Dalotuzumab

Cat. No.:	HY-P99284
CAS No.:	1005389-60-5
Target:	IGF-1R; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description

Dalotuzumab (MK-0646) is a recombinant humanized monoclonal antibody (IgG1 type) targeting IGF-1R. Dalotuzumab acts by inhibiting IGF-1- and IGF-2-mediated tumor cell proliferation, IGF-1R autophosphorylation, and Akt phosphorylation. Dalotuzumab also induces apoptosis and cycle arrest. Dalotuzumab in combination with other anticancer agents such as statins can enhance the antitumor activity of Dalotuzumab in vitro and in vivo[1][2][3].

In Vitro

Dalotuzumab (h7C10; 33 nM; 24 h) inhibits IGF-1- and IGF-2-induced proliferation of MCF7 estrogen-dependent breast cancer cells with IC_{50} values of 4.2 and 3.1 nM, respectively[1].

Dalotuzumab (33 nM; 24 h) induces cycle arrest and inhibits autophosphorylation of the IGF-IR and IRS-1, in MCF7 cells (IGF-1-induced)[1].

Dalotuzumab increases NK cell-mediated lysis of MCF7 and A459 cells by 26 and 25%, respectively[1].

Dalotuzumab (MK-0646; 10 μg/mL; 24, 48 h) abrogates the anti-apoptotic effect of IGF1 in endometrial cancer cells[2].

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

Cell Proliferation Assay[1]

Cell Line:	MCF7 cells (IGF-1 and IGF-2-induced)
Concentration:	33 nM
Incubation Time:	24 h
Result:	Showed anti-proliferation activity to IGF-1- and IGF-2-induced MCF7, with IC_{50} values of 4.2 and 3.1 nM, respectively.

Cell Cycle Analysis[1]

Cell Line:	MCF7 cells (IGF-1-induced)
Concentration:	33 nM
Incubation Time:	24 h
Result:	Prevented cell cycle progression from the G1 to S and G2/M phases.

Apoptosis Analysis[2]

Cell Line:	ECC-1 and USPC-1 cells (IGF-1-induced)
Concentration:	10 μg/mL
Incubation Time:	24, 48 h
Result:	Reversed the effect of IGF1 on caspase-3 cleavage (Caspase-3 is activated in apoptotic cells and cleaves several cellular proteins, including PARP).

Western Blot Analysis[1]

Cell Line:	MCF7 cells (IGF-1-induced)
Concentration:	33 nM
Incubation Time:	24 h
Result:	Led to a decrease of phosphorylation for both β-chain and IRS-1.

In Vivo

Dalotuzumab (h7C10; i.p.; 250 μg/mice for the first time, then 125 μg/mice twice weekly for 40 days) shows anti-tumor effects on MCF-7 and A549 xenograft tumor models[1].

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

Animal Model:	Swiss Nude mice (MCF-7 and A549 xenograft tumor models)[1].
Dosage:	125 and 250 (first time) μg/mice
Administration:	Intraperitoneal injection; 250 μg/mice for the first time, then 125 μg/mice twice weekly for 40 days
Result:	Led to average tumor volume at 6 weeks post-cell injection was reduced by 70% and 72% in the MCF-7 and A549 models, respectively.

REFERENCES

[1]. Goetsch L, et al. A recombinant humanized anti-insulin-like growth factor receptor type I antibody (h7C10) enhances the antitumor activity of vinorelbine and anti-epidermal growth factor receptor therapy against human cancer xenografts. Int J Cancer. 2005 Jan 10;113(2):316-28.

[2]. Bitelman C, et al. IGF1R-directed targeted therapy enhances the cytotoxic effect of chemotherapy in endometrial cancer. Cancer Lett. 2013 Jul 10;335(1):153-9.

[3]. Scartozzi M, et al. Dalotuzumab, a recombinant humanized mAb targeted against IGFR1 for the treatment of cancer. Curr Opin Mol Ther. 2010 Jun;12(3):361-71.

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