Pyrotinib

Cat. No.: HY-104065
CAS No.: 1269662-73-8
Molecular Formula: C₃₂H₃₁ClN₆O₃
Molecular Weight: 583.08
Target: EGFR
Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
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: 0.172 mg/mL (0.29 mM; Need ultrasonic and warming)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>1.7150 mL</td>
<td>8.5752 mL</td>
<td>17.1503 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3430 mL</td>
<td>1.7150 mL</td>
<td>3.4301 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1715 mL</td>
<td>0.8575 mL</td>
<td>1.7150 mL</td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description
Pyrotinib (SHR-1258) is a potent and selective EGFR/HER2 dual inhibitor with IC₅₀s of 13 and 38 nM, respectively.

IC₅₀ & Target

<table>
<thead>
<tr>
<th>EGFR</th>
<th>HER2</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 nM (IC₅₀)</td>
<td>38 nM (IC₅₀)</td>
</tr>
</tbody>
</table>

In Vitro
Pyrotinib has high potency in HER2-dependent cell lines (BT474, SK-OV-3), while showing much weaker inhibition in the HER2 negative cell line (MDA-MB-231). It inhibits BT474 and SK-OV-3 Pyrotinib cells with IC₅₀s of 5.1 and 43 nM, respectively. Pyrotinib displays high selectivity as HKI-272 when tested in a panel of different kinases such as KDR, c-Kit, PDGFRβ, c-Src and C-Met (c-Src with an IC₅₀ of 790 nM, and others over 3000 nM)[1].

In Vivo
Pyrotinib has acceptable bioavailability of 20.6%, 43.5% and 13.5% in nude mice, rats and dogs, respectively. Pyrotinib has favorable drug-like physicochemical properties and shows relatively higher oral exposure in human subjects with a much longer half life than that of preclinical animal species such as mouse, rat and dog. The TGI % (tumor growth inhibition) of Pyrotinib on day 21 is 109%, 157%, 159% at the doses of 5 mg/kg, 10 mg/kg, 20 mg/kg respectively.
Pyrotinib in SK-OV-3 ovarian xenograft model shows TGI% on day 21 of 2%, 12%, 83% at the doses of 2.5 mg/kg, 5 mg/kg, 10 mg/kg respectively), which further confirms its robust in vivo antitumor efficacy at 10 mg/kg\(^1\).

**PROTOCOL**

**Cell Assay**\(^1\)

Cancer cells (A431, SK-BR-3 and NCI-N87) are treated with a series of concentrations of Pyrotinib for 72 hours. Cell proliferation is determined by a sulforhodamine B (SRB) method. The IC\(_{50}\) values are calculated by the data of inhibition rates of serial concentrations of test compounds\(^1\).

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

**Animal Administration**\(^1\)

Rats: Test compounds (include Pyrotinib) are administrated in both intravenous (i.v.) and intragastric (i.g.) for mice to obtain their bioavailability. Plasma samples of nude mice is collected at pre-dose and 0.083, 0.25, 0.5, 1, 2, 4, 6, 8, 12, 24 h after the IV administration\(^1\).

Mice: In vivo efficacy studies are performed on BALB/Ca-nude mice (6 to 7 weeks, female) from SLAC. Nude mice are hypodermic inoculated BT-474 human breast cancer cell or SK-OV-3 ovarian cancer cell. After tumor grows to 150-250 mm\(^3\), mice are randomly divided into groups and dosed with Pyrotinib (2.5, 5, 10, 20 mg/kg) once daily. The volume of tumors and the weight of the mice are measured and recorded for 2-3 times per week\(^1\).

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

**REFERENCES**


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

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