Product Data Sheet

Product Name: Daratumumab
Cat. No.: GC19785

Chemical Properties

Cas. No.	945721-28-8		
Formula		M.Wt	
Solubility	Soluble in water	Storage	Store at -30℃
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	Daratumumab		

Protocol

Cell experiment [1]:

Cell lines	bone marrow mononuclear cells (BM-MNC)
Preparation Method	Freshly isolated BM-MNCs, containing 2% to 35% malignant plasma cells as determined by flow cytometry, were immediately used in ex vivo experiments. The BM-MNCs, containing the malignant plasma cells, as well as the patient's own effector cells, were incubated with daratumumab (10 μg/mL), lenalidomide (3 μmol/L), and bortezomib (3 nmol/L) alone or in combination in RPMI + 10% FBS in 96-well round bottom plates in fully humified incubators at 37°C, 5% CO2-air mixture for 48 hours. The survival of primary CD138+ multiple myeloma cells was determined by flow cytometry.

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Reaction Conditions	10 μg/mL for 48 hours
Applications	PF-07104091 inhibited T47D and KPL1 cells with IC50s of 0.785 and 0.603 μM, respectively.

Animal experiment [2]:

Animal models	human multiple myeloma model in the RAG2-/-γc-/- mice
Preparation Method	A humanized microenvironment was generated in mice by subcutaneous implantation of ceramic scaffolds that were seeded with human MSC (2 × 105 cells/scaffold) and in vitro cultured for 7 days in osteogenic medium, containing ascorbic acid and dexamethasone. Eight weeks after implantation, mice received a sublethal irradiation dose (3 Gy, 200 kV, 4 mA) and luciferase-gene-marked primary multiple myeloma cells were injected directly into the scaffolds (1 × 106 cells/scaffold). Luciferase transduction of primary multiple myeloma cells was carried out using the lentiviral construct pRRL-cPPT-CMV-Luc2-IRES-GFP-PRE-SIN. When tumors became clearly detectable, mice were distributed over the following treatment groups: (i) control, (ii) T-cell depleted PBMC (PBMC-T), (iii) PBMC-T plus lenalidomide, (iv) PBMC-T plus daratumumab, and (v) PBMC-T plus lenalidomide plus daratumumab. Lenalidomide (1 mg/kg) was given in 5 days on 2 days off schedule for 2 weeks (days 49-53 and 56-60) and both daratumumab (8 mg/kg) and PBMC-T (8 × 106 cells/mouse) were given on days 49 and 56.
Dosage form	8 mg/kg on days 49 and 56.

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Applications	Treatment with daratumumab alone suppressed the tumor growth significantly. And the combination of daratumumab plus lenalidomide was able to reduce the tumor volume.

References:

[1]: Nijhof IS, Groen RW, Noort WA, van Kessel B, de Jong-Korlaar R, Bakker J, Van Bueren JJ, Parren PW, Lokhorst HM, Van De Donk NW, Martens AC. Preclinical evidence for the therapeutic potential of CD38-targeted immuno-chemotherapy in multiple myeloma patients refractory to lenalidomide and bortezomib. Clinical cancer research. 2015 Jun 15;21(12):2802-10.

Background

Daratumumab (DARA) is a human IgG1 mAb targeting CD38, a 46-kDa type II transmembrane glycoprotein that is expressed at high levels on malignant cells in multiple myeloma (MM) [1,2].

Daratumumab elicits cell death through complement-dependent cytotoxicity (CDC),

antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), induction of apoptosis, and modulation of CD38 enzyme activities [1]. Macrophages to engulf multiple Daratumumab -opsonized target cells in a relatively short time span with a time-lapse imaging microscopy [1]. Daratumumab -dependent phagocytosis is related to CD38 expression levels, uptake into macrophages and substantial elimination of target cells was consistently observed for CD38-transduced UM9-CD38 and L363-CD38 variants with high levels of CD38 expression [1].

Phagocytosis contributed to the antitumor activity of daratumumab in vivo in 2 different xenograft models: subcutaneous Daudi-luc tumor xenograft model and intravenous leukemic Daudi-luc xenograft model [1]. Daratumumab (8 mg/kg, twice) alone suppressed the tumor growth significantly. And the combination of daratumumab plus lenalidomide was able to reduce the tumor volume [3].

References:
[1]. Overdijk MB, Verploegen S, BÖgels M, van Egmond M, van Bueren JJ, Mutis T, Groen RW, Breij E, Martens AC, Bleeker WK, Parren PW. Antibody-mediated phagocytosis contributes to the anti-tumor activity of the therapeutic antibody daratumumab in lymphoma and multiple myeloma. InMAbs 2015 Mar 4 (Vol. 7, No. 2, pp. 311-320). Taylor & Francis.
[2]. Nooka AK, Kaufman JL, Hofmeister CC, Joseph NS, Heffner TL, Gupta VA, Sullivan HC, Neish AS, Dhodapkar MV, Lonial S. Daratumumab in multiple myeloma. Cancer. 2019 Jul 15;125(14):2364-82.
[3]. Nijhof IS, Groen RW, Noort WA, van Kessel B, de Jong-Korlaar R, Bakker J, Van Bueren JJ, Parren PW, Lokhorst HM, Van De Donk NW, Martens AC. Preclinical evidence for the therapeutic potential of CD38-targeted immuno-chemotherapy in multiple myeloma patients refractory to lenalidomide and bortezomib. Clinical cancer research. 2015 Jun 15;21(12):2802-10.

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