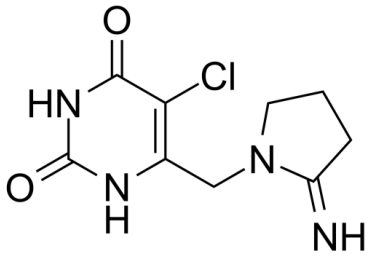
Data Sheet

Product Name:	Tipiracil
Cat. No.:	CS-5895
CAS No.:	183204-74-2
Molecular Formula:	C9H11ClN4O2
Molecular Weight:	242.66
Target:	Nucleoside Antimetabolite/Analog; Thymidylate Synthase
Pathway:	Apoptosis; Cell Cycle/DNA Damage
Solubility:	DMSO : < 1 mg/mL (insoluble or slightly soluble)



BIOLOGICAL ACTIVITY:

Tipiracil is a thymidine phosphorylase (**TPase**) inhibitor. IC50 & Target: thymidine phosphorylase[1] **In Vitro:** Tipiracil is an inhibitor of thymidine phosphorylase. Tipiracil increases trifluridine exposure by inhibiting its metabolism by thymidine phosphorylase. The combination of Trifluridine and Tipiracil is a new oral treatment for metastatic colorectal cancer[2]. Tipiracil prevents degradation of FTD through a first-pass effect as a thymidine phosphorylase inhibitor[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Tipiracil is dissolved with DMSO and diluted with appropriate media[3].[3]HeLa cells are seeded in 96-well plates at 500 cells/180 μL/well in triplicate, pre-cultured for 24 h, and then 20 μL of each drug solution is added for 24 or 72 h. For the 24 h treatment, cells are washed with phosphate-buffered saline (PBS) after treatment, drug-free medium is added to each well, and the culture is further incubated for 48 h. Cell growth inhibition is evaluated using a Cell Counting Kit-8. The 50% inhibitory concentration (IC_{50}) values are calculated from the absorbance data using SAS[3]. **Animal Administration:** Tipiracil (TPI) is dissolved in a 0.5% aqueous solution of HPMC at a molar ratio of 1:0.5 (Mice)[3].[3]Mice[3]

For experiments, 8 mm^3 cubic fragments of tumor are implanted subcutaneously into the axilla of mice. For preparation of the orally administered FTD solution, FTD is dissolved in a 0.5% aqueous solution of hydroxypropyl methyl-cellulose (HPMC). The FTD solution for continuous infusion is prepared by dissolving FTD in physiological saline. The TAS-102 dosing solution is composed of FTD and TPI dissolved in a 0.5% aqueous solution of HPMC at a molar ratio of 1:0.5. The dose of TAS-102 is expressed on the basis of the amount of FTD. For preparation of the S-1 solution, FT, CDHP and Oxo are dissolved in a 0.5% aqueous solution of HPMC at a molar ratio of 1:0.4:1. The dose of S-1 is expressed on the basis of the amount of FT. When the tumor volume reaches 100 mm^3, the mice are randomly assigned into different treatment groups. Nude mice in the treatment group receive the test compounds. The control group receive no treatment. For continuous infusion, the compound is administered with an osmotic pump. Tumor volume is measured twice a week throughout the experiments. Tumor volume and relative tumor volume are calculated. Body weight changes (BWCs) are used as a proxy measure of side-effects, and calculated. The tumor growth inhibition rate (IR) % on day 15 is used to quantify the antitumor effect.

References:

[1]. Lee SJ, et al. Thymidine phosphorylase influences [(18)F]fluorothymidine uptake in cancer cells and patients with non-small cell lung cancer. Eur J Nucl Med Mol Imaging. 2014 Jul;41(7):1327-35.

[2]. Raedler LA. Lonsurf (Trifluridine plus Tipiracil): A New Oral Treatment Approved for Patients with Metastatic Colorectal Cancer. Am Health Drug Benefits.

2016 Mar;9(Spec Feature):97-100.

[3]. Tanaka N, et al. Repeated oral dosing of TAS-102 confers high trifluridine incorporation into DNA and sustained antitumor activity in mouse models. Oncol Rep. 2014 Dec;32(6):2319-26.

CAIndexNames:

2,4(1H,3H)-Pyrimidinedione, 5-chloro-6-[(2-imino-1-pyrrolidinyl)methyl]-

SMILES:

O=C1NC(C(Cl)=C(CN2C(CCC2)=N)N1)=O

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

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