PROTAC BTK Degrader-5

Cat. No.: HY-155072

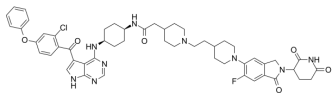
Molecular Formula: $C_{52}H_{57}ClFN_9O_6$

Molecular Weight: 958.52

Target: Btk

Pathway: Protein Tyrosine Kinase/RTK

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



BIOLOGICAL ACTIVITY

Description

PROTAC BTK degraders-5(compound 3e) is a selective BTK degrader with a DC_{50} value of 7.0 nM in JeKo-1 cells. PROTAC BTK degraders-5 has no off-target effect on degrading CRBN neosubstates. PROTAC BTK degraders-5 has anti-proliferation effect on various lymphoma tumor cells and can be used in chronic lymphoid malignancies research[1].

In Vitro

PROTAC BTK Degrader-5 (Compound 3e) (1.6~1000 nM; 24 h) induces BTK degradation with DC_{50} value of 7.0 nM in JeKo-1 cells[1].

PROTAC BTK Degrader-5 (100 and 1000 nM) possesses the metabolic stability with the $T_{1/2}$ of 145 min[1].

PROTAC BTK Degrader-5 (100 nM;12 h) induced - BTK degradation blocks by proteasome inhibitor MG - 132 (HY-13259) (5 μM)[1].

PROTAC BTK Degrader-5 (1.6~1000 nM; 24 h) has no effect on the levels of IKZF1 and GSPT1 and mild effect on the level of IKZF3[1].

PROTAC BTK Degrader-5 (72 h) has anti- proliferation effect in OCI-ly10, TMD8, JeKo-1 and BTK ^{C481S} Ba/F3 cells with the IC_{50} values of 2.3, 4.5, 38.1 and 86.0 nM, which were higher than Ibrutinib (HY-10997)(IC_{50} value of 4.5, 4.7, 79.8, and 1546.0 nM, respectively)[1].

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

In Vivo

PROTAC BTK Degrader-5 (2 mg/kg for i.v, sigle dose) is metabolically stable in mice[1].

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Animal Model:	The male Balb/c mice[1]
Dosage:	a single dose 2 mg/kg or 100 mg/kg, 5% DMSO, 10% Solutol, 85% saline
Administration:	Intravenous injection (i.v.); Oral gavage (p.o.)
Result:	Maintained above 10 nM for at least 4 h after administration of PROTAC BTK Degrader-5 at a single dose of 2 mg/kg via intravenous (IV) injection in the plasma (the effective BTK degradation DC_{50}50 = 7.0nM). Had poor oral bioavailability at a dose of 100 mg/kg.

REFERENCES

[1]. Song Chen, et al. Discovery of novel BTK PROTACs with improved metabolic stability via linker rigidification strategy. European Journal of Medicinal Chemistry.Volume 255, 5 July 2023, 115403.

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