Product Data Sheet

Product Name: Zenocutuzumab
Cat. No.: GC70169

Chemical Properties

Cas. No.	1969309-56-5	
Formula	M.Wt	145.76 kDa
Solubility	Storage	Store at -80°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	Zenocutuzumab	

Protocol

Cell experiment [1]:

Cell lines	Isogenic human bronchiolar epithelial cell lines (HBEC) expressing either a CD74-NRG1 or a VAMP2-NRG1 fusion
Preparation Method	Cells were treated with 0.001-1000nM Zenocutuzumab for 96h, and then growth was determined using AlamarBlue viability dye. Values are expressed relative to the vehicle-treated control (100%). Data were analyzed by nonlinear regression to determine IC_{50} for inhibition of growth.
Reaction Conditions	0.001-1000nM; 96h

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Applications	Growth of isogenic human bronchiolar epithelial cell lines (HBEC) expressing either a CD74-NRG1 or a VAMP2-NRG1 fusion was reduced by subnanomolar concentrations of Zenocutuzumab. In contrast, growth of the isogenic control HBEC line remained largely unaffected by Zenocutuzumab treatment. HBEC cells with NRG1 fusions were approximately 40,000 times more sensitive to Zenocutuzumab than the parental control cells.

Animal experiment [1]:

Animal models	NSG (LUAD-0061AS3)，BALB/c nude (OV-10-0050)， athymic nude (ST2891, ST3204, and CTG-0953) mice
Preparation Method	Crushed patient-derived xenograft (PDX) tumor samples were mixed with matrigel (50%) and injected into the subcutaneous flank of 6- to 12-week-old female NSG (LUAD-0061AS3), BALB/c nude (OV-10-0050), or athymic nude (ST2891, ST3204, and CTG-0953) mice. When tumors reached Approximately 125 to 250mm^3, mice were randomized into groups of 5 to 10 and treatment commenced. Animals bearing established PDX tumors were treated once per week with Zenocutuzumab (2.5, 8, or 25mg/kg). Zenocutuzumab was administered in phosphate-buffered saline by injection into the peritoneal cavity once per week. Mice were observed daily throughout the treatment period for signs of morbidity and mortality. Tumor length and width as well as animal weights were measured twice weekly.
Dosage form	2.5, 8, 25mg/kg; once per week; i.p.

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Applications	Each of the three Zenocutuzumab doses caused a significant reduction in tumor volume.

References:
[1]Schram A M, Odintsov I, Espinosa-Cotton M, et al. Zenocutuzumab, a HER2xHER3 bispecific antibody, is effective therapy for tumors driven by NRG1 gene rearrangements[J]. Cancer Discovery, 2022, 12(5): 1233-1247.

Background

Zenocutuzumab is a bispecific humanized IgG1 antibody containing two different Fab arms that target the extracellular domains of HER2 and HER3[1]. Zenocutuzumab specifically binds to the HER3 receptor, blocks its interaction with the ligand, and inhibits downstream PI3K/AKT and MAPK/ERK signaling pathway activation[2, 3]. Zenocutuzumab can be used to treat NRG1 fusion-positive cancers, which are oncogenic drivers of pancreatic cancer and other solid tumors[4].

In vitro, treatment of homologous human bronchial epithelial cell lines (HBEC) expressing CD74-NRG1 or VAMP2-NRG1 fusions with Zenocutuzumab (0.001-1000nM) for 96h significantly inhibited cell growth. HBEC cells with NRG1 fusions were approximately 40,000-fold more sensitive to Zenocutuzumab than parental control

cells[5]. Zenocutuzumab (0.1-1000nM) treatment of HBEC-CD74NRG1, LUAD-0061AS3 and MDA-MB-175-VII cells dose-dependently reduced the phosphorylation of HER3, HER2 and HER4[5].

In vivo, Zenocutuzumab (2.5-25mg/kg) treated with patient-derived xenograft (PDX) model mice by intraperitoneal injection inhibited tumor growth in a dose-dependent manner and caused tumor regression[5].

References:
[1] Antonarelli G, Giugliano F, Corti C, et al. Research and clinical landscape of bispecific antibodies for the treatment of solid malignancies[J]. Pharmaceuticals, 2021, 14(9): 884.
[2] Yin L. Gene Editing in ErbB/HER Family-Mediated Cancer Immunology[J]. 2025.
[3] Bhagyalalitha M, Shankaranarayana A H, Kumar S A, et al. Advances in HER2-Targeted Therapies: From monoclonal antibodies to dual inhibitors developments in cancer treatment[J]. Bioorganic Chemistry, 2024: 107695.
[4] Schram A M, O'Reilly E M, O'Kane G M, et al. Efficacy and safety of zenocutuzumab in advanced pancreas cancer and other solid tumors harboring NRG1 fusions[J]. 2021.
[5] Schram A M, Odintsov I, Espinosa-Cotton M, et al. Zenocutuzumab, a HER2xHER3 bispecific antibody, is effective therapy for tumors driven by NRG1 gene rearrangements[J]. Cancer Discovery, 2022, 12(5): 1233-1247.

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