
Product Data Sheet

Product Name: Spebrutinib besylate

Cat. No.: GC37672

Chemical Properties

Cas. No. 1360053-81-1

SMILES COCCOC1=CC=C(NC2=NC=C(F)C(NC3=CC=CC(NC(C=C)=O)=C3)=N2)C=C1.O=S(C4=CC=CC=C4)(O)=OFormula C₂₈H₂₈FN₅O₆S M.Wt 581.62

Solubility Soluble in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure

Protocol

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

Cell experiment: 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].

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

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.

Background

Spebrutinib besylate (AVL-292 benzenesulfonate; CC-292 besylate) is a potent inhibitor of Btk kinase activity ($IC_{50} < 0.5$ nM, $K_{inact}/K_i = 7.69 \times 10^4$ M⁻¹s⁻¹) in biochemical assays. IC_{50} : < 0.5 nM (Btk)[1]

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 μ M, 2.43 μ M, 4.4 μ M, and 7.15 μ M, respectively. 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].

[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.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA