

产品名称: **CC122**
 产品别名: **Avadomide**

生物活性:																		
Description	Avadomide (CC 122) is an orally available cereblon modulator. Avadomide modulates cereblon E3 ligase activity and exhibits potent antitumor and immunomodulatory activities[1].																	
In Vitro	Avadomide inhibits proliferation and induces apoptosis in ABC and GCB DLBCL. In DLBCL cell lines, Avadomide-induced degradation or short hairpin RNA-mediated knockdown of Aiolos and Ikaros correlates with increased transcription of IFN-stimulated genes independent of IFN- α , - β , and - γ production and/or secretion and results in apoptosis in both activated B-cell (ABC) and germinal center B-cell DLBCL.[1]																	
In Vivo	Treatment of female CB-17 SCID mice with Avadomide (CC122) at 3 or 30 mg/kg once daily significantly decreased tumor growth in OCI-LY10 ABC-DLBCL (P = .028 and P < .001, respectively) and WSU-DLCL2 GCB-DLBCL derived xenograft models (P < .01) compared with the vehicle control. In a separate study, we assessed the ability of Avadomide (CC122) to promote degradation of Ikaros and Aiolos in vivo. In the 21-day efficacy study of WSU-DLCL2 xenograft transplanted mice, tumors were excised 1, 6, or 24 hours post final dosing. Aiolos and Ikaros expression was interrogated through immunohistochemistry (IHC) and was found to be decreased 64% and 30%, respectively, compared with vehicle within 1 hour of treatment, with a maximal reduction of 94% and 69%, respectively, observed at 6 hours. Aiolos and Ikaros levels partially recovered 24 hours postdosing with protein level within 20% and 34% of vehicle, respectively. The 24-hour postdose Aiolos and Ikaros expression represents the trough compound level following multiple doses of Avadomide (CC122). When the 1-hour time point is compared with the 24-hour postdose time point, there is a significant reduction in Aiolos but not Ikaros expression; however, at the 6-hour time point, both transcription factors are significantly different from the 24-hour time point. Taken together, these data reveal that Avadomide (CC122) inhibited DLBCL tumor growth in vivo and that this activity was associated with the degradation of Aiolos and Ikaros in both ABC- and GCB-DLBCL xenograft models.[1]																	
Solvent&Solubility	<p>In Vitro: DMSO : ≥ 33 mg/mL (115.27 mM) * "≥" means soluble, but saturation unknown.</p>																	
	<table border="1"> <thead> <tr> <th rowspan="2">Preparing Stock Solutions</th> <th>Solvent Mass Concentration</th> <th>1 mg</th> <th>5 mg</th> <th>10 mg</th> </tr> </thead> <tbody> <tr> <td>1 mM</td> <td>3.4930 mL</td> <td>17.4648 mL</td> <td>34.9296 mL</td> </tr> <tr> <td>5 mM</td> <td>0.6986 mL</td> <td>3.4930 mL</td> <td>6.9859 mL</td> </tr> <tr> <td>10 mM</td> <td>0.3493 mL</td> <td>1.7465 mL</td> <td>3.4930 mL</td> </tr> </tbody> </table>	Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg	10 mg	1 mM	3.4930 mL	17.4648 mL	34.9296 mL	5 mM	0.6986 mL	3.4930 mL	6.9859 mL	10 mM	0.3493 mL	1.7465 mL	3.4930 mL
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<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。 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。</p>																		
References	<p>[1]. Rasco DW, et al. A First-in-Human Study of Novel Cereblon Modulator Avadomide (CC-122) in Advanced Malignancies. Clin Cancer Res. 2019 Jan 1;25(1):90-98.</p> <p>[2]. Hagner, P.R.et al.CC-122, a pleiotropic pathway modifier, mimics an IFN response and has antitumor activity in DLBCL.Blood.Aug 6;126(6):779-89.</p>																	
实验参考:																		

<p>Animal Administration</p>	<p>Female SCID mice (CB17/lcr-Prkdcscid, Charles River) were 8 weeks old, with body weights ranging from 15.0 to 23.2 g, on day 1 of these studies. Each SCID mouse was injected subcutaneously in the right flank with 5x10⁶ OCI-LY10 cells (0.2 ml cell suspension). Tumors were calipered in two dimensions to monitor growth as their mean volume approached 100–150 mm³. Fourteen days (WSU-DLCL2) or twenty-one days (OCI-LY10) after tumor cell implantation, mice were sorted into treatment groups (n=10/group). Tumors were callipered twice weekly during the study. Avadomide (CC122) was suspended in 0.5% carboxymethyl cellulose: 0.25% Tween-80 in de-ionized water. Vehicle and Avadomide (CC122) were each administered via oral gavage (p.o.) once daily for twenty-eight days (qd x28). [1]</p>
<p>References</p>	<p>[1]. Rasco DW, et al. A First-in-Human Study of Novel Cereblon Modulator Avadomide (CC-122) in Advanced Malignancies. Clin Cancer Res. 2019 Jan 1;25(1):90-98.</p> <p>[2]. Hagner, P.R.et al.CC-122, a pleiotropic pathway modifier, mimics an IFN response and has antitumor activity in DLBCL.Blood.Aug 6;126(6):779-89.</p>



源叶生物