Product Data Sheet

Chemical Properties

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Ponatinib (AP24534)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cas No.:</td>
<td>943319-70-8</td>
</tr>
<tr>
<td>M.Wt:</td>
<td>532.56</td>
</tr>
<tr>
<td>Formula:</td>
<td>C29H27F3N6O</td>
</tr>
<tr>
<td>Chemical Name:</td>
<td>3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methylpiperazin-1-yl)methyl]-3-(trifluoromethyl)phenyl]benzamide</td>
</tr>
<tr>
<td>Canonical SMILES:</td>
<td>CC1=C(C=C(C=C1)C(=O)NC2=CC(=C(C=C2)CN3CCN(CC3)C(F)(F)F)C#CC4=CN=C5N4N=CC=C5</td>
</tr>
<tr>
<td>Solubility:</td>
<td>&gt;53.3mg/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

| Targets:              | Bcr-Abl |
| Pathways:             | TGF-β / Smad Signaling >> Bcr-Abl |
| Description:          | BCR-ABL fusion gene forms when the ABL gene from chromosome 9 joins to the BCR gene on chromosome 22. BCR-ABL is translated into a constitutively active tyrosine kinase, which is oncogenic. Depending on the fusion location, multiple protein variants are formed with molecular weight ranging from 185 to 210 kDa. BCR-ABL activates JAK/STAT pathway and MAPK signaling. [3] This gene is found in most patients with chronic myelogenous leukemia (CML), and in some patients with acute lymphoblastic leukemia (ALL) or acute myelogenous leukemia (AML). |
Ponatinib is the second-generation pan inhibitor of BCR-Abl kinases, which is also effective against the mutant form of BCR-Abl (T315I). [1, 2] IC50 for WT and mutant form are 0.5 and 11 nM. [4] Ponatinib also inhibits several other clinically relevant kinases (RET, FLT3, KIT, PDGFRα, PDGFRβ, and FGFR1) in vitro, with IC50s of 5, 25, 100, 5, 9, and 23) in Ba/F3 cells lines. [4]

Reference:

Protocol

**Cell experiment:**

**Cell lines**

BaF3 cells stably expressing ZMYM2-FGFR1 and CEP110-FGFR1 or BCR-FGFR1

**Preparation method**

The solubility of this compound in DMSO is >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**

48 hours, 50 nM for BaF3-ZMYM2, BAF3-CEP 100 nM for BaF3-BCR

**Applications**

Ponatinib treatment reduced phosphorylation FGFR1 levels. The percentage of cells in S-phase was also dramatically decreased, while the percentage of apoptotic cells was increased in the three different chimeric kinase-transformed BaF3 cells which suggested that their survival depended on activated FGFR1.
Animal experiment [3]:

Animal models
Female CB.17 severe combined immunodeficient mice injected with MV4-11 cells

Dosage form
Oral administration, 1–25 mg/kg, once daily for 4 weeks

Applications
Ponatinib potently inhibited tumor growth in a dose-dependent manner. Administration of 1 mg/kg, the lowest dose tested, led to significant inhibition of tumor growth (TGI = 46%, P < 0.01) and doses of 2.5 mg/kg or greater resulted in tumor regression. Notably, dosing with 10 or 25 mg/kg led to complete and durable tumor regression with no palpable tumors detected during a 31-day follow up.

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


Product Validation

Cell death induced by 2.5 μM ponatinib treatment is mediated via the caspase 3/7 pathway (*P=0.0029,**P=0.0027,***P=0.0017,****P=0.0001).
Treatment of Ponatinib induces apoptosis

Analysis on TIE2/ABL1 axes in NHEJ repair. Immunoblot of whole cell lysates derived from U251.EV and U251.Tie2 cells after transfection with 10nM siRNAs against TIE2 or ABL1, or treatment with ponatinib or imatinib at the indicated doses. SCIENCE ADVANCES01 APR 2016 : E1501290.

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. Short-term 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.

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