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# 产品名称：2-[(2R)-2-甲基-2-吡咯烷基]-1H-苯并咪唑-4-甲酰胺二盐酸盐
# 产品别名：Veliparib dihydrochloride；维利帕尼二盐酸盐；ABT-888 dihydrochloride

## 生物活性：

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| **Description** | Veliparib (dihydrochloride) is a potent inhibitor of PARP1 and PARP2 with $K_i$s of 5.2 nM and 2.9 nM in cell-free assays, respectively. | |
| **$IC_{50}$ & Target** | PARP-2 | PARP-1 |
| | 2.9 nM (Ki) | 5.2 nM (Ki) |
| **In Vitro** | Veliparib is inactive to SIRT2 (>5 μM)[1]. Veliparib inhibits the PARP activity with EC50 of 2 nM in C41 cells[2]. Veliparib can decrease the PAR levels in both irradiated and nonirradiated H460 cells. Veliparib reduces clonogenic survival and inhibits DNA repair by PARP-1 inhibition in H460 cells. Veliparib increases apoptosis and autophagy in H460 cells when combination with radiation[3]. Veliparib inhibits PARP activity in H1299, DU145 and 22RV1 cells and the inhibition is independent of p53 function. Veliparib (10 μM) suppresses the surviving fraction (SF) by 43% in the clonogenic H1299 cells. Veliparib shows effective radiosensitivity in oxic H1299 cells. Veliparib can attenuate the SF of hypoxic-irradiated cells including H1299, DU145 and 22RV1[4]. | |
| **In Vivo** | The oral bioavailability of Veliparib is 56%-92% in mice, SD rats, beagle dogs, and cynomolgus monkeys after oral administration[1]. Veliparib (25 mg/kg, i.p.) can improve tumor growth delay in a NCI-H460 xenograft model. Combination with radiation, veliparib decreases the tumor vessel formation[3]. Veliparib reduces intratumor PAR levels by more than 95% at a dose of 3 and 12.5 mg/kg in A375 and Colo829 xenograft models and the suppression can be maintained over time[4]. | |
| **Solvent&Solubility** | ***In Vitro:*** | |
| | **$H_2O$ : ≥ 50 mg/mL (157.62 mM)** | |
| | **DMSO : ≥ 3.2 mg/mL (10.09 mM)** | |
| | * "≥" means soluble, but saturation unknown. | |

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 3.1525 mL | 15.7624 mL | 31.5249 mL |
| | 5 mM | 0.6305 mL | 3.1525 mL | 6.3050 mL |
| | 10 mM | 0.3152 mL | 1.5762 mL | 3.1525 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。

[1]. Donawho CK, et al. ABT-888, an orally active poly(ADP-ribose) polymerase inhibitor that potentiates DNA-damaging agents in preclinical tumor models. Clin Cancer Res. 2007 May 1;13(9):2728-37.

[2]. Penning TD, et al. Discovery of the Poly(ADP-ribose) polymerase (PARP) inhibitor 2-[(R)-2-methylpyrrolidin-2-yl]-1H-benzimidazole-4-carboxamide (ABT-888) for the treatment of cancer. J Med Chem. 2009 Jan 22;52(2):514-23.

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| **References** | [3]. Albert JM, et al. Inhibition of poly(ADP-ribose) polymerase enhances cell death and improves tumor growth delay in irradiated lung cancer models. Clin Cancer Res. 2007 May 15;13(10):3033-42.<br>[4]. Robert J. Kinders, et al. Preclinical Modeling of a Phase 0 Clinical Trial: Qualification of a Pharmacodynamic Assay of Poly (ADP-Ribose) Polymerase in Tumor Biopsies of Mouse Xenografts. Clin Cancer Res. Author manuscript; available in PMC 2009 Nov 1. |

**实验参考：**

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| **Animal Administration** | For B16F10 syngeneic studies, $6\times10^4$ cells are mixed with 50% Matrigel and inoculated by s.c. injection into the flank of 6- to 8-week-old female C57BL/6 mice (20 g). For cisplatin efficacy studies, female nude mice are implanted s.c. by trocar with fragments (20-30 $mm^3$) of human tumors harvested from s.c. grown tumors in nude mice hosts. For the carboplatin and MX-1 cyclophosphamide studies, female scid mice are inoculated with 200 μL of a 1:10 dilution of tumor brei in 45% Matrigel and 45% Spinner MEM. For these established tumor studies, tumors are allowed to grow to the indicated size and then randomized to therapy groups. For DOHH-2 xenograft studies, $1\times10^6$cells are mixed with 50% Matrigel and inoculated by s.c. injection into the flank of male scid mice. Veliparib is delivered by either oral route or continuous infusion using s.c. placement of 14-day Alzet OMP model 2002 in a vehicle containing 0.9% NaCl adjusted to pH 4.0. The OMP delivers at a rate of 12 μL daily and Veliparib doses are calculated accordingly. Temozolomide, cisplatin, carboplatin, and cyclophosphamide are formulated according to the manufacturers' recommendations. [1] |
| **Kinase Assay** | PARP assays are conducted in a buffer containing 50 mM Tris (pH 8.0), 1 mM DTT, 1.5 μM [$^3$H]$NAD^+$ (1.6 μCi/mmol), 200 nM biotinylated histone H1, 200 nM slDNA, and 1 nM PARP-1 or 4 nM PARP-2 enzyme. Reactions are terminated with 1.5 mM benzamide, transferred to streptavidin Flash plates, and counted using a TopCount microplate scintillation counter. [1] |
| **References** | [1]. Donawho CK, et al. ABT-888, an orally active poly(ADP-ribose) polymerase inhibitor that potentiates DNA-damaging agents in preclinical tumor models. Clin Cancer Res. 2007 May 1;13(9):2728-37.<br>[2]. Penning TD, et al. Discovery of the Poly(ADP-ribose) polymerase (PARP) inhibitor 2-[(R)-2-methylpyrrolidin-2-yl]-1H-benzimidazole-4-carboxamide (ABT-888) for the treatment of cancer. J Med Chem. 2009 Jan 22;52(2):514-23.<br>[3]. Albert JM, et al. Inhibition of poly(ADP-ribose) polymerase enhances cell death and improves tumor growth delay in irradiated lung cancer models. Clin Cancer Res. 2007 May 15;13(10):3033-42.<br>[4]. Robert J. Kinders, et al. Preclinical Modeling of a Phase 0 Clinical Trial: Qualification of a Pharmacodynamic Assay of Poly (ADP-Ribose) Polymerase in Tumor Biopsies of Mouse Xenografts. Clin Cancer Res. Author manuscript; available in PMC 2009 Nov 1. |