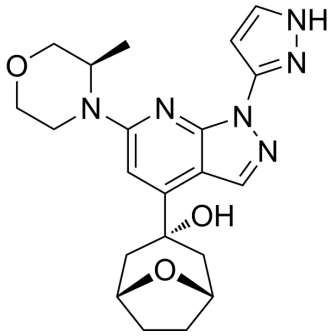
Camonsertib

Cat. No.:	HY-139609
CAS No.:	2417489-10-0
Molecular Formula:	$C_{21}H_{26}N_6O_3$
Molecular Weight:	410.47
Target:	ATM/ATR; mTOR
Pathway:	Cell Cycle/DNA Damage; PI3K/Akt/mTOR
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (121.81 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4362 mL	12.1812 mL	24.3623 mL
	5 mM	0.4872 mL	2.4362 mL	4.8725 mL
	10 mM	0.2436 mL	1.2181 mL	2.4362 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (3.05 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (3.05 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (3.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Camonsertib (RP-3500) is an orally active, selective ATR kinase inhibitor (ATRi) with an IC_{50} of 1.00 nM in biochemical assays. Camonsertib shows 30-fold selectivity for ATR over mTOR (IC_{50}=120 nM) and >2,000-fold selectivity over ATM, DNA-PK, and PI3Kα kinases. Camonsertib has potent antitumor activity[1].

IC_{50} & Target	ATR	ATM	mTOR
		>30 μM (IC_{50})	120 nM (IC_{50})

In Vitro

Camonsertib (RP-3500; 1 μM; 1-24 hours) inhibits CHK1(Ser345) phosphorylation from 1 to 3 hours[1].

Camonsertib inhibits Gemcitabine stimulated ATR phosphorylation of its substrate pCHK1(Ser345) with an IC_{50} of 0.33 nM in a LoVo cell-based assay[1].

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

Western Blot Analysis[1]

Cell Line:	LoVo and CW-2 human colon cancer cell lines
Concentration:	1 μM
Incubation Time:	1, 2, 4, 6, 8, 16, 24 hours
Result:	Inhibited CHK1(Ser345) phosphorylation from 1 to 3 hours. Starting at 4 hours, CHK1(Ser345) became re-phosphorylated as DNA-PKcs became activated in treated cells, along with its substrates KAP1 and H2AX.

In Vivo

Camonsertib (RP-3500; 3, 7, 15 mg/kg; Orally; once daily for 18 days) produces dose-dependent tumor growth inhibition with a minimum effective dose (MED) of 7 mg/kg in LoVo xenografts[1].

Camonsertib (5, 10 mg/kg; Orally; once daily) produces statistically significant tumor growth inhibition in the CW-2 colon xenograft model[1].

Camonsertib (7 mg/kg; for 7 days) results in 8.1- and 2.7-fold inductions of KAP1 and DNA-PKcs phosphorylation in mice bearing LoVo tumors[1].

Camonsertib has a more profound anti-tumor effect occurred at higher doses on the 3 days on/4 days off (30 mg/kg) and 5 days on/2 days off (25 mg/kg) schedules compared with consecutive daily administrations (10 mg/kg) at a lower dose for 14 days[1].

Camonsertib (15mg/kg) combined PARPi Olaparib (80mg/kg; both agents days 1-3 on/4 days off) or sequential (PARPi for 3 days followed by RP-3500 for 3 days then 1 day off) schedules produces greater antiTumor effects compared with sequential administration without affecting tolerability[1].

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

Animal Model:	Female mice (6-8 weeks old) bearing LoVo xenografts[1]
Dosage:	3, 7, 15 mg/kg (0.5% methylcellulose/0.02% SDS vehicle)
Administration:	Orally; once daily for 18 days
Result:	Produced dose-dependent tumor growth inhibition with a minimum effective dose (MED) of 7 mg/kg. The maximum tolerated dose (MTD) was 10 mg/kg once daily on a continuous dosing schedule.

REFERENCES

[1]. Anne Roulston, et al. RP-3500: A Novel, Potent and Selective ATR Inhibitor that is Effective in Preclinical Models as a Monotherapy and in Combination with PARP Inhibitors. Mol Cancer Ther

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