Venetoclax

Cat. No.: HY-15531
CAS No.: 1257044-40-8
Molecular Formula: C₄₅H₅₀ClN₇O₇S
Molecular Weight: 868.44
Target: Bcl-2 Family; Autophagy
Pathway: Apoptosis; Autophagy
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 : 77.5 mg/mL (89.24 mM; Need ultrasonic)
Ethanol : < 1 mg/mL (insoluble)
H₂O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Mass (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>1.1515 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.2303 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1151 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: ≥ 2.58 mg/mL (2.97 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (2.88 mM); Suspended solution; Need ultrasonic and warming

BIOLOGICAL ACTIVITY

Description
Venetoclax (ABT-199; GDC-0199) is a highly potent, selective and orally bioavailable Bcl-2 inhibitor with a Kᵢ of less than 0.01 nM. Venetoclax induces autophagy[1][2][3].

IC₅₀ & Target

<table>
<thead>
<tr>
<th>Target</th>
<th>IC₅₀ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bcl-2</td>
<td>0.01 nM (Ki)</td>
</tr>
<tr>
<td>Bcl-xL</td>
<td>48 nM (Ki)</td>
</tr>
<tr>
<td>Bcl-W</td>
<td>245 nM (Ki)</td>
</tr>
</tbody>
</table>

In Vitro
Venetoclax (ABT-199) potently kills FL5.12-BCL-2 cells (EC₅₀=4 nM); Venetoclax (ABT-199) shows much weaker
activity against FL5.12-BCL-XL cells (EC\textsubscript{50}=261 nM). ABT-199 also shows selectivity in cellular mammalian two-hybrid assays, where it disrupts BCL-2-BIM complexes (EC\textsubscript{50}=3 nM) but is much less effective against BCL-XL-BCL-XS (EC\textsubscript{50}=2.2 μM) or MCL-1-NOXA complexes\textsuperscript{[1]}.

**In Vivo**

After a single oral dose of 12.5 mg per kg body weight in xenografts derived from RS4;11 cells (ALL), Venetoclax (ABT-199) causes a maximal tumor growth inhibition (TGI\textsubscript{max}) of 47% (P<0.001) and tumor growth delay (TGD) of 26% (P<0.05)\textsuperscript{[1]}. Treatment of established xenografted (a mouse xenograft model of the T-ALL cell line LOUCY) tumors with Venetoclax (ABT-199) 100 mg/kg for 4 days results in a significant reduction of leukemic burden\textsuperscript{[2]}.

**PROTOCOL**

**Cell Assay**\textsuperscript{[1]}

RS4;11 cells are seeded at 50,000 per well in 96-well plates and treated with compounds diluted in half-log steps starting at 1 μM and ending at 0.00005 μM. All other leukemia and lymphoma cell lines are seeded at 15,000-20,000 cells per well in the appropriate medium and incubated with Venetoclax or Navitoclax for 48 h. Effects on proliferation are determined using Cell TiterGlo reagent. EC\textsubscript{50} values are determined by nonlinear regression analysis of the concentration-response data. Mouse FL5.12-BCL-2 and FL5.12-BCL-XL cells are propagated and assessed. Bak\textsuperscript{-/-}/Bax\textsuperscript{-/-} double knockout mouse embryonic fibroblasts are seeded into 96-well microtiter plates at 5,000 cells per well in DMEM supplemented with 10% FBS. Venetoclax (ABT-199) in the same culture medium is added in half-log dilutions starting at 5 μM. The cells are then incubated at 37°C (5% CO\textsubscript{2}) for 48 h, and the effects on proliferation are determined using Cell TiterGlo reagent\textsuperscript{[1]}.

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

**Animal Administration**\textsuperscript{[2]}

Mice\textsuperscript{[2]} Nonobese diabetic/severe combined immunodeficient γ (NSG) mice are injected at 6 weeks of age in the tail vein with 150 μL phosphate-buffered saline containing 5×10\textsuperscript{6} luciferase-labeled LOUCY cells. At regular time points, the bioluminescence is measured using the IVIS Lumina II imaging system. At 6 weeks, the cells are engrafted and the mice are randomly divided into 2 groups (with an equal number of males and females in both groups), and the treatment is started on day 0. Mice are treated with Venetoclax (ABT-199) 100 mg/kg body weight or with vehicle via oral gavage for 4 consecutive days. At days 0, 2, and 4 the bioluminescence is measured.

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

**CUSTOMER VALIDATION**

- Cell Metab. 2018 Oct.
- Immunity. 2019 May.

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

**REFERENCES**
