Product Name: Rocilinostat (ACY-1215)

Chemical Properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product Name</td>
<td>Rocilinostat (ACY-1215)</td>
</tr>
<tr>
<td>Cas No.</td>
<td>1316214-52-4</td>
</tr>
<tr>
<td>M.Wt</td>
<td>433.5</td>
</tr>
<tr>
<td>Formula</td>
<td>C24H27N5O3</td>
</tr>
<tr>
<td>Chemical Name</td>
<td>N-[7-(hydroxyamino)-7-oxoheptyl]-2-(N-phenylanilino)pyrimidine-5-carboxamide</td>
</tr>
<tr>
<td>Canonical SMILES</td>
<td>C1=CC=C(C=C1)N(C2=CC=CC=C2)C3=NC=C(C=N3)C(=O)NCCCCCCO(=O)NO</td>
</tr>
<tr>
<td>Solubility</td>
<td>≥21.675mg/mL in DMSO</td>
</tr>
<tr>
<td>Storage</td>
<td>Store at -20°C</td>
</tr>
<tr>
<td>General tips</td>
<td>For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.</td>
</tr>
<tr>
<td>Shopping Condition</td>
<td>Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request</td>
</tr>
</tbody>
</table>

Biological Activity

<table>
<thead>
<tr>
<th>Targets</th>
<th>DNA Damage/DNA Repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathways</td>
<td>HDAC</td>
</tr>
<tr>
<td>Description</td>
<td>Rocilinostat (ACY-1215) is a selective inhibitor of HDAC6 with IC50 of 5 nM [1]. HDAC6 (histone deacetylase 6) is an enzyme which encoded by the HDAC6 gene and plays an important role in translational regulation, cell cycle progression and developmental events. It has been revealed that over-expression of HDAC6 is correlated with tumorigenesis and cell survival and HDAC6 also involves in cancer cells metastasis [2] [3]. Rocilinostat (ACY-1215) is a selective HDAC6 inhibitor. When tested with human MM cell lines</td>
</tr>
</tbody>
</table>
(MM.1S), treatment with ACY-1215 in increasing dose for 6 hours increased acetylated α-tubulin at a concentration of 0.62μM via inhibiting HDAC6 [1]. In multiple myeloma cells, used ACY-125 as an adjuvant with carfilzomib triggered synergistic anti-MM effects, even in bortezomib-resistant cells which resulted in enhance cells apoptosis [2].

In mouse model with xenografted human MM cells, administration of ACY-125 only or with bortezomib could markedly delay tumor growth and the combination showed best efficacy [1]. It is also reported that ACY-1215 has minimal activity against HDAC4, HDAC5, HDAC7, HDAC9, HDAC11, Sirtuin1, and Sirtuin2 (IC50 > 1μM), and has slight activity against HDAC8 (IC50 = 0.1μM) [1]. When tested with mouse xenografted MM cells, combination carfilzomib with ACY-1215 showed a decreased effect on tumor volume and cells apoptosis [2].

Reference:

Protocol

Cell experiment:

Cell lines

MM cells; PBMCs.

Preparation method

Soluble in DMSO > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting conditions

0.16, 0.8, 4, 20 nM; MM cells: 24 h, PBMCs: 48 h.

Applications

ACY-1215 induces less cytotoxicity in PHA-stimulated or unstimulated PBMCs. In purified CD4+ T cells, ACY-1215 induces toxicity with IC50 value of 2.5 μM. In MM cell lines, ACY-1215 dose-dependently decreases viability with IC50 value of 2-8 μM and induces significant cytotoxicity. In MM.1S cells, ACY-1215 dose-dependently reduces DNA synthesis of MM cells adherent to BMSCs and also inhibits growth induced by IL-6 and IGF-1.

Animal experiment [3]:

Animal models

Male SCID mice inoculated subcutaneously with MM.1S cells.
Dosage form
50 mg/kg; 5 days a week for 3 weeks; administrated orally.

Applications
In human MM xenograft mouse model, ACY-1215 (50 mg/kg) significantly delays tumor growth. Treatment mice with ACY-1215 plus bortezomib significantly prolonged overall survival (OS) and induces a significant accumulation of polyubiquitinated proteins. Treatment with ACY-1215 plus bortezomib is well tolerated and have no significant influence on the body weight. In female SCID-beige mice inoculated intravenously with MM.1S-LucNeo cells, treatment with ACY-1215 (75 mg/kg) and bortezomib (1.5 mg/kg) significantly inhibits tumor growth and prolongs OS.

Preparation method
Dissolved in 10% DMSO in 5% dextrose in water

Other notes
Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:

Product Citations

Caution
FOR RESEARCH PURPOSES ONLY.
NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.