

产品名称：马立马司他
产品别名：Marimastat

生物活性:					
Description	Marimastat (BB2516) is a broad spectrum and orally bioavailable inhibitor of MMPs, with potent activity against MMP-9 (IC ₅₀ =3 nM), MMP-1 (IC ₅₀ =5 nM), MMP-2 (IC ₅₀ =6 nM), MMP-14 (IC ₅₀ =9 nM) and MMP-7 (IC ₅₀ =13 nM), used in the treatment of cancer. Marimastat (BB2516) is an angiogenesis and metastasis inhibitor, which limits the growth and production of blood vessels. As an antimetastatic agent it prevents malignant cells from breaching the basement membranes[1][2].				
IC ₅₀ & Target	MMP-3	MMP-1	MMP-2	MMP-14	MMP-7
	3 nM (IC ₅₀)	5 nM (IC ₅₀)	6 nM (IC ₅₀)	9 nM (IC ₅₀)	13 nM (IC ₅₀)
In Vitro	Marimastat (BB2516) (1 μM) shows inhibition of vascular outgrowth, and selectively affects angiogenesis[3].				
In Vivo	Animals receiving chemoradiation + Marimastat (BB2516) (8.7 mg/kg) have statistically significant delayed growth, compared to animals receiving chemoradiation alone. Marimastat (BB2516) may work in combination with chemotherapy and radiation to inhibit tumor growth[4].				
Solvent&Solubility	In Vitro: DMSO : 100 mg/mL (301.74 mM; Need ultrasonic)				
	Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
		1 mM	3.0174 mL	15.0871 mL	30.1741 mL
		5 mM	0.6035 mL	3.0174 mL	6.0348 mL
		10 mM	0.3017 mL	1.5087 mL	3.0174 mL
	<p>*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。</p> <p>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。</p> <p>In Vivo:</p> <p>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：</p> <p>——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</p>				
	<p>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: ≥ 2.5 mg/mL (7.54 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (7.54 mM, 饱和度未知) 的澄清溶液。</p> <p>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。</p>				
	<p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 2.5 mg/mL (7.54 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (7.54 mM, 饱和度未知) 的澄清溶液。</p> <p>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</p>				

	<p>盐水水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (7.54 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (7.54 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 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</p>
References	<p>[1]. Rasmussen HS, et al. Matrix metalloproteinase inhibition as a novel anticancer strategy: a review with special focus on batimastat and marimastat. <i>Pharmacol Ther.</i> 1997;75(1):69-75.</p> <p>[2]. Yu M, et al. Incorporation of Bulky and Cationic Cyclam-Triazole Moieties into Marimastat Can Generate Potent MMP Inhibitory Activity without Inducing Cytotoxicity. <i>ChemistryOpen.</i> 2013 Jun;2(3):99-105.</p> <p>[3]. van Wijngaarden J, et al. An in vitro model that can distinguish between effects on angiogenesis and on established vasculature: actions of TNP-470, marimastat and the tubulin-binding agent Ang-510. <i>Biochem Biophys Res Commun.</i> 2010 Jan 8;391(2):1161-5.</p> <p>[4]. Skipper JB, et al. In vivo efficacy of marimastat and chemoradiation in head and neck cancer xenografts. <i>ORL J Otorhinolaryngol Relat Spec.</i> 2009;71(1):1-5.</p>
实验参考：	
Animal Administration	<p>Three-month-old female nude mice are inoculated using a trochar needle with 2 mm² established SCC-1 tissue subcutaneously in the flank. Treatment started once the tumors are 5-6 mm in diameter. Mice are randomly divided into groups of 8 mice to receive different treatments: (1) control, (2) marimastat alone, (3) cisplatin + radiation in combination and (4) marimastat + cisplatin + radiation in combination. All animals receive a 14-day osmotic pump containing dimethylsulfoxide (DMSO) as a control for both the pump and vehicle. Animals treated with marimastat receive the same osmotic pump containing 200 μL of marimastat with DMSO to result in a daily dose of 8.7 mg/kg 10 days after the initiation of treatment. Lead-shielded animals receive 8 Gy of 60Co radiation to the exposed tumor, divided into 4 fractions on days 8, 12, 16 and 20. A dose of 8 Gy is chosen because 7.5 Gy (7,500 rad) has been shown in previous experiments to inhibit tumor growth without being a curative dose. Animals receive 4 intraperitoneal doses of cisplatin (3 mg/kg) 1 h before each fraction of radiation. Tumors are measured biweekly for 32 days. Potential treatment toxicity is monitored using mouse weight. Tumor size (surface area equal to product of two largest diameters) and regression rates are determined in each treatment group. After 32 days, tumors are harvested for immunohistochemistry. Day 32 is chosen due to death of control group animals and euthanization of animals showing clinical signs of illness to allow for statistical analysis of data acquired from surviving animals. [3]</p>
Kinase Assay	<p>Compounds 1, 2, 7-9 and 11-16 are pre-incubated with MMP-1 or MMP-3 (10 nM) at different concentrations (0-10 μM) in a mixture of Tris-HCl (50 mM, pH 7.5), NaCl (150 mM), CaCl₂ (10 mM), NaN₃ (0.02%) and Brij-35 (0.05%) for 1 hour at 37°C. Residual activity is measured using the fluorogenic MMP substrate (2 μM) by fluorescence increase (emission at 393 nm and excitation at 325 nm) on a fluorescence plate reader. The data are fitted to the tight binding inhibitor equation: $v = \frac{[E-I-k+[(E-I-k)^2+4Ek]^{1/2}]}{(2E)}$, where v is the velocity of the reaction, E is the enzyme concentration, I is the initial inhibitor concentration, and k is the apparent inhibition constant, using</p>

	the software Prism. [1]
References	<p>[1]. Rasmussen HS, et al. Matrix metalloproteinase inhibition as a novel anticancer strategy: a review with special focus on batimastat and marimastat. <i>Pharmacol Ther.</i> 1997;75(1):69-75.</p> <p>[2]. Yu M, et al. Incorporation of Bulky and Cationic Cyclam-Triazole Moieties into Marimastat Can Generate Potent MMP Inhibitory Activity without Inducing Cytotoxicity. <i>ChemistryOpen.</i> 2013 Jun;2(3):99-105.</p> <p>[3]. van Wijngaarden J, et al. An in vitro model that can distinguish between effects on angiogenesis and on established vasculature: actions of TNP-470, marimastat and the tubulin-binding agent Ang-510. <i>Biochem Biophys Res Commun.</i> 2010 Jan 8;391(2):1161-5.</p> <p>[4]. Skipper JB, et al. In vivo efficacy of marimastat and chemoradiation in head and neck cancer xenografts. <i>ORL J Otorhinolaryngol Relat Spec.</i> 2009;71(1):1-5.</p>



源叶生物