Mubritinib

Cat. No.: HY-13501
CAS No.: 366017-09-6
Molecular Formula: C₂₅H₂₃F₃N₄O₂
Molecular Weight: 468.47
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 : 50 mg/mL (106.73 mM; Need ultrasonic)
H₂O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions
<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg</td>
<td></td>
</tr>
<tr>
<td>5 mg</td>
<td></td>
</tr>
<tr>
<td>10 mg</td>
<td></td>
</tr>
<tr>
<td>1 mM</td>
<td>2.1346 mL</td>
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<tr>
<td></td>
<td>10.6730 mL</td>
</tr>
<tr>
<td></td>
<td>21.3461 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4269 mL</td>
</tr>
<tr>
<td></td>
<td>2.1346 mL</td>
</tr>
<tr>
<td></td>
<td>4.2692 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2135 mL</td>
</tr>
<tr>
<td></td>
<td>1.0673 mL</td>
</tr>
<tr>
<td></td>
<td>2.1346 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 >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.34 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (5.34 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description
Mubritinib (TAK-165) is a potent and selective EGFR2/HER2 inhibitor with an IC₅₀ of 6 nM.

IC₅₀ & Target
HER2
6 nM (IC₅₀)

In Vitro
TAK-165 specifically inhibits HER2 tyrosine kinase with an IC₅₀ 6 nM and does not inhibit other types tyrosine kinase up to 25 000 nM. TAK-165 inhibits HER2 phosphorylation and its down-stream Akt and MAPK in HER2 strongly expressing cells (BT474 breast cancer cell line). TAK-165 sensitivity depends on HER2 levels of each cell line.
Especially, BT474 cells which over-express HER2 strongly is highly sensitive (IC\textsubscript{50}=0.005 \( \mu \)M) and PC-3 cells which express HER2 very weakly is less sensitive (IC\textsubscript{50}=4.62 \( \mu \)M). But, HT1376 and ACHN cells that over-expressed EGFR showed high IC\textsubscript{50} (IC\textsubscript{50}>25 \( \mu \)M)[1].

In Vivo

In the xenograft model, treatment with TAK-165 significantly inhibits growth of UMUC-3, ACHN, and LN-REC4. The antitumor effect after 14 days treatment are 22.9\%, 26.0\%, and 26.5\% in UMUC3, ACHN and LN-REC4, respectively[1].

PROTOCOL

Cell Assay[1]

Cells are treated with TAK-165 at various concentrations for 72 h. After the incubation period, the cells are counted. The IC\textsubscript{50} value is calculated from a dose–response curve generated by least-squares linear regression of the response [1].

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

Animal Administration[1]

Mice: UMUC-3 and LN-REC4 cells are implanted with 50\% Matrigel solution. After the tumor volume reaches 200–300 mm\textsuperscript{3} in LN-REC4 and UMUC-3 cells and to 100–200 mm\textsuperscript{3} in ACHN, the mice are treated orally twice daily for 14 days with vehicle (control) or 10 or 20 mg/kg per day of TAK-165. In the Herceptin study against UMUC-3, treatments consist of a twice weekly intraperitoneal injection of 20 mg/kg Herceptin in PBS for 2 weeks. Tumor growth is assessed by electronic caliper measurement of tumor diameter in two dimensions, and tumor volume is calculated[1].

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

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REFERENCES