**Inhibitors, Agonists, Screening Libraries**

**Data Sheet**

**Product Name:** Trametinib  
**Cat. No.:** HY-10999  
**CAS No.:** 871700-17-3  
**Molecular Formula:** C_{26}H_{23}FIN_{5}O_{4}  
**Molecular Weight:** 615.39  
**Target:** MEK  
**Pathway:** MAPK/ERK Pathway  
**Solubility:** DMSO: ≥ 69 mg/mL (Heating Trametinib at 80°C in DMSO for 10 min-30 min to get a clear solution and then cool to room temperature)[3]

**BIOLOGICAL ACTIVITY:**

Trametinib is a potent MEK inhibitor that specifically inhibits MEK1/2, with an IC_{50} value of about 2 nM. Due to the poor solubility of Trametinib, Trametinib DMSO solvate (Cat. No.: HY-10999A) is the more commonly used form.

**IC50 & Target:** IC_{50}: 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 collagen-induced 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 (Extracted from published papers and Only for reference)**

**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]. **Cell Assay:** Heating Trametinib at 80°C in DMSO for 10 min-30 min to get a clear solution and then cool to room temperature[3]. 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].

**Animal Administration:** Trametinib is dissolved in 10% Cremophor EL-10% PEG400 (Mice)[2][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×W×W/2.

**References:**


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

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