Product Data Sheet

Product Name: Cevidoplenib
Cat. No.: GC63429

Chemical Properties

Cas. No.	1703788-21-9		
Formula	$C_{25}H_{27}N_7O_3$	M.Wt	473.53
Solubility	DMSO:35 mg/mL	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	Cevidoplenib		

Protocol

Cell experiment [1]:

Cell lines	Mouse primary B cells
Preparation method	Mouse primary B cells were labeled with CP670, and stimulated with either anti-IgM mAb, CD40L and IL-4 or LPS for 72 h in the presence or absence of Cevidoplenib (0-5μM) and tofacitinib at the indicated concentrations.
Reaction Conditions	0-5μM; 72 h

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Applications	Cevidoplenib inhibits B-cell receptor (BCR) cross-linking-induced cell proliferation in a concentration-dependent manner.
Animal experiment [2]:	
Animal models	Male WT or Mincle KO mice
Preparation method	After control diet feeding for 5 days, mice received 10 mg/kg Cevidoplenib or vehicle control by oral administration every 10 days during EtOH-diet feeding.
Dosage form	10mg/kg; p.o.
Applications	EtOH-fed mice treated with Cevidoplenib had reduced liver neutrophil infiltration, liver damage, and steatosis.

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References:
[1] Cho S, Jang E, Yoon T, et al. A novel selective spleen tyrosine kinase inhibitor SKI-O-703 (cevidoplenib) ameliorates lupus nephritis and serum-induced arthritis in murine models[J]. Clinical and Experimental Immunology, 2023, 211(1): 31-45.
[2] Kim J W, Roh Y S, Jeong H, et al. Spliceosome-associated protein 130 exacerbates alcohol-induced liver injury by inducing NLRP3 inflammasome–mediated IL-1β in mice[J]. The American journal of pathology, 2018, 188(4): 967-980.

Background

Cevidoplenib (SKI-O-703) is an orally active and selective spleen tyrosine kinase (Syk) inhibitor[1]. Syk is a crucial regulatory molecule in the signal transduction pathways involved in autoimmune diseases such as immune thrombocytopenia (ITP)[2]. Cevidoplenib is also the mesylate form of SKI-O-592, with an IC_{50} value of 6.2 nM for Syk[3].

In vitro, Cevidoplenib (0-5μM) treated primary mouse B cells for 72 hours, inhibiting B cell receptor (BCR) cross-linking-induced cell proliferation in a concentration-dependent manner. It increased the proportion of early and late apoptotic cells. This cytotoxic effect was stronger when B cells were activated by anti-IgM mAb compared to LPS activation[3].

In vivo, Cevidoplenib (84 mg/kg) was administered orally to mice with systemic lupus erythematosus (SLE), significantly reducing levels of IgG autoantibodies, proteinuria, and glomerulonephritis. It also decreased the levels of germinal centers (GC) involved in humoral immune responses and serum B cell-activating factor (BAFF) signaling from the TNF family[3]. Cevidoplenib (42, 84 mg/kg) was administered orally to mice with antiphospholipid syndrome (APS), significantly reducing antiphospholipid antibody (APLs)

levels and preventing myocardial arteriolar thrombosis in mice[4]. Cevidoplenib (10 mg/kg) was administered orally to mice with alcoholic liver disease (ALD), effectively reducing hepatic neutrophil infiltration, inhibiting liver injury, and steatosis[5].

References:

[1] Provan D, Newland A C. Investigational drugs for immune thrombocytopenia[J]. Expert Opinion on Investigational Drugs, 2022, 31(7): 715-727.
[2] Cooper N, Ghanima W, Hill Q A, et al. Recent advances in understanding spleen tyrosine kinase (SYK) in human biology and disease, with a focus on fostamatinib[J]. Platelets, 2023, 34(1): 2131751.
[3] Cho S, Jang E, Yoon T, et al. A novel selective spleen tyrosine kinase inhibitor SKI-O-703 (cevidoplenib) ameliorates lupus nephritis and serum-induced arthritis in murine models[J]. Clinical and Experimental Immunology, 2023, 211(1): 31-45.
[4] Jang E, Hwang H, Yoon T, et al. S307: CEVIDOPLENIB (SKI-O-703), A NOVEL SYK INHIBITOR, REDUCES ANTIPHOSPHOLIPID ANTIBODY TITERS AND PREVENTS INTRAMYOCARDIAL SMALL ARTERIAL THROMBOSIS IN A MOUSE MODEL OF ANTIPHOSPHOLIPID SYNDROME[J]. HemaSphere, 2023, 7(S3): e3562913.
[5] Kim J W, Roh Y S, Jeong H, et al. Spliceosome-associated protein 130 exacerbates alcohol-induced liver injury by inducing NLRP3 inflammasome–mediated IL-1β in mice[J]. The American journal of pathology, 2018, 188(4): 967-980.