Obiltoxaximab

Cat. No.: HY-P9932

CAS No.: 1351337-07-9

Molecular Weight: 145.5 kDa

Target: Bacterial

Pathway: Anti-infection

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

BIOLOGICAL ACTIVITY

Description

Obiltoxaximab (ETI 204) is the second and potent anti-protective antigen (PA) monoclonal antibody with immunogenicity. Obiltoxaximab plays a central role in anthrax toxin assembly and target cell intoxication, promoting survival, and inhibiting bacterial spread to the periphery in animal models. Obiltoxaximab can be used in the research of inhalational anthrax, bacteremia and toxemia[1][2][3][4].

In Vivo

Obiltoxaximab (16 mg/kg, i.v., a single dose for 70 days) for simulated populations of healthy and infected humans is comparable in overall serum exposures in individual infected macaques following obiltoxaximab, similar results in rabbit experiments[1].

Obiltoxaximab (16 mg/kg, i.m., 24, 48, 72 h prior to lethal challenge with B. anthracis spores) leads to 100% survival challenged with B. anthracis spores in cynomolgus macaques and prevents systemic bacteremia in the vast majority of animals[2].

Obiltoxaximab (4 and 8 mg/kg, i.v. and i.m., a single dose for 9 h) postexposure prophylaxis (PEP) leads to 100% survival with the combination of Levofloxacin (HY-B0330) challenged with B. anthracis spores in rabbits[2].

Obiltoxaximab (8 mg/kg, i.v., a single dose, 29 days) combined with antibiotics or Doxycycline (HY-N0565) lowers bacteremia levels in protective antigen (PA) of anthrax induced rabbits[5].

Pharmacokinetics of intramuscular Obiltoxaximab[2]

Study and dose (mg/kg)	Postchallenge dosing schedule	C_{max} (μg/mL)	T_{max} (days)	$AUC_{0-\infty}$ (μg·day/mL)	$T_{1/2}$ (days)	CL /F(mL/day/kg)	V_z/F (mL/kg)
PEP 2							
8	18 h	80.8	1.0	1030	7.50	7.76	84.0
8	24 h	86.5	1.0	788	5.20	10.2	76.2
16	18 h	165	1.0	2120	8.44	7.54	91.9

16	24 h	119	1.0	1990	9.85	8.03	114
PEP 3							
16	24 h	142	1.0	2190	10.4	7.00	110
16	36 h	132	0.50	1540	7.09	10.0	106
16	48 h	104	3.0	2040	12.6	8.00	143

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

Animal Model:	Human, macaques and rabbits[1]
Dosage:	16 mg/kg
Administration:	i.v., a single dose, 70 days
Result:	Overall serum exposures were comparable following obiltoxaximab in human, macaques and rabbits.

Animal Model:	Cynomolgus macaques[2]
Dosage:	16 mg/kg
Administration:	i.m., 24, 48, 72 h prior to lethal challenge with B. anthracis spores
Result:	Resulted in transient low levels of bacteremia in several animals, resolving in all animals after day 4, and the majority of animals remained abacteremic until day 56.

Animal Model:	Rabbits[2]
Dosage:	4 and 8 mg/kg
Administration:	i.v. and i.m. at 4 and 8 mg/kg, a single dose, 9 h
Result:	Effectiveness in the PEP setting was initially examined in rabbits.

Animal Model:	Protective antigen (PA) of anthrax induced rabbits[5]
Dosage:	8 mg/kg
Administration:	i.v., a single dose, 29 days
Result:	Lowered bacteremia levels between days 1 and 2 combined with antibiotics, eliminated bacteremia levels combined with Doxycycline (HY-N0565) in protective antigen (PA) of anthrax induced rabbits.

REFERENCES

[1]. Nagy CF, et al. Animal-to-Human Dose Translation of Obiltoxaximab for Treatment of Inhalational Anthrax Under the US FDA Animal Rule. Clin Transl Sci. 2017 Jan;10(1):12-19.

[2]. Yamamoto BJ, et al. Obiltoxaximab Prevents Disseminated Bacillus anthracis Infection and Improves Survival during Pre- and Postexposure Prophylaxis in Animal Models of Inhalational Anthrax. Antimicrob Agents Chemother. 2016 Sep 23;60(10):5796-805.

[3]. Hou A W, et al. Obiltoxaximab: adding to the treatment arsenal for Bacillus anthracis infection[J]. Annals of Pharmacotherapy, 2017, 51(10): 908-913.

[4]. Yamamoto B J, et al. Obiltoxaximab prevents disseminated Bacillus anthracis infection and improves survival during pre-and postexposure prophylaxis in animal models of inhalational anthrax[J]. Antimicrobial agents and chemotherapy, 2016, 60(10): 5796-5805.

[5]. Biron B, et al. Efficacy of ETI-204 monoclonal antibody as an adjunct therapy in a New Zealand white rabbit partial survival model for inhalational anthrax[J]. Antimicrob Agents Chemother. 2015 Apr;59(4):2206-14.

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