Trifluridine-tipiracil hydrochloride mixture

Cat. No.: HY-16478
CAS No.: 733030-01-8
Molecular Formula: C₁₀H₁₁F₃N₂O₅ · ½C₉H₁₁ClN₄O₂ · ½HCl
Molecular Weight: 435.76
Target: Nucleoside Antimetabolite/Analogue; Thymidylate Synthase
Pathway: Cell Cycle/DNA Damage; Apoptosis
Storage: Powder
              -20°C  3 years
              4°C   2 years
In solvent
              -80°C  6 months
              -20°C  1 month

SOLVENT & SOLUBILITY

<table>
<thead>
<tr>
<th></th>
<th>In Vitro</th>
<th>DMSO : 2.34 mg/mL (5.37 mM; Need ultrasonic and warming)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H₂O : &lt; 0.1 mg/mL (insoluble)</td>
<td></td>
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<tr>
<td>Preparing Stock Solutions</td>
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<tr>
<td></td>
<td>DMSO</td>
<td>1 mg</td>
</tr>
<tr>
<td></td>
<td>1 mM</td>
<td>2.2948 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.4590 mL</td>
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<tr>
<td></td>
<td>10 mM</td>
<td>0.2295 mL</td>
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</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description
Trifluridine-tipiracil hydrochloride mixture (TAS-102) is a novel oral 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
Trifluridine-tipiracil hydrochloride mixture (TAS-102), a novel antimetabolite combination chemotherapy agent, consists of a rediscovered antimetabolite agent, trifluorothymidine (trifluridine, FTD) combined with the metabolic inhibitor of thymidine phosphorylase, tipiracil (TPI), in a 1:0.5 molar ratio[1]. FTD is the active antitumor component of Trifluridine-tipiracil hydrochloride mixture (TAS-102); its monophosphate form inhibits thymidylate synthase, and its triphosphate form is incorporated into DNA in tumor cells. The incorporation into DNA is known to have antitumor effects, since the inhibition of thymidylate synthase caused by oral FTD rapidly disappears after the drug’s elimination. When FTD is administered orally, it is rapidly degraded to its inactive form by thymidine phosphorylase in the intestines and liver (first-pass effect). Consequently, TPI is synthesized to maintain adequate plasma concentrations of orally-administered FTD and to potentiate the antitumor activity of FTD[2].
Trifluridine-tipiracil hydrochloride mixture (TAS-102) and CPT-11 is a promising treatment option for colorectal or gastric cancer. Trifluridine-tipiracil hydrochloride mixture monotherapy has a significant antitumor activity against KM12C/5-FUFU-bearing nude mice. The combination-treated (CPT-11-and Trifluridine-tipiracil hydrochloride mixture) group is significantly superior to monotherapy[2]. FTD systemic exposure in plasma increases dose-dependently. The tumor growth rate and body weight gain decrease dose-dependently, but FTD concentrations in the DNA of tumor tissues and white blood cells increase dose-dependently. FTD inhibits colony formation of bone marrow cells in a concentration-dependent manner[3].

**PROTOCOL**

**Animal Administration** [2]

Mice: Trifluridine-tipiracil hydrochloride mixture is prepared by mixing FTD and TPI at a molar ratio of 1:0.5 in 0.5% HPMC. The dose of TAS-102 is expressed according to the amount of FTD. Trifluridine-tipiracil hydrochloride mixture is administered orally from day 1 to 14, twice a day, with approximately a 6-hour interval at the reported effective dose (150 mg/kg/day) (7,11). For the control group, 0.5% HPMC alone is administered at 10 ml/kg according to a similar schedule. CPT-11 (40 mg/kg) is administered intravenously on days 1 and 8, once a day. The tumor diameters are measured twice a week, and the tumor volume is estimated[2].

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

**REFERENCES**

