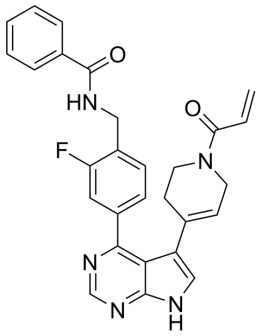
BTK-IN-15

Cat. No.:	HY-150752
CAS No.:	2820426-92-2
Molecular Formula:	$C_{28}H_{24}FN_5O_2$
Molecular Weight:	481.52
Target:	Btk; Pyroptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis; Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

BTK-IN-15 (compound 42) is a potent Bruton's tyrosine kinase (BTK) inhibitor with high oral absorption. BTK-IN-15 inhibits BTK with an IC_{50} value of 0.7 nM. BTK-IN-15 displays excellent kinase selectivity, antitumor activity, and induces apoptosis[1].

IC_{50} & Target

IC50: 0.7 nM (BTK)[1]

In Vitro

BTK inhibition is an effective approach against B-cell malignancies[1].
BTK-IN-15 (compound 42) demonstrates inhibitory against TMD8 with an IC_{50} value of 2.6 nM[1].
BTK-IN-15 (1 μM; 1 h) displays significant selectivity to BTK over EGFR kinase with 0.05% and 44% of the control, respectively[1].
BTK-IN-15 (0-1 mM; 72 h) exerts potent anti-proliferative activity against a human mantle cell lymphoma cell line (REC-1) with an IC_{50} value of 1.7 nM[1].
BTK-IN-15 (0-1 mM; 2 h) inhibits BTK auto-phosphorylation with an IC_{50} value of 1.49 nM[1].
BTK-IN-15 (0-100 nM; 48 h) arrests cell cycle at G1 phase and (0-1 mM; 72 h) induces apoptosis in TMD8[1].
BTK-IN-15 shows low hERG channel activity (IC_{50}=4.38 μM), indicating low cardiotoxicity[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	B-cell lymphoma (DLBCL) TMD8 cancer cells
Concentration:	0, 0.15, 0.46, 1.37, 4.12, 12.35, 37.04, 111, 333, 1000 nM
Incubation Time:	2 hours
Result:	Inhibited BTK auto-phosphorylation at the Tyr223 site with an IC_{50} value of 1.49 nM.

Cell Cycle Analysis[1]

Cell Line:	B-cell lymphoma (DLBCL) TMD8 cancer cells
Concentration:	0, 10, 100 nM
Incubation Time:	48 hours
Result:	Arrested cell cycle progression at G1 phase in a dose-dependent manner, the percentage of cells in the G0/G1 phase increased from 33.0 to 63.0% with a dose range of 1-100 nM.

Apoptosis Analysis[1]

Cell Line:	B-cell lymphoma (DLBCL) TMD8 cancer cells
Concentration:	0, 10, 100, 1000 nM
Incubation Time:	72 hours
Result:	Induced apoptosis of TMD8 cells in a weakly triggered concentration-dependent manner, with the apoptosis cell values of 19% (10 nM), 25.2% (100 nM), and 31.4% (1000 nM), respectively.

In Vivo

BTK-IN-15 (compound 42) (12.5-50 mg/kg; p.o.; twice daily; 21 d) inhibits tumor growth (TGI = 104%) at a dosage of 50 mg/kg in mice[1].

BTK-IN-15 (300, 400, 500 mg/kg; p.o.; twice daily; 14 d) has biological safety and displays no affect against body weight in mice compared with control[1].

BTK-IN-15 (10 mg/kg; p.o.) shows a high oral bioavailability of 40.98% in mice[1].

Pharmacokinetics of BTK-IN-15 in Mice[1]

Route	Dose (mg/kg)	T_{max} (h)	C_{max} (ng/mL)	$AUC_{(0-t)}$ (h•ng/mL)	$AUC_{(0-\infty)}$ (h•ng/mL)	$T_{1/2}$ (h)	V_z (L/kg)	CL (L/h/kg)	F (%)
i.v.	2	0.03	2245.39	1471.35	718.33	0.67	2.79	2.87	40.98
p.o.	10	0.39	1441.59	718.33	1472.06	0.59			

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

Animal Model:	Female CB-17 SCID nude mice with TMD8 xenograft model[1]
Dosage:	12.5 mg/kg, 25 mg/kg, and 50 mg/kg
Administration:	Oral gavage; twice daily; 21 days
Result:	Inhibited tumor growth at a dosage of 50 mg/kg and reduced tumor volume after 21 days with a TGI of 104%. Reduced the content of white blood cells, lymphocytes and monocytes, while showed no effect on red blood cell and platelets.

Animal Model:	ICR mice (acclimation for 5 days, 18-20 g)[1]
Dosage:	300, 400, 500 mg/kg
Administration:	Oral gavage; 14 days
Result:	Demonstrated no affect against body weight in mice compared with control.

REFERENCES

[1]. Minjian Yang, et al. Design, synthesis, and biological evaluation of pyrrolopyrimidine derivatives as novel Bruton's tyrosine kinase (BTK) inhibitors. EUR J MED. 2022 Jul. 114611.

Caution: Product has not been fully validated for medical applications. For research use only.

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