Iberdomide

Cat. No.: HY-101291

CAS No.: 1323403-33-3

Molecular Formula: $C_{25}H_{27}N_3O_5$

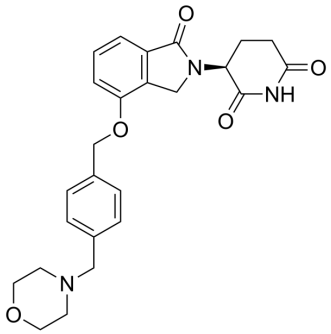
Molecular Weight: 449.5

Target: Ligands for E3 Ligase; Apoptosis; Molecular Glues

Pathway: PROTAC; 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 : 125 mg/mL (278.09 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2247 mL	11.1235 mL	22.2469 mL
	5 mM	0.4449 mL	2.2247 mL	4.4494 mL
	10 mM	0.2225 mL	1.1123 mL	2.2247 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: ≥ 2.08 mg/mL (4.63 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.63 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.63 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Iberdomide (CC-220) is an orally active and potent cereblon (CRBN) E3 ligase modulator (CELMoD) with an IC_{50} of ~150 nM for cereblon-binding affinity. Iberdomide, a derivative of Thalidomide (HY-14658), has antitumor and immunostimulatory activities[1][2].

In Vitro

Iberdomide (CC-220; 0.01, 0.1, 1, 10 μM; 72-96 hrs) has antiproliferative effects in a panel of multiple myeloma (MM) cell lines (EJM, H929, KMS11, KMS128M, KMS12PE, MM1.S, MM1.R, RPM-8226, U266 cells) across a range of concentrations[1].
Iberdomide (0.1 μM; 96 hrs) induces apoptosis in all MM cell lines[1].

	Iberdomide (0.1 μM; 24, 48, 72 hrs) results in time-dependent increases in G0/G1 and sub-G1 cell cycle fractions on H929 cells [1]. Iberdomide leads to rapid Aiolos depletion in the KMS12BM line[1]. Iberdomide (0.1 μM) displays some anti-proliferative activity in two of the Pomalidomide-resistant (PR) lines with cereblon mutations (EJM/PR and H929/PR) along with decreased levels of cereblon protein[1]. Iberdomide (0.1-1000 nM; 72 hrs) equally induces PBMC-mediated killing of both parental MM1.S cells and MM1.S/PR cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Iberdomide (CC-220; 10 mg/kg; oral gavage) after 6 or 24 hours causes higher hCRBN expression in hC343 splenocytes correlated to deeper IKZF1/3 downregulation in WT (C57BL/6), hC123, or-343, (representing two different transgenic founder lines expressing hCRBN) and mCrbn$^{-/-}$ mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Iberdomide is dissolved in DMSO. In the assay, 60 nM 6Xhis-tagged CRBN-DDB1 is combined with 30 nM cy5-conjugated cereblon modulator and 3 nM LanthaScreen Eu-anti-His Tag antibody in 20 mM HEPES pH 7, 150 mM NaCl, 0.005% Tween-20 assay buffer. FRET is observed by exciting at 340 nm and monitoring emission at 615 nm and 665 nm, and FRET efficiency is determined by the ratio of FRET to non-FRET emission. Competing cereblon modulating compound (Iberdomide) or DMSO carrier is titrated and incubated for 10 min before scanning[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Host Microbe. 2020 Mar.
- Nat Cancer. 2022 May;3(5):595-613.
- Nat Commun. 2022 Sep 10;13(1):5324.
- Blood Cancer J. 2019 Feb 11;9(2):19.
- Cell Chem Biol. 2020 Jul 16;27(7):866-876.e8.

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REFERENCES

[1]. Chad C Bjorklund, et al. Iberdomide (CC-220) is a potent cereblon E3 ligase modulator with antitumor and immunostimulatory activities in lenalidomide- and pomalidomide-resistant multiple myeloma cells with dysregulated CRBN. Leukemia. 2020 Apr;34(4):1197-1201.

[2]. Erin W Meermeier, et al. Tumor burden limits bispecific antibody efficacy through T cell exhaustion averted by concurrent cytotoxic therapy. Blood Cancer Discov. 2021 Jul;2(4):354-369.

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

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