UCT943

Cat. No.: HY-112435

CAS No.: 1450666-80-4

Molecular Formula: $C_{22}H_{20}F_3N_5O$

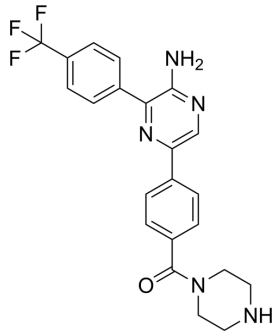
Molecular Weight: 427.42

Target: PI4K; Parasite

Pathway: PI3K/Akt/mTOR; Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (584.90 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3396 mL	11.6981 mL	23.3962 mL
5 mM	0.4679 mL	2.3396 mL	4.6792 mL
10 mM	0.2340 mL	1.1698 mL	2.3396 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: ≥ 2.08 mg/mL (4.87 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.87 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.87 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

UCT943 is a next-generation Plasmodium falciparum PI4K inhibitor. UCT943 inhibits the P. vivax PI4K (PvPI4K) enzyme with an IC_{50} of 23 nM[1].

IC_{50} & Target

PvPI4K 23 nM (IC_{50})	Plasmodium

In Vitro

UCT943 maintains high in vitro selectivity (>200-fold) for the parasite PvPI4K versus the human PI4Kβ isozyme (IC_{50} of PI4Kβ,

5.4 μM), inhibition of which is linked to immunosuppressive effects[1].
In vitro cytotoxicity of UCT943 is tested against L6 cells, chinese hamster ovarian (CHO), Vero, and HepG2 cells, with 50% cytotoxic concentrations (CC_{50}s) of 12, 17, 113, and 13 μM, respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

UCT943 shows excellent in vivo efficacy in the Plasmodium berghei (10 mg/kg and 3 mg/kg; oral administration; daily; 4 days) and P. falciparum NSG (NOD-scid IL-2Rγ^{null}) mouse models (0.01, 0.1, 0.3, 1.1 and 10 mg/kg; oral administration; once per day; 4 days). When dosed at 10 mg/kg per os (p.o.), UCT943 reduces parasitemia by >99.9% in the mouse P. berghei infection model and cures all mice, with >30 mean survival days (MSD). At 3 mg/kg p.o., no complete cure is achieved, and MSD is 10 days, albeit parasitemia is reduced by 99%. The resulting 90% effective dose (ED_{90}) is 1.0 mg/kg p.o. in the P. berghei infection model. The ED_{90} is 0.25 mg/kg in the P. falciparum-infected NSG mouse model[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Mice with P. berghei and P. falciparum NOD-scid IL-2Rγ^{null} (NSG) models[1]
Dosage:	10 mg/kg and 3 mg/kg for P. berghei model; 0.01, 0.1, 0.3, 1.1 and 10 mg/kg for P. falciparum NOD-scid IL-2Rγ^{null} (NSG) model
Administration:	Oral administration; daily; 4 days for P. berghei model Oral administration; once per day; 4 days for P. falciparum NOD-scid IL-2Rγ^{null} (NSG) model
Result:	The ED_{90} is 1.0 mg/kg in the P. berghei infection model. The ED_{90} is 0.25 mg/kg in the P. falciparum-infected NSG mouse model.

REFERENCES

[1]. Brunschwig C, et al. UCT943, a Next-Generation Plasmodium falciparum PI4K Inhibitor Preclinical Candidate for the Treatment of Malaria. Antimicrob Agents Chemother. 2018 Aug 27;62(9). pii: e00012-18.

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