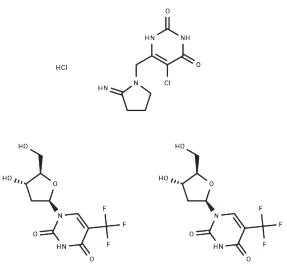
Data Sheet (Cat.No.T3658)

TargetMol

Trifluridine/tipiracil hydrochloride mixture

Chemical Properties



CAS No. : 733030-01-8

Formula: C29H34Cl2F6N8O12

Molecular Weight: 871.53

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Trifluridine/tipiracil hydrochloride mixture (TAS-102) is a novel oral combination drug containing trifluridine (TFT) and tipiracil hydrochloride (TTP) in a 2:1 molar ratio.
Targets(IC50)	Nucleoside Antimetabolite/Analog,DNA/RNA Synthesis
In vitro	Trifluridine/tipiracil hydrochloride mixture is an oral combination drug consisting of trifluridine (FTD), which is a thymidine-based nucleoside analog, and tipiracil hydrochloride (TPI), which improves the bioavailability of FTD by inhibiting its catabolism by thymidine phosphorylase (TP)[1]. Phosphorylated form of trifluridine is incorporated into DNA resulting in DNA dysfunction and cell cycle arrest. Thymidine phosphorylase inhibitor inhibits degradation of FTD and inhibits angiogenesis. Thus, Trifluridine/tipiracil hydrochloride mixture treatment results in massive trifluridine incorporation into DNA and in activation of similar DNA damage response pathways, which involve phosphorylation of Chk1 and cycle arrest during the G2/M-phase[2].
In vivo	The elimination half-life of FTD after intravenous administration to humans is very rapid (18 minutes), due to the rapid degradation of FTD to its major metabolite, 5-trifluoromethyl-2,4(1H,3H)-pyrimidinedione. In monkeys, the plasma FTD level after oral administration alone is very low, suggesting extensive first-pass metabolism by the liver and intestine TPase. However, the addition of TPI(tipiracil hydrochloride) is found to enable oral administration. By inhibiting TP, TPI inhibits the degradation of FTD in the liver and intestines following oral administration and thereby improves its bioavailability. The TP enzyme catalyzes the phosphorolysis of pyrimidine 2'-deoxynucleosides such as FTD. Studies using human CRC tumor xenografts in mice determine that the maximum antitumor activity is achieved with a 1:0.5 molar ratio, and studies in mice and monkeys show that the maximum plasma concentration of FTD is almost achieved with the same ratio. Moreover, this ratio produces a favorable balance between antitumor activity and toxicity. Lower toxicity in mice is observed with TPI coadministration than with FTD alone. Trifluridine/tipiracil hydrochloride mixture (FTD) can overcome acquired resistance to 5-FU because the main mechanism of Trifluridine/tipiracil hydrochloride mixture is not associated with main metabolic enzymes of 5-FU, such as TS and OPRT. Trifluridine/tipiracil hydrochloride mixture has demonstrated efficacy in 5-FU-refractory cancers[1].
Kinase Assay	IC50 determination of compounds against EGFR enzymes: The inhibition potency of compounds against EGFR WT and mutant enzymes is assessed using CisBio

Kinase Assay	homogenous time resolved fluorescence approach (HTRF, Cat No. 62TK0PEJ) according to manufacturer's instruction. The final enzyme concentrations used in this assay are 0.1 nM, 0.03 nM, and 0.026 nM for EGFR wild type, L858R and Exon19Del, respectively, and 0.8 μM, 4 μM and 25 μM ATP, corresponding to the Km values of EGFR enzymes, are applied accordingly. In brief, 3 μL of ATP and 2 μM TK biotin-peptide substrate are incubated in the presence or absence of serially diluted compound at room temperature in 384-well Greiner white polystyrene assay plates. The reaction is initiated by addition of 3 μL kinase which could phosphorylate the substrate peptide, and the assay buffer contains 1 mM DTT, 5 mM MgCl2, 1 mM MnCl2, and 0.01% CHAPS. After 30 minutes incubation, the reaction is stopped by the addition of 6 μl detection reagent mix containing 250 nM Strep-XL665 and TK Ab Europium Cryptate diluted in detection buffer. The plates are incubated for 1 h before the fluorescence is then measured at 615 nm and 665 nm, respectively with excitation wavelength at 320 nm by EnVision Multilabel Reader from Perkin Elmer using standard HTRF settings. The calculated signal ratio of 665 nm/615 nm is proportional to the kinase activity. The concentration of compound producing 50% inhibition of the respective kinase (IC50) is calculated using four-parameter logistic fit.

Solubility Information

Solubility	H2O: 50 mg/mL (57.37 mM),Sonication is recommended. Ethanol: 100 mg/mL (114.74 mM),Sonication is recommended. DMSO: 100 mg/mL (114.74 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.1474 mL	5.737 mL	11.4741 mL
5 mM	0.2295 mL	1.1474 mL	2.2948 mL
10 mM	0.1147 mL	0.5737 mL	1.1474 mL
50 mM	0.0229 mL	0.1147 mL	0.2295 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Lenz HJ, et al. Cancer Treat Rev. 2015, 41(9):777-83.
Luo P Q, Zhang L X, Chen Z M, et al.Effects and mechanisms of trifluridine alone or in combination with cryptotanshinone in inhibiting malignant biological behavior of gastric cancer.Cell Cycle.2023: 1-15.
Nukatsuka M, et al. Anticancer Res. 2015, 35(9):4605-15.
Li R, Liu L, Liu Y, et al.Unraveling the Role of PCDH9 in Breast Cancer and Identifying Therapeutic Strategies for PCDH9-Deficient Tumors.Breast Cancer: Targets and Therapy.2024: 583-593.

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481