NVP-TNKS656

Cat. No.: HY-13990

CAS No.: 1419949-20-4

Molecular Formula: $C_{27}H_{34}N_4O_5$

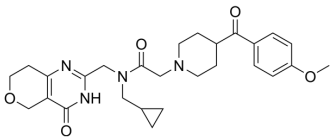
Molecular Weight: 494.58

Target: PARP; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 35 mg/mL (70.77 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0219 mL	10.1096 mL	20.2192 mL
5 mM	0.4044 mL	2.0219 mL	4.0438 mL
10 mM	0.2022 mL	1.0110 mL	2.0219 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: ≥ 3.5 mg/mL (7.08 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 3.5 mg/mL (7.08 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3.5 mg/mL (7.08 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NVP-TNKS656 is a highly potent, selective, and orally active TNKS2 inhibitor with IC_{50} of 6 nM, and is > 300 fold selectivity against PARP1 and PARP2.

IC_{50} & Target

TNKS2	PARP2
6 nM (IC_{50})	32 μM (IC_{50})

In Vivo

NVP-TNKS656 (30 or 100 mg/kg, p.o.) exhibits good exposure and moderate oral bioavailability of 32% and 53%,

respectively. Some slight overproportional increase in oral exposure is observed between 30 and 100 mg/kg with the dose normalized AUC for the 100 mg/kg dose being 2-fold higher than for the 30 mg/kg dose. Mice treated with NVP-TNKS656 (350 mg/kg, p.o.) show good plasma and tumor exposures corresponding to $AUC_{0\text{-}24h}$ of 515 and 325 μM·h, respectively[1].

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

PROTOCOL

Animal Administration [1]

Athymic female nude mice weighing 19-22 g are implanted subcutaneously with a 3×3×3 mm^3 tumor fragment from an MMTV-Wnt1 tumor-bearing mouse. Tumors are grown to approximately 250-300 mm^3. Individual mice are given a single oral dose of vehicle (n=3) (4% HCl:10% propylene glycol:20% Solutol HS15:60.5% D5W:0.5% NaOH) or TNKS656 at 350 mg/kg (n=18). At 0.5, 1, 2, 4, 8, 16, or 24 h following dosing (n=3/time point), mice are euthanized, and blood is collected via cardiac puncture and processed for plasma. Tumors are excised from mice and frozen at −80°C for PD analysis.

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

REFERENCES

[1]. Shultz MD, et al. Identification of NVP-TNKS656: the use of structure-efficiency relationships to generate a highly potent, selective, and orally active tankyrase inhibitor. J Med Chem. 2013 Aug 22;56(16):6495-511.

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