Product Data Sheet

Product Name: Fresolimumab
Cat. No.: GC65539

Chemical Properties

Cas. No.	948564-73-6		
Formula		M.Wt	
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	Fresolimumab		

Protocol

Cell experiment [1]:

Cell lines	OE19□031M cells
Preparation Method	OE19 and 031M cells were subjected to chemoradiation for 14 days and Fresolimumab (10μg/mL) was added to the therapy schedule during the last 7 days of chemoradiation.
Reaction Conditions	10μg/mL; 7 days
Applications	Fresolimumab could reverse the mesenchymal morphology of both OE19 and 031M cells, even during chemoradiation.

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Animal experiment [2]:

Animal models	Female athymic nude-NU (NCr)-Foxn1n homozygous (HOM) mice
Preparation Method	Female athymic nude-NU (NCr)-Foxn1n homozygous (HOM) mice received 5×10^6 Lovo cells/200μL (s.c.) in the right flank. Mice were pooled and randomized (8-10 mice/group) when tumor size reached approximately 50-90mm^3. SAR439459, Fresolimumab (10, 25, 50mg/kg) or HuIgG4 isotype were injected intraperitoneally (i.p.) and tumor growth was measured as described above. Antitumor efficacy was evaluated by tumor volume measurement, and animal body weights assessed. Tumors were measured with a caliper 2-3 times weekly. When a tumor reached approximately 2000mm^3 or there was 10% body weight loss or 20% tumor ulceration, animals were euthanized.
Dosage form	10, 25, 50mg/kg; i.p.
Applications	In Lovo model, we compared the ability of SAR439459 and Fresolimumab as a monotherapy to inhibit active TGFβ1 at various doses and observed that treatment with either of these antibodies reduced intratumoral TGFβ levels at all the doses.

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References:
[1]Steins A, Ebbing E A, Creemers A, et al. Chemoradiation induces epithelial? to?mesenchymal transition in esophageal adenocarcinoma[J]. International journal of cancer, 2019, 145(10): 2792-2803.
[2]Greco R, Qu H, Qu H, et al. Pan-TGF? inhibition by SAR439459 relieves immunosuppression and improves antitumor efficacy of PD-1 blockade[J]. Oncoimmunology, 2020, 9(1): 1811605.

Background

Fresolimumab is a high-affinity humanized monoclonal antibody that binds to and inhibits all isoforms of the protein transforming growth factor β (TGFβ)[1]. The K_d values of Fresolimumab for TGFβ1, TGFβ2, and TGFβ3 are 1.7±0.6nM, 3.0±1.2nM, and 2.0±1.2nM, respectively[2]. Fresolimumab can treat idiopathic pulmonary fibrosis (IPF), focal segmental glomerulosclerosis, and cancer[3, 4].

In vitro, treatment of esophageal adenocarcinoma OE19 and 031M cells with

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Fresolimumab (10μg/mL) for 1 week reversed the mesenchymal morphology of the cells and reduced the expression of the mesenchymal marker VIM[5]. Fresolimumab (12.5, 50nM) treated MC38, EMT6 and HCT116 cells expressing human TGFβRII blocked TGFβ1-induced SMAD2/3 phosphorylation[6].

In vivo, Fresolimumab (10, 25, 50mg/kg) treated mice with human colon cancer Lovo cell xenografts by intraperitoneal injection significantly reduced TGFβ levels in tumors[6].

References:
[1] Lacouture M E, Morris J C, Lawrence D P, et al. Cutaneous keratoacanthomas/squamous cell carcinomas associated with neutralization of transforming growth factor β by the monoclonal antibody fresolimumab (GC1008)[J]. Cancer Immunology, Immunotherapy, 2015, 64: 437-446.
[2] Moulin A, Mathieu M, Lawrence C, et al. Structures of a pan-specific antagonist antibody complexed to different isoforms of TGFβ reveal structural plasticity of antibody–antigen interactions[J]. Protein Science, 2014, 23(12): 1698-1707.
[3] Trachtman H, Goyal S, Finn P, et al. Neutralizing TGF-β in fibrotic renal disorders: focus on fresolimumab[J]. Drugs Future, 2012, 37(787): 10.1358.
[4] Vincenti F, Fervenza F C, Campbell K N, et al. A phase 2, double-blind, placebo-controlled, randomized study of fresolimumab in patients with steroid-resistant primary focal segmental glomerulosclerosis[J]. Kidney international reports, 2017, 2(5): 800-810.
[5] Steins A, Ebbing E A, Creemers A, et al. Chemoradiation induces epithelial-to-mesenchymal transition in esophageal adenocarcinoma[J]. International journal of cancer, 2019, 145(10): 2792-2803.
[6] Greco R, Qu H, Qu H, et al. Pan-TGFβ inhibition by SAR439459 relieves immunosuppression and improves antitumor efficacy of PD-1 blockade[J]. Oncoimmunology, 2020, 9(1): 1811605.

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