Product Data Sheet

Product Name: Ipilimumab (MDX-010)
Cat. No.: GC31951

Chemical Properties

Cas. No.	477202-00-9		
SMILES	[Ipilimumab]		
Formula	$C_{6742}H_{9972}N_{1732}O_{2004}S_{40}$	M.Wt	145313.36
Solubility		Storage	Store at -80°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C 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			

Protocol

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Cell Experiment	
Cell lines	PBMCs
Preparation method	Add ipilimumab at the initiation of ATC expansion cultures from healthy donors at various concentrations ranging from 0 to 50 μg/mL. ATC(activated T cells) are harvested on day 14, armed with EGFRBi or CD20Bi, and co-cultured at 25:1 E:T(effector:target) ratio for 18 hours with EGFR positive pancreatic cancer cell line (COLO356/FG) or 4 hours with CD20 positive Burkitt's lymphoma cell line (Daudi) for cytotoxicity assay. BiAb-mediated tumor specific cytotoxicity is measured by 51Cr release assay.
Concentrations	0, 0.5, 5.0, and 50 μg/mL
Incubation time	14 days

Animal Experiment	
Animal models	Purpose-bred cynomolgus monkeys
Formulation	Saline
Dosages	3 mg/kg or 10 mg/kg
Administration	i.v.

Conversion of different model animals based on BSA (Value based on data from FDA Draft Guidelines)

Species	Mouse	Rat	Rabbit	Guinea pig	Hamster	Dog
Weight (kg)	0.02	0.15	1.8	0.4	0.08	10

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Body Surface Area (m^2)	0.007	0.025	0.15	0.05	0.02	0.5
K_m factor	3	6	12	8	5	20

Animal A (mg/kg) = Animal B (mg/kg) multiplied by $\frac{\text{Animal B Km}}{\text{Animal A Km}}$

For example, to modify the dose of resveratrol used for a mouse (22.4 mg/kg) to a dose based on the BSA for a rat, multiply 22.4 mg/kg by the K_m factor for a mouse and then divide by the K_m factor for a rat. This calculation results in a rat equivalent dose for resveratrol of 11.2 mg/kg

Background

Biological Activity

In vitro: Ipilimumab, is a fully humanized IgG1k monoclonal antibody produced by recombinant DNA technology in a CHO mammalian cell expression system, binding with high affinity to the extracellular domain of human (and Cynomolgus monkey) CTLA-4, and acting as an inhibitor of its complex functions. This essentially results in T-cell activation and proliferation, and in lymphocyte infiltration leading to tumor cell death. However, the enhancement of T effector cell function, combined with the inhibition of CD4+ Treg and CD8+ suppressive cell types, are considered essential for mediating the full therapeutic effects of ipilimumab. Ipilimumab can improve ATC proliferation, enhance the BiAb-mediated tumor-specific cytotoxicity, and increase cytokine synthesis, while it attenuates Treg activity as shown by decreased level of IL-10 secretion and reduced Treg population. Ipilimumab and nivolumab treatments could collaboratively enhance effector and memory T cell responses without inappropriately activating naive T cells.

In vivo: Ipilimumab is shown in phase III clinical trials to have a survival benefit in metastatic melanoma that is durable in 10% to 20% of patients. Conceivably, the main adverse effects of ipilimumab are autoimmunein nature. Ipilimumab enhances antitumor immunity by inhibiting immunosuppressive activity of regulatory T cells (Treg).

References:
[1].Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate

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032): a multicentre, open-label, phase 1/2 trial.
Antonia SJ, et al. Lancet Oncol. 2016 Jul;17(7):883-895. PMID: 27269741.
[2].Pembrolizumab versus Ipilimumab in Advanced Melanoma.
Robert C, et al. N Engl J Med. 2015 Jun 25;372(26):2521-32. PMID: 25891173.

Caution: Product has not been fully validated for medical applications. For research use only.
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