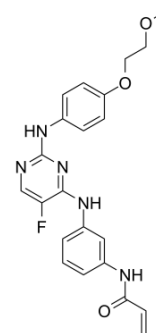


Spebrutinib

Cat. No.:	HY-18012		
CAS No.:	1202757-89-8		
Molecular Formula:	C ₂₂ H ₂₂ FN ₅ O ₃		
Molecular Weight:	423.44		
Target:	Btk		
Pathway:	Protein Tyrosine Kinase/RTK		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 45 mg/mL (106.27 mM)
 * "≥" means soluble, but saturation unknown.

Concentration	Mass		
	1 mg	5 mg	10 mg
1 mM	2.3616 mL	11.8080 mL	23.6161 mL
5 mM	0.4723 mL	2.3616 mL	4.7232 mL
10 mM	0.2362 mL	1.1808 mL	2.3616 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (5.90 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (5.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Spebrutinib (AVL-292; CC-292) is a covalent, orally active, and highly selective with an IC₅₀ of 0.5 nM.

IC₅₀ & Target

IC₅₀: <0.5 nM (Btk)^[1]

In Vitro

Spebrutinib (CC-292) is a covalent, highly selective, orally active inhibitor of Btk with IC₅₀ value of 0.5 nM. Spebrutinib also less potently inhibits Yes, c-Src, Brk, Lyn, and Fyn with IC₅₀s of 723 nM, 1.729 μM, 2.43 μM, 4.4 μM, and 7.15 μM, respectively. Extensive analysis has revealed that the EC₅₀ of Btk occupancy from a Spebrutinib dose-response in Ramos cells (EC₅₀=6 nM) correlated directly with the cellular EC₅₀ of Btk kinase inhibition with Spebrutinib (EC₅₀=8 nM). Furthermore, the concentration at which Spebrutinib inhibits 90% of Btk activity in Ramos cells is 35 nM while the concentration of

Spebrutinib required for 90% occupancy of Btk is 39 nM^[1].

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

PROTOCOL

Cell Assay ^[1]

Cells are incubated in serum-free RPMI media for 1-1.5 hours. Isolated human B cells are incubated with Spebrutinib at a final concentration of 0.001, 0.01, 0.1 and 1 μ M. Ramos cells are incubated with 0.1 nM-3 μ M Spebrutinib. Cells are then incubated in the presence of compound for 1 hour at 37°C. Following incubation, cells are centrifuged and resuspended in 100 μ L of serum-free RPMI and BCR is stimulated with addition of 5 μ g/mL α -human IgM. Samples are centrifuged, washed in phosphate-buffered saline (PBS), and lysed in 100 μ L of Cell Extraction Buffer plus 1:10 (v/v) PhosSTOP Phosphatase Inhibitor and 1:10 (v/v) Complete Protease Inhibitor. Antibodies used for immunoblot analysis include P-PLC γ 2, PLC γ 2 (3871; CST), Syk (2712; CST), P-Syk (2710; CST), Btk, P-Btk, and Tubulin. Membranes are scanned on a Li-Cor Odyssey scanner using infrared fluorescence detection^[1].

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

CUSTOMER VALIDATION

- Blood. 2016 Jun 23;127(25):3237-52.
- Br J Pharmacol. 2019 Dec;176(23):4491-4509.
- Stem Cell Reports. 2019 May 14;12(5):996-1006.
- R Soc Open Sci. 2019 Jun 5;6(6):190434.
- Leukemia Res. 2019 Dec.

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REFERENCES

[1]. Evans EK, et al. Inhibition of Btk with CC-292 provides early pharmacodynamic assessment of activity in mice and humans. J Pharmacol Exp Ther. 2013 Aug;346(2):219-28.

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

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