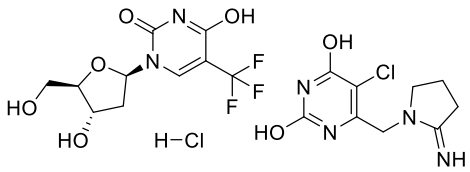
Product data sheet

MedKoo Cat#: 205641 Name: TAS-102 (Trifluridine/Tipiracil HCl) CAS#: 733030-01-8 Chemical Formula: $C_{19}H_{23}Cl_2F_3N_6O_7$ Molecular Weight: 575.3232	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

TAS-102 is an investigational drug candidate for metastatic colorectal cancer. It contains trifluridine (TFT) and Tipiracil hydrochloride (TTP) in a molar ratio of 1;0.5. Trifluridine is a nucleoside analog, and tipiracil hydrochloride is a thymidine phosphorylase inhibitor, which prevents rapid metabolism of trifluiridine, increasing the bioavailability of trifluiridine. After oral administration of TAS-102, TFT is phosphorylated to the active monophosphate form TF-TMP, which binds covalently to the active site of thymidylate synthase, thereby reducing the nucleotide pool levels required for DNA replication. Furthermore, the triphosphate form TF-TTP can be incorporated into DNA, which induces DNA fragmentation and leads to the inhibition of tumor growth. TPI exhibits a dual effect: 1) an anti-angiogenic effect mediated through the inhibition of thymidine phosphorylase, which plays an important role in nucleotide metabolism and a variety of development processes, including angiogenesis, 2) increased bioavailability of the normally short-lived antimetabolite TFT by preventing its degradation into the inactive form trifluorothymine (TF-Thy). The synergistic effect of the components in TAS-102 may demonstrate antitumor activity in 5-FU-resistant cancer cells.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under “QC And Documents” section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	51.17	88.94
DMF	20.0	34.76
Ethanol	100.0	173.82
Water	32.5	56.49

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.74 mL	8.69 mL	17.38 mL
5 mM	0.35 mL	1.74 mL	3.48 mL
10 mM	0.17 mL	0.87 mL	1.74 mL
50 mM	0.03 mL	0.17 mL	0.35 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of “Calculator”

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Li G, Liu H, He J, Li Z, Wang Z, Zhou S, Zheng G, He Z, Yang J. TAS-102 has a tumoricidal activity in multiple myeloma. Am J Cancer Res. 2020 Nov 1;10(11):3752-3764. PMID: 33294265; PMCID: PMC7716153.

2. Matsuoka K, Nakagawa F, Kobunai T, Takechi T. Trifluridine/tipiracil overcomes the resistance of human gastric 5-fluorouracil-refractory cells with high thymidylate synthase expression. Oncotarget. 2018 Feb 5;9(17):13438-13450. doi: 10.18632/oncotarget.24412. PMID: 29568368; PMCID: PMC5862589.

In vivo study

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1. Tanaka N, Sakamoto K, Okabe H, Fujioka A, Yamamura K, Nakagawa F, Nagase H, Yokogawa T, Oguchi K, Ishida K, Osada A, Kazuno H, Yamada Y, Matsuo K. 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. doi: 10.3892/or.2014.3487. Epub 2014 Sep 17. PMID: 25230742; PMCID: PMC4240496.
2. Temmink OH, Emura T, de Bruin M, Fukushima M, Peters GJ. Therapeutic potential of the dual-targeted TAS-102 formulation in the treatment of gastrointestinal malignancies. Cancer Sci. 2007 Jun;98(6):779-89. doi: 10.1111/j.1349-7006.2007.00477.x. Epub 2007 Apr 18. PMID: 17441963.

7. Bioactivity

Biological target:

Trifluridine-tipiracil hydrochloride mixture (TAS-102) is a combination drug that consists of an antineoplastic thymidine-based nucleoside analog, trifluorothymidine, and a potent thymidine phosphorylase inhibitor, tipiracil, in a 1:0.5 molar ratio.

In vitro activity

In Figure 1, TAS-102 treatment also induced apoptosis in the p53-null myeloma cells ARP-1 and JJN3, which indicated that there might be other signaling pathways involved in TAS-102 induced myeloma cell apoptosis. Previous studies have shown that the cytosolic DNA sensing cGAS-STING pathway is greatly important for the cells in response to DNA damage. This pathway can promote cellular apoptosis through the transcriptional activation of apoptotic regulators as well as through a transcription-independent role of IRF3. The expression level of cGAS, STING, the cleaved level of PARP, Caspase 3, and the phosphorylated level of IRF3, TBK1 were upregulated in either wide-type MM.1S myeloma cells or the p53-knockout cells (MM.1S p53 KO), while the level of non-cleaved PARP, Caspase 3, the level of non-phosphorylated TBK1, IRF3 were not changed, and the level of GAPDH protein served as protein loading controls (Figure 3A). STING expression was knocked down in wild type or MM.1S p53 KO myeloma cells using the specific small interfering RNAs (siRNAs) against STING (siSTING). Reduced apoptosis was observed in the siSTING myeloma cells, compared with that in siCtrl cells, after TAS-102 treatment (Figure 3B and 3C). These results indicate an additional mechanism of TAS-102-induced myeloma cell apoptosis through activation of the cGAS-STING pathway.

Reference: Am J Cancer Res. 2020; 10(11): 3752–3764. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7716153/

In vivo activity

To investigate the kinetics of FTD (trifluridine) incorporation into DNA, this study followed the process during TAS-102 treatment of mice harboring KM20C human colon cancer xenografts (Fig. 5A and B). TAS-102 treatment (150 mg/kg/day, twice daily for 14 days) was compared to oral administration of S-1 once daily for 14 days. TAS-102 and S-1 had similar antitumor effects (IR of 50.2 and 51.4%, respectively). FTD accumulated in the DNA of KM20C xenografts in a time-dependent manner throughout the administration of TAS-102. Compared to S-1 treatment, the growth suppressive effect of TAS-102 appeared more sustained (Fig. 5A).

Reference: Oncol Rep. 2014 Dec; 32(6): 2319–2326. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4240496/