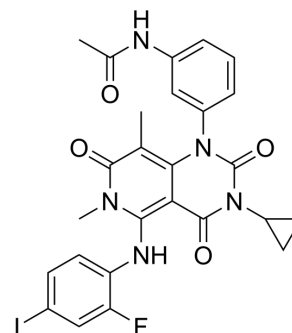


Trametinib

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; 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 : 25 mg/mL (40.62 mM; ultrasonic and warming and heat to 60°C)					
		Solvent Concentration	Mass	1 mg	5 mg	10 mg
	Preparing Stock Solutions	1 mM	1.6250 mL	8.1249 mL	16.2499 mL	
		5 mM	0.3250 mL	1.6250 mL	3.2500 mL	
10 mM		0.1625 mL	0.8125 mL	1.6250 mL		
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 0.5% HPMC/1% Tween-80 in Saline water Solubility: 6.67 mg/mL (10.84 mM); Suspended solution; Need ultrasonic 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 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 an orally active MEK inhibitor that inhibits MEK1 and MEK2 with IC ₅₀ s of about 2 nM. Trametinib activates autophagy and induces apoptosis ^{[1][2]} .	
IC₅₀ & Target	MEK1 2 nM (IC ₅₀)	MEK2 2 nM (IC ₅₀)
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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 HWA486^[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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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 μ M 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 μ M 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 μ L/mL RNase and 25 μ L/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 5×10^6 cells/100 μ L/site or 1×10^6 cells/100 μ L/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

- Cell. 2024 Feb 1;187(3):624-641.e23.
- Cell. 2024 Jan 4;187(1):166-183.e25.
- Cell. 2018 Aug 9;174(4):843-855.e19.
- Cancer Cell. 2024 Jun 21:S1535-6108(24)00226-5.
- Cancer Cell. 2023 Dec 11;41(12):2083-2099.e9.

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REFERENCES

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- [1]. Yamaguchi T, et al. Suppressive effect of an orally active MEK1/2 inhibitor in two different animal models for rheumatoid arthritis: a comparison with HWA486. *Inflamm Res*, 2012, 61(5), 445-454.
- [2]. Yamaguchi T, et al. Antitumor activities of JTP-74057 (GSK1120212), a novel MEK1/2 inhibitor, on colorectal cancer cell lines in vitro and in vivo. *Int J Oncol*, 2011, 39(1), 23-31.
- [3]. Abe H, et al. Discovery of a Highly Potent and Selective MEK Inhibitor: GSK1120212 (JTP-74057 DMSO Solvate). *ACS Med Chem Lett*. 2011 Feb 28;2(4):320-4.
- [4]. Liu H, et al. Identifying and Targeting Sporadic Oncogenic Genetic Aberrations in Mouse Models of Triple Negative Breast Cancer. *Cancer Discov*. 2018 Mar;8(3):354-369.
- [5]. Lai J, et al. Elimination of melanoma by sortase A-generated TCR-like antibody-drug conjugates (TL-ADCs) targeting intracellular melanoma antigen MART-1. *Biomaterials*. 2018 Sep;178:158-169.
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Caution: Product has not been fully validated for medical applications. For research use only.

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