Maritoclax

Cat. No.: HY-15613

CAS No.: 1227962-62-0

Molecular Formula: $C_{22}H_{12}Cl_4N_2O_4$

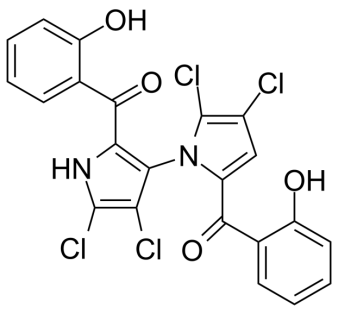
Molecular Weight: 510.15

Target: Bcl-2 Family

Pathway: 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 : ≥ 43 mg/mL (84.29 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9602 mL	9.8010 mL	19.6021 mL
	5 mM	0.3920 mL	1.9602 mL	3.9204 mL
	10 mM	0.1960 mL	0.9801 mL	1.9602 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: ≥ 2.5 mg/mL (4.90 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.90 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Maritoclax (Marinopyrrole A) is a novel and specific Mcl-1 inhibitor with an IC_{50} value of 10.1 μM, and shows >8 fold selectivity than BCL-xl (IC_{50} > 80 μM).

IC_{50} & Target

Mcl-1

10.1 μM (IC_{50})

In Vitro

Maritoclax (Marinopyrrole A) blocks the binding of Bim BH3 α-helix to Mcl-1 but not Bcl-XL. Maritoclax (Marinopyrrole A) markedly inhibits the viability of Mcl-1-IRES-BimEL cells (EC_{50}=1.6 μM) with a selectivity greater than 40-fold over Bcl-2-IRES-BimEL (EC_{50}=65.1 μM) and Bcl-XL-IRES-BimEL (EC_{50}=70.0 μM) cells. Maritoclax (Marinopyrrole A) induces cell death selectively in Mcl-1-dependent but not Bcl-2- or Bcl-XL-dependent leukemia cells. Maritoclax (Marinopyrrole A) induces proteasome-mediated Mcl-1 degradation without induction of Mcl-1 phosphorylation and Noxa expression. Maritoclax (Marinopyrrole A) inhibits Mcl-1 interaction with Bim in intact cells and triggers cytochrome c release from isolated mitochondria. Maritoclax (Marinopyrrole A) synergistically sensitizes lymphoma/leukemia cells to ABT-737[1]. Maritoclax (Marinopyrrole A) shows activity against all tested S. aureus strains, including glycopeptide-intermediate and vancomycin-resistant MRSA, and has potent activities against other Gram-positive organisms. In addition, Maritoclax (Marinopyrrole A) is active against H. influenzae but is inactive against other tested Gram-negative strains. Maritoclax (Marinopyrrole A) displays substantial concentration-dependent killing against MRSA strain TCH1516 and is far more rapid in its antibiotic action than either vancomycin or linezolid. Maritoclax exhibits a favorable therapeutic index, with 50% inhibitory concentrations (IC_{50}) in excess of 20× above the MIC in each case: 32 to 64 μg/mL against HeLa cells and 8 to 32 μg/mL against L929 cells[2]. Maritoclax (Marinopyrrole A) (3 μM) induced-cell death is associated with MCL1 decrease and translation inhibition. Maritoclax (Marinopyrrole A) induces a dephosphorylation of EIF4EBP1 concomitant to a decrease of EIF4E phosphorylation [3]. Maritoclax (Marinopyrrole A) is much more effective against Bcl-2-dependent RS4;11 cells (IC_{50}: 2 μM) when compared to Mcl-1-dependent HeLa cells (IC_{50}: 20 μM)[4].

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

PROTOCOL

Cell Assay [2]

Maritoclax (Marinopyrrole A) cytotoxicity is assessed by seeding 2×10^4 HeLa or L929 cells per well in sterile 96-well tissue culture-treated plates. After 24 h, the medium is replaced with fresh medium containing increasing concentrations of marinopyrrole A, and the plates are incubated at 37°C in 5% CO_2 for 24 h. Cytotoxicity is assayed at 24 h by measuring the reduction of MTS [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium] using the CellTiter 96 Aqueous nonradioactive cell proliferation assay according to the manufacturer's instructions.

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

CUSTOMER VALIDATION

- Cell Metab. 2019 May 7;29(5):1045-1060.e10.
- Cell Death Differ. 2020 Mar;27(3):999-1007.
- bioRxiv. 2020 May.
- bioRxiv. 2018 Nov.
- Biochem Biophys Rep. 2018 Jul 13;15:69-75.

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REFERENCES

[1]. Doi K, et al. Discovery of marinopyrrole A (maritoclax) as a selective Mcl-1 antagonist that overcomes ABT-737 resistance by binding to and targeting Mcl-1 for proteasomal degradation. J Biol Chem. 2012 Mar 23;287(13):10224-35.

[2]. Haste NM, et al. Pharmacological properties of the marine natural product marinopyrrole A against methicillin-resistant Staphylococcus aureus. Antimicrob Agents Chemother. 2011 Jul;55(7):3305-12.

[3]. Gomez-Bougie P, et al. The selectivity of Marinopyrrole A to induce apoptosis in MCL1high BCL2low expressing myeloma cells is related to its ability to impair protein translation. Br J Haematol. 2016 Aug 14.

[4]. Eichhorn JM, et al. Purported Mcl-1 inhibitor marinopyrrole A fails to show selective cytotoxicity for Mcl-1-dependent cell lines. Cell Death Dis. 2013 Oct 24;4:e880

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