Trametinib

Cat. No.: HY-10999
CAS No.: 871700-17-3
Molecular Formula: C₂₆H₂₃FIN₅O₄
Molecular Weight: 615.39
Target: MEK
Pathway: MAPK/ERK Pathway
Storage:
- Powder: -20°C 3 years, 4°C 2 years, In solvent -80°C 6 months, -20°C 1 month

Solvent & Solubility

In Vitro
10 mM in DMSO

<table>
<thead>
<tr>
<th>Solvent Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 mM</td>
<td>1.6250 mL</td>
<td>8.1249 mL</td>
<td>16.2499 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3250 mL</td>
<td>1.6250 mL</td>
<td>3.2500 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1625 mL</td>
<td>0.8125 mL</td>
<td>1.6250 mL</td>
</tr>
</tbody>
</table>

In Vivo
1. Trametinib is dissolved in 0.5% hydroxypropyl methylcellulose with 0.2% Tween 80[^5].
2. Trametinib (GSK1120212) is prepared in vehicle (10% Cremophor EL/10% PEG400)[^4].

BIOLOGICAL ACTIVITY

Description
Trametinib is a potent MEK inhibitor that inhibits MEK1 and MEK2 with IC₅₀ of about 2 nM. Due to the poor solubility of Trametinib, Trametinib DMSO solvate (Cat. No.: HY-10999A) is recommended.

IC₅₀ & Target
IC₅₀: 2 nM (MEK1/2)[^1]

In Vitro
Trametinib (0.1–100 nM) blocks tumor necrosis factor-α and interleukin-6 production from peripheral blood mononuclear cells (PBMCs). Trametinib (JTP-74057) inhibits the growth of 9 out of 10 human colorectal cancer cell lines, and they shows cell-cycle arrest at the G1 phase after drug treatment[^1]. The combination of GSK2118436 and Trametinib (GSK1120212) effectively inhibits cell growth, decreases ERK phosphorylation, decreases cyclin D1 protein, and increases p27(kip1) protein in the resistant clones[^2].
In Vivo

Adjuvant-induced arthritis (AIA) and type II collageninduced arthritis (CIA) development are suppressed almost completely by 0.1 mg/kg of Trametinib (JTP-74057) or 10 mg/kg of Leflunomide[1]. Trametinib (0.3 mg/kg, 1 mg/kg, p.o.) is effective in inhibiting the HT-29 xenograft growth in a nude mouse xenograft model[2].

PROTOCOL

Kinase Assay [2]

The nonphosphorylated myelin basic protein (MBP) is coated onto an ELISA plate, and the active form of B-Raf/c-Raf is mixed with unphosphorylated MEK1/MEK2 and ERK2 in 10 µM ATP and 12.5 mM MgCl₂ containing MOPS buffer in the presence of various concentrations of Trametinib (JTP-74057). The phosphorylation of MBP is detected by the anti-phosphoMBP antibody. Kinase inhibitory activities against a total of 99 kinases are tested at 10 µM ATP[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [2]

Cells are treated with various concentrations of Trametinib (JTP-74057) in 100 mm dishes for 3 or 4 days. Both floating and adherent cells are collected and fixed with 70% ethanol. After washing with PBS, the cells are suspended in 100 µL/mL RNase and 25 µL/mL Propidium iodide (PI) and incubated at 37°C for 30 min in the dark. The DNA content of each single cell is determined using the flow cytometer Cytomics FC500 or Guava EasyCyte plus[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [2]

Mice[2]
Female BALB/c-nu/nu mice are used. On day 0, HT-29 cells or COLO205 cells suspended in ice-cold HBSS (-) are inoculated subcutaneously into the right flank of the mice at 5×10⁶ cells/100 µL/site or 1×10⁶ cells/100 µL/site, respectively. The acetic acid-solvated form of Trametinib (JTP-74057, 0.3 mg/kg, 1 mg/kg) is dissolved in 10% Cremophor EL-10% PEG400 and is administered orally once daily for 14 days from the day when the mean tumor volume reached 100 mm³. The tumor length [L(mm)] and width [W(mm)] are measured using a microgauge twice a week after commencement of dosing, and the tumor volume is calculated using the following formula: tumor volume (mm³)=L×W×W/2.

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

CUSTOMER VALIDATION

- Cancer Discov. 2015 Sep;5(9):960-71.

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REFERENCES


