Talacotuzumab

Cat. No.: HY-P99395

CAS No.: 1826831-79-1

Target: Interleukin Related

Pathway: Immunology/Inflammation

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description

Talacotuzumab (JNJ 56022473; CSL 362) is an IgG1-type fully humanized, CD123-neutralizing monoclonal antibody containing a modified Fc structure. Talacotuzumab has K_Ds of 0.43 nM, 188 nM, 46 nM, 16.8 nM for CD123, CD32b/c, CD16-158F, CD16-158V, respectively. Talacotuzumab inhibits IL-3 binding to CD123, antagonizing IL-3 signaling in target cells. Talacotuzumab has mutated the Fc region to increase affinity for CD16 (FcγRIIIa), thereby enhancing antibody-dependent cell-mediated cytotoxicity (ADCC). Talacotuzumab is highly effective in vivo reducing leukemic cell growth in acute myeloid leukemia (AML) xenograft mouse models[1][2][3][4].

In Vitro

Talacotuzumab (JNJ 56022473; CSL 362) strongly mediates ADCC of TF-1 cells with an ic50 of 5 ng/ml (33 pM)[1].

Talacotuzumab (1 μg/ml; pretreatment for 24 hours) inhibits TLR7-stimulated (Imiquimod; HY-B0180; 0.5 μM; for 6 days) and TLR9-stimulated (CpG C; 0.5 μM; for 6 days) IFN-α production in both SLE donors and healthy donors plasmacytoid dendritic cells (pDCs) and basophils, whereas TLR4-stimulated (LPS; HY-D1056; 10 μg/ml) production is not significantly reduced. Talacotuzumab inhibits TLR7- and TLR9-induced plasmablast expansion and proliferation by depletion of plasmacytoid dendritic cells (pDCs)[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Talacotuzumab (JNJ 56022473; CSL 362; 300 μg; ip; thrice weekly for 5 weeks) results in a significant delay in tumor growth compared with an isotype control in acute myeloid leukaemia mice xenografts[1].

Talacotuzumab (1, 10, 30 mg/kg; s.c.; single injection) has maximal serum concentrations at 48 hours of ~12, 190, and 380 μg/ml at doses of 1, 10, and 30 mg/kg in naive cynomolgus monkeys, respectively[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Nonobese diabetic/severe combined immunodeficiency mice injected intravenously AML xenograft cells (AML-5)[1]
Dosage:	300 μg
Administration:	IP; thrice weekly for 5 weeks
Result:	Resulted in a significant delay in tumor growth compared with an isotype control.

REFERENCES

[1]. S J Busfield, et al. Targeting of acute myeloid leukemia in vitro and in vivo with an anti-CD123 mAb engineered for optimal ADCC. Leukemia. 2014 Nov;28(11):2213-21.

[2]. Shereen Oon, et al. A cytotoxic anti-IL-3Rα antibody targets key cells and cytokines implicated in systemic lupus erythematosus. JCI Insight. 2016 May 5;1(6):e86131.

[3]. Erwin M Lee, et al. Efficacy of an Fc-modified anti-CD123 antibody (CSL362) combined with chemotherapy in xenograft models of acute myelogenous leukemia in immunodeficient mice. Haematologica. 2015 Jul;100(7):914-26.

[4]. L H Xie, et al. CD123 target validation and preclinical evaluation of ADCC activity of anti-CD123 antibody CSL362 in combination with NKs from AML patients in remission. Blood Cancer J. 2017 Jun 2;7(6):e567.

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