Trametinib

Cat. No.: HY-10999  
CAS No.: 871700-17-3  
Molecular Formula: C₂₆H₂₃FIN₅O₄  
Molecular Weight: 615.39  
Target: MEK; Autophagy; Apoptosis  
Pathway: MAPK/ERK Pathway; Autophagy; Apoptosis  
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 : 33.33 mg/mL (54.16 mM; Need ultrasonic)

<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>1.6250 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. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (4.06 mM); Clear solution  
2. Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (4.06 mM); Clear solution

BIOLOGICAL ACTIVITY

Description  
Trametinib (GSK1120212;JTP-74057) is a potent MEK inhibitor that inhibits MEK1 and MEK2 with IC₅₀s of about 2 nM.

IC₅₀ & Target  
<table>
<thead>
<tr>
<th>IC₅₀</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 nM</td>
<td>MEK1</td>
</tr>
<tr>
<td>2 nM</td>
<td>MEK2</td>
</tr>
</tbody>
</table>

In Vitro  
Trametinib (GSK1120212;JTP-74057) (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 collagen-induced arthritis (CIA) development are suppressed almost completely by 0.1 mg/kg of Trametinib (GSK1120212;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 MgCl\(_2\) 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\(^2\).

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### 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 5×10\(^6\) cells/100 µL/site or 1×10\(^6\) 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 mm\(^3\). 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 \((mm^3) = L \times W \times W / 2\).

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## CUSTOMER VALIDATION

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

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## REFERENCES


