Investigation of immune responses against Staphylococcus aureus * analysis of antibodies and antibody producing cells in patients with Staphylococcus aureus infections and patients whose wounds are colonised by Staphylococcus aureus

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The objective of this study is to obtain whole blood from patients with S. aureus infections and/or patients whose wounds are colonized by S. aureus for in vitro development of human monoclonal antibodies against S. aureus.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON33490

Source
ToetsingOnline

Brief title
AntiStaph

Condition

- Bacterial infectious disorders
- Skin and subcutaneous tissue disorders

Synonym

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hospital infections, S. aureus colonization and infection

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Top Intitute Pharma

Intervention

Keyword: colonisation, infection, monoclonal antibody, Staphylococcus aureus

Outcome measures

Primary outcome

The primary study parameter is a detectable IgA or IgG response against

staphylococcal antigens relevant for the development of therapeutic antibodies.

The endpoint will be defined by the absence of a detectable IgA or IgG response

against antigens relevant for the development of therapeutic antibodies.

Secondary outcome

Not applicable

Study description

Background summary

Staphylococcus aureus is a Gram-positive bacterium that colonizes the skin and anterior nares of about 25-30% of the healthy human population. Although mainly a harmless coloniser, S. aureus can cause severe infection. Its methicillin-resistant form (MRSA) is the most important cause of antibiotic-resistant health care-associated infections worldwide. Glycopeptides, especially vancomycin, are currently used as first-line treatment of MRSA infections. Unfortunately, this has led to the emergence of vancomycin-intermediate and vancomycin-resistant MRSA (VISA and VRSA). This raises concern that the current first-line treatment for MRSA infection will become increasingly ineffective. New classes of antimicrobials are thus urgently needed to treat infections with multi-drug resistant S. aureus.

The aim of the research and development in question is to generate human monoclonal antibodies recognizing S. aureus - associated antigens and to develop these antibodies into therapeutics for the prophylactic and/or therapeutic treatment of infectious diseases. Using the technology to generate and develop fully human human monoclonal antibodies from the blood of infected patients, we in collaboration with IQ Corporation, want to develop a number of human monoclonal antibodies against pathogenic S. aureus strains and their toxins. After a whole blood donation, the peripheral blood mononuclear cells (PBMC) will be isolated from the donated blood. The subsequent in vitro procedure for processing of the donated blood includes sorting single human B lymphocytes, and isolating RNA for the expression of the antibody-encoding genes in an antibody production platform. The resulting fusion products will be screened for relevant specificities against S. aureus. A selection of the most promising antibodies will, after in vitro efficacy studies, be subjected to pre-clinical and clinical research for the purpose of developing an antibody-based drug for the treatment of certain infectious diseases mediated by S. aureus. In addition, the sera isolated from the blood will be tested for the presence of antibodies against S. aureus cell-wall, exoproteins and toxins. This will be done by immunoproteomics (collaboration with Dr. B. Bröker, University of Greifswald) and by protein chip technology (collaboration with PepScan).
To develop the human monoclonal antibodies, whole blood is necessary from patients with an invasive S. aureus infection, from patients who suffer from detectable toxins produced by S. aureus and from patients whose wounds are colonised by S. aureus (Epidemolysis bullosa). The study will include both adult patients and minors.
Risks for patients who donate 12 ml of whole blood are deemed to be minimal. After blood donation the identity of the volunteers will be anonimised to safeguard their privacy. The patients will not have any personal therapeutic benefits from participating in this study but developing human monoclonal antibodies may be beneficial to patient populations in general.

Study objective

The objective of this study is to obtain whole blood from patients with S. aureus infections and/or patients whose wounds are colonized by S. aureus for in vitro development of human monoclonal antibodies against S. aureus.

Study design

The protocol concerns a mono-center, cohort study. It will take 4 years to include 120 patients from which 40 are diagnosed with invasive S. aureus infection and 20 who are infected with S. aureus strains producing one of the major staphylococcal toxins (PVL, ETA, TSST). Patients with S. aureus infections and patients whose wounds are colonized with S. aureus will be recruited to donate 12 milliliters blood during regular blood sampling. Most of

the patients will donate blood only once, and perhaps a few patients will be ask for an additional blood donation. Adults will donate blood maximally 3 times and minors maximally 2 times over a period of one year with minimal intervals of 3 days.
The study will take place at the University Medical Center Groningen (UMCG). Whole blood will be taken during regular blood sampling.

Study burden and risks

Risks for patients donating 12 ml of whole blood are deemed to be minimal. The blood will be taken during regular blood sampling. The patients will not have any personal therapeutic benefits in participating in this study, but the development of human monoclonal antibodies may be beneficial to patient populations in general.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)

Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Provision of written informed consent and history of S. aureus infection, presence of toxin producing strains or wound colonisation

Exclusion criteria

1. A history of, or presence of diseases or other conditions in which no blood donation can take place (as judged by the investigator or the treating physician).
2.Evidence of having serum hepatitis or carrying the hepatitis B surface antigen or Hepatitis C antibodies or being HIV positive.
3. Abuse of alcohol or drugs or any other condition.
4. Pregnancy.
5. Positive drug screen for Benzodiazepines, methadone, metamphetamine, morphine, PCP, tricyclic antidepressants, amphetamines, cocaine, cannabinoids, barbiturates and ethanol
6. Subjects, who in the opinion of the investigator or the treating physician should not, for reasons of safety, participate in the study.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-12-2009
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL27471.042.09