcl-XL-IRES-BimEL (EC50=70.0 μM) cells. Maritoclax (Marinopyrrole A) induces cell death selectively in Mcl-1-dependent but not Bcl-2- or Bcl-XL-dependent leukemia cells. Maritoclax (Marinopyrrole A) induces proteasome-mediated Mcl-1 degradation without induction of Mcl-1 phosphorylation and Noxa expression. Maritoclax (Marinopyrrole A) inhibits Mcl-1 interaction with Bim in intact cells and triggers cytochrome c release from isolated mitochondria. Maritoclax (Marinopyrrole A) synergistically sensitizes lymphoma/leukemia cells to ABT-737[1]. Maritoclax (Marinopyrrole A) shows activity against all tested S. aureus strains, including glycopeptide-intermediate and vancomycin-resistant MRSA, and has potent activities against other Gram-positive organisms. In addition, Maritoclax (Marinopyrrole A) is active against H. influenzae but is inactive against other tested Gram-negative strains. Maritoclax (Marinopyrrole A) displays substantial concentration-dependent killing against MRSA strain TCH1516 and is far more rapid in its antibiotic action than either vancomycin or linezolid. Maritoclax exhibits a favorable therapeutic index, with 50% inhibitory concentrations (IC50) in excess of 20× above the MIC in each case: 32 to 64 μg/mL against HeLa cells and 8 to 32 μg/mL against L929 cells[2]. Maritoclax (Marinopyrrole A) (3 μM) induced-cell death is associated with MCL1 decrease and translation inhibition. Maritoclax (Marinopyrrole A) induces a dephosphorylation of EIF4EBP1 concomitant to a decrease of EIF4E phosphorylation[3]. Maritoclax (Marinopyrrole A) is much more effective against Bcl-2-dependent RS4;11 cells (IC50: 2 μM) when compared to Mcl-1-dependent HeLa cells (IC50: 20 μM)[4].

In Vitro:

DMSO : ≥ 43 mg/mL (84.29 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	1.9602 mL	9.8010 mL	19.6021 mL
	5 mM	0.3920 mL	1.9602 mL	3.9204 mL
	10 mM	0.1960 mL	0.9801 mL	1.9602 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。

Solvent&Solubility	***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 (4.90 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.90 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 (4.90 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (4.90 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 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 (4.90 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.90 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]. Doi K, et al. Discovery of marinopyrrole A (maritoclax) as a selective Mcl-1 antagonist that overcomes ABT-737 resistance by binding to and targeting Mcl-1 for proteasomal degradation. J Biol Chem. 2012 Mar 23;287(13):10224-35. [2]. Haste NM, et al. Pharmacological properties of the marine natural product marinopyrrole A against methicillin-resistant Staphylococcus aureus. Antimicrob Agents Chemother. 2011 Jul;55(7):3305-12. [3]. Gomez-Bougie P, et al. The selectivity of Marinopyrrole A to induce apoptosis in MCL1high BCL2low expressing myeloma cells is related to its ability to impair protein translation. Br J Haematol. 2016 Aug 14. [4]. Eichhorn JM, et al. Purported Mcl-1 inhibitor marinopyrrole A fails to show selective cytotoxicity for Mcl-1-dependent cell lines. Cell Death Dis. 2013 Oct 24;4:e880
实验参考：	
Cell Assay	Maritoclax (Marinopyrrole A) cytotoxicity is assessed by seeding 2×10^4 HeLa or L929 cells per well in sterile 96-well tissue culture-treated plates. After 24 h, the medium is replaced with fresh medium containing increasing concentrations of marinopyrrole A, and the plates are incubated at 37°C in 5% CO_2 for 24 h. Cytotoxicity is assayed at 24 h by measuring the reduction of MTS [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium] using the CellTiter 96 Aqueous nonradioactive cell proliferation assay

	according to the manufacturer's instructions. [2]
References	[1]. Doi K, et al. Discovery of marinopyrrole A (maritoclax) as a selective Mcl-1 antagonist that overcomes ABT-737 resistance by binding to and targeting Mcl-1 for proteasomal degradation. J Biol Chem. 2012 Mar 23;287(13):10224-35. [2]. Haste NM, et al. Pharmacological properties of the marine natural product marinopyrrole A against methicillin-resistant Staphylococcus aureus. Antimicrob Agents Chemother. 2011 Jul;55(7):3305-12. [3]. Gomez-Bougie P, et al. The selectivity of Marinopyrrole A to induce apoptosis in MCL1high BCL2low expressing myeloma cells is related to its ability to impair protein translation. Br J Haematol. 2016 Aug 14. [4]. Eichhorn JM, et al. Purported Mcl-1 inhibitor marinopyrrole A fails to show selective cytotoxicity for Mcl-1-dependent cell lines. Cell Death Dis. 2013 Oct 24;4:e880