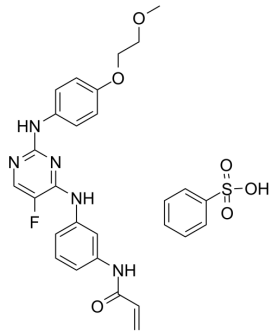
Spebrutinib besylate

Cat. No.:	HY-18012A
CAS No.:	1360053-81-1
Molecular Formula:	$C_{28}H_{28}FN_5O_6S$
Molecular Weight:	581.62
Target:	Btk
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Spebrutinib besylate (AVL-292 benzenesulfonate; CC-292 besylate) is a potent inhibitor of Btk kinase activity (IC_{50}<0.5 nM, K_{inact}/K_i=7.69×10^4 M^{-1}s^{-1}s) in biochemical assays.
IC_{50} & Target	IC50: <0.5 nM (Btk)[1]
In Vitro	Spebrutinib (CC-292) is a covalent, highly selective, orally active inhibitor of Btk with IC_{50} value of 0.5 nM. Spebrutinib also less potently inhibits Yes, c-Src, Brk, Lyn, and Fyn with IC_{50}s of 723 nM, 1.729 μM, 2.43 μM, 4.4 μM, and 7.15 μM, rspectively. Extensive analysis has revealed that the EC_{50} of Btk occupancy from a Spebrutinib dose-response in Ramos cells (EC_{50}=6 nM) correlated directly with the cellular EC_{50} of Btk kinase inhibition with Spebrutinib (EC_{50}=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 μM. Ramos cells are incubated with 0.1 nM-3 μM 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 μL of serum-free RPMI and BCR is stimulated with addition of 5 μg/mL α-human IgM. Samples are centrifuged, washed in phosphate-buffered saline (PBS), and lysed in 100 μL 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-PLCγ2, PLCγ2 (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.
- Leuk Res. 2020 Jan;88:106286.

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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.

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