Berzosertib

Cat. No.: HY-13902  
CAS No.: 1232416-25-9  
Molecular Formula: C₂₄H₂₅N₅O₃S  
Molecular Weight: 463.55  
Target: ATM/ATR  
Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR  
Storage: Powder -20°C 3 years  
4°C 2 years  
In solvent -80°C 6 months  
-20°C 1 month

SOLVENT & SOLUBILITY

In Vitro  
DMSO : ≥ 35 mg/mL (75.50 mM)  
* " ≥ " means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass</th>
<th>Solvent Concentration</th>
<th>Solvent Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td></td>
<td></td>
<td></td>
<td>2.1573 mL</td>
<td>10.7863 mL</td>
<td>21.5726 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td></td>
<td></td>
<td>0.4315 mL</td>
<td>2.1573 mL</td>
<td>4.3145 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td></td>
<td></td>
<td>0.2157 mL</td>
<td>1.0786 mL</td>
<td>2.1573 mL</td>
</tr>
</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

In Vivo  
1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (5.39 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (5.39 mM); Clear solution

3. Add each solvent one by one: 10% Vitamin E d-alpha tocopheryl polyethylene glycol 1000 succinate
Solubility: 9.38 mg/mL (20.24 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description  
Berzosertib (VE-822) is an ATR inhibitor with a Kᵢ value of less than 0.2 nM. It also inhibits ATM with a Kᵢ of 34 nM.

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>ATR</th>
<th>ATM</th>
<th>PI3Kγ</th>
</tr>
</thead>
<tbody>
<tr>
<td>IC₅₀</td>
<td>0.2 nM (Kᵢ)</td>
<td>34 nM (Kᵢ)</td>
<td>220 nM (Kᵢ)</td>
</tr>
</tbody>
</table>

In Vitro  
Berzosertib (VE-822) also inhibits DNK-PA, mTOR, PI3Kγ with IC₅₀ of >4, >1, and 0.22 μM, respectively. In PSN-1 and MiaPaCa-
2 cells, Berzosertib (VE-822) inhibits ATR and ATM with IC_{50} of 19 nM and 2.6 μM, respectively. VE-822 (80 nM) reduces phosphorylation of Chk1 after NSC 613327 (100 nM), radiation (XRT) (6 Gy) or both in PDAC. Additionally, Berzosertib (VE-822) does not inhibit ATM, Chk2 or DNA-PK phosphorylation in response to radiation, which further supports the selectivity of Berzosertib (VE-822) for ATR. VE-822 decreases survival of irradiated PDAC (all lines used are p53-mutant; K-Ras mutant). Knock down of Chk1 by siRNA sensitizes PSN-1 and MiaPaCa-2 cells to radiation but the radiosensitising effect is less profound compared with Berzosertib (VE-822). Adding Berzosertib (VE-822) to NSC 613327 reduces survival ~2-3-fold and dramatically more after chemoradiotherapy[^1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### In Vivo

<table>
<thead>
<tr>
<th>PSN-1 xenografts are treated with Berzosertib (VE-822) (60 mg/kg; d0, 1), NSC 613327 (100 mg/kg; d0) and/or XRT (6 Gy; d1). Tumors are then harvested 2 h post-XRT. Berzosertib (VE-822) inhibits p-Ser-345-Chk1 in xenografts after DNA-damaging agents, establishing VE-822 as a potent inhibitor of ATR in vivo. Besides, Berzosertib (VE-822) enhances the therapeutic efficacy of radiation (XRT) in MiaPaCa-2 and PSN-1 xenograft models[^1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</th>
</tr>
</thead>
</table>

### PROTOCOL

**Cell Assay[^1]**

| NSC 613327 (10 nM) is added 24 h pre-XRT and is replaced with fresh medium before addition of Berzosertib (VE-822). PSN-1 cells are treated with Berzosertib (VE-822) (80 nM) for 1 h before, through to 18 h after, XRT (6 Gy). Apoptosis is analyzed 48 h after XRT by flow cytometry using an Annexin V-FITC kit with PI[^1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

**Animal Administration[^1]**

| MiaPaCa-2 cells and PSN-1 cells (10^6 in 50 μL serum-free medium mixed with 50 μL of Matrigel) are inoculated subcutaneously in female Balb/c nude mice. When the xenograft tumors reach 80 mm^3, the mice are randomized. Berzosertib (VE-822) (60 mg/kg) is administered by oral gavage on one of three alternate schedules; either daily on days 0-5 (total of six days dosing), daily on days 0 through to 3 (total of 4 days dosing) or on days 1, 3 and 5. XRT (6 Gy) is given either on days 0 or 1 or days 1-5 (total of 5 days dosing; 2 Gy). NSC 613327 is dosed at 100 mg/kg by intraperitoneal injection on day 0. XRT to the tumor is given 2 h after initiation of Berzosertib (VE-822) treatment. MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

### CUSTOMER VALIDATION


See more customer validations on [www.MedChemExpress.com](http://www.MedChemExpress.com)

### REFERENCES

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898  Fax: 609-228-5909  E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA