

Product Data Sheet

Product Name: CB-5339

Cat. No.: GC20117

Chemical Properties

Cas. No. 1863952-15-1

Chemical Name 1-(4-(benzylamino)-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-2-yl)-2-methyl-1H-indole-4-carboxamide

SMILES O=C(N)C1=CC=CC2=C1C=C(C)N2C3=NC(NCC4=CC=CC=C4)=C(CCCN5)C5=N3

Formula $C_{24}H_{24}N_6O$ M.Wt 412.49

Solubility DMSO : 41.67 mg/mL Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

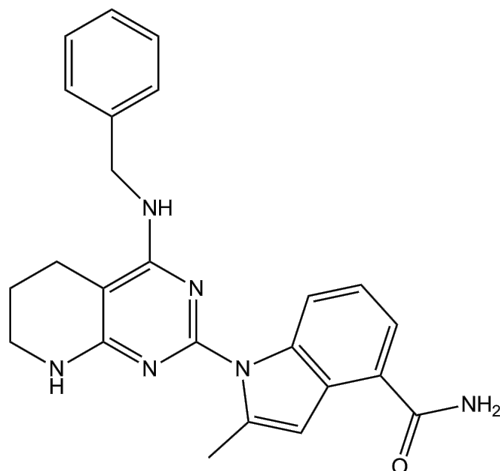
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment [1]:

Cell lines HCT-116 cells

HCT-116 cells (2000 cells per well) were seeded in 96-well cell culture plates at a volume of 90µl per well, and cultured at 37°C with 5% CO₂ for 24 hours. CB-5339 was dissolved in DMSO (concentration less than 0.1%) and diluted to Preparation Method different concentrations (0, 0.1, 0.5, 1, 2, 4, 6, 8, and 10µM). Then, different concentrations of CB-5339 were incubated with the cells together under 37°C and 5% CO₂ conditions. After 72 hours of treatment, the absorbance at 450 nm was measured to determine the cell viability.

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Reaction Conditions 0, 0.1, 0.5, 1, 2, 4, 6, 8, and 10 μ M; 72h

Applications CB-5339 treatment significantly inhibited the viability of HCT-116 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models Male NSG mice

Preparation Method Male NSG mice were raised under standard conditions. 2×10^5 MLL-AF9 cells were injected into the tail veins of 8-week-old male NSG mice. After confirming the successful establishment of the xenograft model, the mice were randomly divided into two groups and treated with CB-5339 (90mg/kg/day; p.o.) or normal saline (0.5% methylcellulose) for 4 days. Then, peripheral blood samples of the mice were collected for analysis.

Dosage form 90mg/kg/day for 4 days; p.o.

Applications CB-5339 treatment decreased circulating leukemic cells and prolonged mice survival.

References:

[1] Wang X, Wen T, Miao H, et al. Discovery of a new class of valosine containing protein (VCP/P97) inhibitors for the treatment of colorectal cancer[J]. Bioorganic & Medicinal Chemistry, 2022, 74: 117050.

[2] Roux B, Vaganay C, Vargas J D, et al. Targeting acute myeloid leukemia dependency on VCP-mediated DNA repair through a selective second-generation small-molecule inhibitor[J]. Science translational medicine, 2021, 13(587): eabg1168.

Background

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CB-5339 is a potent and selective, orally bioavailable small molecule inhibitor of valosin containing protein (VCP)/p97, with an IC_{50} value of 9nM^[1]. CB-5339 targets the D2 ATPase domain of p97, effectively inhibiting p97 function, triggering the accumulation of ubiquitinated proteins, and inducing proteotoxic stress^[2]. CB-5339 has been widely used as an anti-cancer agent to inhibit the proliferation of solid tumors and hematological tumors^[3].

In vitro, CB-5339 treatment for 72 hours significantly inhibited the proliferation of HCT-116 cells, with an IC_{50} value of $0.7 \pm 0.07 \mu M$ ^[4]. After 48 hours of treatment with CB-5339, the viability of 17-71 cells and DH82 cells was significantly inhibited, with IC_{50} values of 188nM and 486nM, respectively^[5]. Treatment with 2 μM CB-5339 for 7 days significantly induced senescence in RBE cells^[6].

In vivo, CB-5339 treatment (90mg/kg; p.o.) for 4 days reduced the number of circulating leukemia cells in the MLL-AF9 syngeneic mouse model and prolonged the survival time of the mice^[7]. CB-5339 (50mg/kg/day; p.o.) combined with venetoclax (30mg/kg/day; p.o.) for 3 weeks significantly reduced the acute myelocytic leukemia (AML) burden in NSG mice, and increased the median survival time and overall survival time, without causing obvious toxicity^[8].

References:

- [1] Kilgas S, Ramadan K. Inhibitors of the ATPase p97/VCP: From basic research to clinical applications[J]. Cell Chemical Biology, 2023, 30(1): 3-21.
- [2] Carrera Espinoza M J, Tucker S K, Sureshkumar S, et al. Harnessing p97/VCP: A Transformative AAA+ ATPase Target for Next-Generation Cancer Therapeutics[J]. Cancers, 2025, 17(18): 2945.
- [3] Benajiba L, Carraway H E, Hamad N, et al. Trials in progress: a phase I study to evaluate the safety and pharmacokinetic profiles of CB-5339 in participants with relapsed/refractory acute myeloid leukemia or relapsed/refractory intermediate or high-risk myelodysplastic syndrome[J]. Blood, 2020, 136: 21.
- [4] Wang X, Wen T, Miao H, et al. Discovery of a new class of valosine containing protein (VCP/P97) inhibitors for the treatment of colorectal cancer[J]. Bioorganic & Medicinal Chemistry, 2022, 74: 117050.
- [5] LeBlanc A K, Mazcko C N, Fan T M, et al. Comparative oncology assessment of a novel inhibitor of valosin-containing protein in tumor-bearing dogs[J]. Molecular cancer therapeutics, 2022, 21(10): 1510-1523.

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- [6] Yang W, Wang S, Ji S, et al. CRISPR screens identify the ATPase VCP as a druggable therapeutic vulnerability in cholangiocarcinoma[J]. Proceedings of the National Academy of Sciences, 2025, 122(39): e2519568122.
- [7] Roux B, Vaganay C, Vargas J D, et al. Targeting acute myeloid leukemia dependency on VCP-mediated DNA repair through a selective second-generation small-molecule inhibitor[J]. Science translational medicine, 2021, 13(587): eabg1168.
- [8] Fiskus W C, Das K, Mill C P, et al. Efficacy of Vcp/p97 inhibitor, CB-5339, alone and in combinations against high-risk AML, including those with genetic lesion in TP53[J]. 2022.

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