Development of Targeted Antibody Therapy to Reduce Antimicrobial Resistance-Related Morbidity and Mortality in the Erasmus Medical Centre

Published: 11-11-2014
Last updated: 22-04-2024

To identify and clone antibodies that can neutralize the bacterial pathogens Escherichia coli and Pseudomonas aeruginosa.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bacterial infectious disorders
Study type	Observational non invasive

Summary

ID

NL-OMON44672

Source
ToetsingOnline

Brief title
TARAME

Condition

- Bacterial infectious disorders

Synonym
blood poisoning

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Antibody, Escherichai coli, Pseudomonas aeruginosa, Sepsis

Outcome measures

Primary outcome

The primary objective of the study is the cloning of recombinant antibodies against E. coli and P. aeruginosa to develop antibody therapy for patients suffering from nosocomial infections, including patients that are immunocompromised and have a reduced cellular immune response.

Secondary outcome

To obtain new insights into the nature of the immune response to E. coli and P. aeruginosa infections.

Study description

Background summary

Blood culture infections are a major contributor to patient morbidity and mortality in hospitals around the world, including here at Erasmus MC. Worryingly, there has been an alarming increase in antibiotic resistance in the previous decade, whereas the discovery of new antibiotics has almost stopped, largely due to the high costs and the long (up to 10 years) *research to market* development process. Therefore, new strategies are required for preventing and treating current and emerging (antibiotic resistant) pathogens that threaten individual patients. A novel mechanism for treating antimicrobial resistant organisms is to utilize the immune system of patients via immunotherapy, utilizing a pool of targeted and specific anti-bacterial antibodies to support and activate the immune system to an infection (passive immunization). This type of therapy could potentially reduce morbidity and mortality associated with bacteremic infections, and help reduce our over-reliance on antibiotics. In the TARAME pre-pilot study, the feasibility of developing pools of protective antibodies for use in immunotherapy will be investigated by identifying and generating complement activating antibodies directed against Escherichia coli and Pseudomonas aeruginosa. Recent publications have indicated that conserved antigens exist in both species of

bacteria and that immunotherapy could be a useful therapy against these 2 major bacterial pathogens.

Study objective

To identify and clone antibodies that can neutralize the bacterial pathogens Escherichia coli and Pseudomonas aeruginosa.

Study design

The study design to be applied is a pilot study in adult wards of the Erasmus MC involving 5 patients with culture-confirmed E. coli and 5 patients with culture-confirmed P. aeruginosa sepsis. The estimated duration of inclusion is 24 months. The study involves one extra blood withdrawal, comprising 2 x 9 ml blood samples taken 7-10 days after suspicion of infection, all from an existing central venous catheter (CVC) and when the antibody response is expected to peak.

Study burden and risks

Two extra 9ml tubes of blood will be drawn (comprising one extra blood withdrawal of 2 x 9 ml blood samples taken 7-10 days after suspicion of infection) from an already installed central venous catheter (CVC) from a defined patient group presenting with sepsis in adult wards of the Erasmus MC. This patient group is defined as those patients with a confirmed positive blood culture result for the bacterial pathogens E. coli or P. aeruginosa. Further, no blood samples will be taken unless informed consent from either the patient or his/her legal representative has been obtained. There are no benefits for study participants. However patients may benefit in the future if high affinity antibodies can be identified and cloned for use as antibody therapy (passive immunization) against sepsis caused by the bacterial pathogens E. coli or P. aeruginosa.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

's-Gravendijkwal 230
Rotterdam 3015CE
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

's-Gravendijkwal 230
Rotterdam 3015CE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Aged between 18- years and 65 years
Diagnosed with sepsis and with a positive blood culture for E. coli or P. aeruginosa
Signed informed consent by the patient or his/her legal representative

Exclusion criteria

Age younger than 18 years
Age older than 65 years
Receiving immunosuppressive medication, including chemotherapy
HIV seropositivity
Hematological malignancies

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-10-2015
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	11-11-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-07-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL50363.078.14