HPK1-IN-40-d_2

Cat. No.: HY-149773S

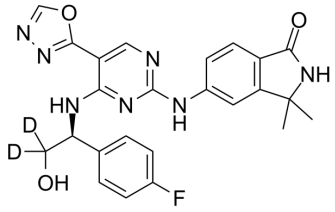
Molecular Formula: $C_{24}H_{20}D_2FN_7O_3$

Molecular Weight: 477.49

Target: MAP4K

Pathway: MAPK/ERK Pathway

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

HPK1-IN-40 (compound 49) is a potent and selective HPK1 inhibitor with an IC_{50} of 0.9 nM. HPK1-IN-40 reinvigorates T-cell receptor (TCR) signaling, promoting T-cell function and cytokine production in T cells while having anti-cancer activity[1].

IC_{50} & Target

HPK1[1] IC_{50}: 0.9 nM[1]

In Vitro

HPK1-IN-40 (0.1 μM, 1 μM) improves the IL-2 secretion of Jurkat cells , leads to augmented T cell function[1].
HPK1-IN-40 (0.03 μM ~ 1 μM)inhibits the HPK1 signaling in T cells[1].

Pharmacokinetic Parameters of HPK1-IN-40 in Rats[1]

Route	Parameter	Rat (1 mg/kg)
IV	$T_{1/2}$(h)	0.898
	AUC_{last}(h*ng/mL)	355
	V_{ss}(L/kg)	2.45
	Cl_{hep} (mL/min/kg)	46.8
Route	Parameter	Rat (3 mg/kg)
PO	$T_{1/2}$ (h)	0.499
	T_{max} (h)	0.250
	AUC_{last}(h*ng/mL)	1.91
	C_{max} (ng/mL)	3.62

F%	0.179

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

Western Blot Analysis[1]

Cell Line:	Jurkat, primary mouse T cells
Concentration:	0.03, 0.1, 0.3, 1 (μM)
Incubation Time:	1h
Result:	Inhibited the HPK1 signaling in T cells.

In Vivo

HPK1-IN-40 alone (25 mg/kg; i.p.; bid for 7 days) in CT26 tumor-bearing mice causes T cell activation[1].
HPK1-IN-40 (25 mg/kg; i.p.; bid for 10 days) combines with anti-PD1 antibody (10 mg/kg; i.p.; bid for 10 days) shows synergistic antitumor effects, the CT26 tumor growth rate of HPK1-IN-40 combined with anti-PD1 antibody is the lowest. No significant body weight loss was observed, indicative of good tolerance of the treatment [1].

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

Animal Model:	CT26 Tumor-bearing mice
Dosage:	25 mg/kg
Administration:	Twice a day by intraperitoneal injection (i.p.), bid for 7 days.
Result:	Increased IFN-γ$^+$CD3$^+$ T in CD3$^+$ TIL, IFN-γ$^+$CD8$^+$ T in CD8$^+$ TIL, Th1 in CD4$^+$ TIL, CD69$^+$CD3$^+$ T in CD3$^+$ TIL, CD69$^+$CD8$^+$ T in CD8$^+$ TIL, CD69$^+$CD4$^+$ T in CD4$^+$ TIL.

Animal Model:	CT26 Tumor-bearing mice
Dosage:	HPK1-IN-40 (25 mg/kg), anti-PD1 antibody (10 mg/kg)
Administration:	HPK1-IN-40 alone / anti-PD1 antibody alone (every 3 days), or the combination treatment, twice a day by intraperitoneal injection (i.p.) for 10 days.
Result:	Showed marginal tumor growth inhibition (TGI = 19.6%). The CT26 tumor growth rate of HPK1-IN-40 combined with anti-PD1 antibody was the lowest, then anti-PD1 alone, then HPK1-IN-40. No significant body weight loss was observed.

REFERENCES

[1]. Jing Ai, et al. Design, Synthesis, and Pharmacological Evaluation of Isoindoline Analogues as New HPK1 Inhibitors. Journal of Medicinal Chemistry. 2023 Article ASAP.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA