

产品名称: **Birinapant**

产品别名: 比瑞那帕

生物活性:

Description	Birinapant (TL32711), a bivalent Smac mimetic, is a potent antagonist for XIAP and cIAP1 with K _d s of 45 nM and less than 1 nM, respectively. Birinapant (TL32711) induces the autoubiquitylation and proteasomal degradation of cIAP1 and cIAP2 in intact cells, which results in formation of a RIPK1: caspase-8 complex, caspase-8 activation, and induction of tumor cell death. Birinapant (TL32711) targets TRAF2-associated cIAPs and abrogates TNF-induced NF-κB activation.				
IC ₅₀ & Target	Kd: 45 nM (XIAP), <1 nM (cIAP1)[1]				
In Vitro	Birinapant (TL32711) (30-10000 nM; 24 hours) significantly decreases the viability of SUM190 cells in a dose-dependent manner[1].				
	Birinapant (TL32711) (30-1000 nM; 4 hours) shows a significant decrease in cIAP1 levels and enhanced PARP cleavage, and induces apoptosis[1].				
	Birinapant (TL32711) binds with high affinity to the isolated BIR3 domains of cIAP1, cIAP2, and XIAP and the single BIR domain of ML-IAP and rapidly degrades TRAF2-bound cIAP1 and cIAP2 thereby inhibiting TNF-mediated NF-κB activation[1].				
	Cell Viability Assay[1]				
	Cell Line:	TRAIL-resistant SUM190 IBC cells			
	Concentration:	30, 100, 300, 1000, 10000 nM			
	Incubation Time:	24 hours			
	Result:	Significantly decreased the viability of SUM190 cells in a dose-dependent manner.			
	Western Blot Analysis[1]				
	Cell Line:	SUM190 cells			
	Concentration:	30, 300, 1000 nM			
	Incubation Time:	4 hours			
Result:	Showed a significant decrease in cIAP1 levels and enhanced PARP cleavage.				
In Vivo	Birinapant (TL32711) (30 mg/kg; i.p.; every third day (*5)) shows antitumor efficacy and are devoid of overt toxicity in preclinical models[2].				
	Animal Model:	Female athymic nude mice (low-passage, patient-derived xenotransplant models of ovarian cancer, colorectal cancer, and melanoma)[2]			
	Dosage:	30 mg/kg			
	Administration:	Intraperitoneal injection; every third day (*5)			
	Result:	Resulted in inhibition of tumor growth.			
	In Vitro:				
	DMSO : ≥ 40 mg/mL (49.57 mM)				
	H ₂ O : < 0.1 mg/mL (insoluble)				
	* "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	<div>SolventMassConcentration</div>	1 mg	5 mg	10 mg
		1 mM	1.2392 mL	6.1962 mL	12.3925 mL
		5 mM	0.2478 mL	1.2392 mL	2.4785 mL
	10 mM	0.1239 mL	0.6196 mL	1.2392 mL	

<p>Solvent&Solubility</p>	<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><i>In Vivo:</i></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 Solubility: ≥ 2.08 mg/mL (2.58 mM); Clear solution</p> <p>此方案可获得 ≥ 2.08 mg/mL (2.58 mM，饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例，取 100 μL 20.8 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) Solubility: 2.08 mg/mL (2.58 mM); Suspended solution; Need ultrasonic</p> <p>此方案可获得 2.08 mg/mL (2.58 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 μL 20.8 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。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.08 mg/mL (2.58 mM); Clear solution</p> <p>此方案可获得 ≥ 2.08 mg/mL (2.58 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</p>
<p>References</p>	<p>[1]. Allensworth JL, et al. Smac mimetic Birinapant induces apoptosis and enhances TRAIL potency in inflammatory breast cancer cells in an IAP-dependent and TNF-α-independent mechanism. <u>Breast Cancer Res Treat. 2013 Jan;137(2):359-71.</u></p> <p>[2]. Krepler C, et al. The novel SMAC mimetic birinapant exhibits potent activity against human melanoma cells. <u>Clin Cancer Res. 2013 Apr 1;19(7):1784-94.</u></p> <p>[3]. Nguyen QD, et al. Temporal and spatial evolution of therapy-induced tumor apoptosis detected by caspase-3-selective molecular imaging. <u>Clin Cancer Res. 2013 Jul 15;19(14):3914-24.</u></p> <p>[4]. Benetatos CA, et al. Birinapant (TL32711), a bivalent SMAC mimetic, targets TRAF2-associated cIAPs, abrogates TNF-induced NF-κB activation, and is active in patient-derived xenograft models. <u>Mol Cancer Ther. 2014 Apr;13(4):867-79.</u></p>