Alisporivir

Cat. No.: HY-12559

CAS No.: 254435-95-5

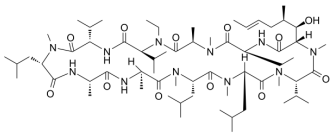
Molecular Formula: $C_{63}H_{113}N_{11}O_{12}$

Molecular Weight: 1216.64

Target: HCV

Pathway: Anti-infection

Storage: Stored under nitrogen, away from moisture
Powder -80°C 2 years
-20°C 1 year
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (82.19 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	0.8219 mL	4.1097 mL	8.2194 mL
5 mM	0.1644 mL	0.8219 mL	1.6439 mL
10 mM	0.0822 mL	0.4110 mL	0.8219 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
Solubility: ≥ 2.62 mg/mL (2.15 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (2.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Alisporivir (Debio-025) is a cyclophilin inhibitor molecule with potent anti-hepatitis C virus (HCV) activity.

In Vitro

DEB025 binds to CypA, a peptidyl-prolyl cis-trans isomerase which is a crucial cofactor for HCV replication[1]. Alisporivir (Debio-025) represents the prototype of a new class of non-immunosuppressive cyclophilin inhibitors. Alisporivir prevents HCV protein-mediated collapse of the respiration-driven mitochondrial membrane potential. Alisporivir prevents HCV protein-mediated mitochondrial dysfunction outside the context of apoptosis, calcium overload, production of ROS, dysfunction[2]. In cell culture models, low-micromolar doses of alisporivir block SARS-CoV and MERS-CoV replication. Combination treatment with Alisporivir and ICN-1229 increases the anti-MERS-CoV activity in cell culture[3]. Alisporivir

	pretreatment stimulates antigen presentation by hepatoma target cells, leading to enhancement of antigen-specific CD8+ T cell activation by 40%. Alisporivir induces an increase of MHC-I and beta-2 microglobulin on the surface of several cell lines [4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Combination treatment with Alisporivir and ICN-1229 does not protect against SARS-CoV infection in a mouse model[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Alisporivir is prepared in DMSO at 4 mM and diluted in cell culture medium at the indicated concentrations (0.1, 0.2, 0.3, 0.4, 0.5 μM). UHCV-32 and UHCVcon-57.3 are U-2 OS human osteosar coma-derived cell lines inducibly expressing the entire open reading frame derived from the HCV H77 prototype and consensus clones, respectively. Cell viability is measured by trypan blue exclusion analysis[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Exp Med. 2021 Apr 5;218(4):e20202207.
- Cell Death Differ. 2022 Jun 20.
- Cell Rep. 2021 Apr 6;35(1):108959.
- iScience. 2022: 105626.
- Antimicrob Agents Chemother. 2022 Nov 14;e0039222.

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REFERENCES

[1]. Coelmont L, et al. DEB025 (Alisporivir) inhibits hepatitis C virus replication by preventing a cyclophilin A induced cis-trans isomerisation in domain II of NS5A. PLoS One. 2010 Oct 27;5(10):e13687.

[2]. Quarato G, et al. The cyclophilin inhibitor alisporivir prevents hepatitis C virus-mediated mitochondrial dysfunction. Hepatology. 2012 May;55(5):1333-43.

[3]. de Wilde AH, et al. Alisporivir inhibits MERS- and SARS-coronavirus replication in cell culture, but not SARS-coronavirus infection in a mouse model. Virus Res. 2017 Jan 15;228:7-13.

[4]. Esser-Nobis K, et al. The cyclophilin-inhibitor alisporivir stimulates antigen presentation thereby promoting antigen-specific CD8(+) T cell activation. J Hepatol. 2016 Jun;64(6):1305-14.

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