Auto-antibodies in patients with epidermolysis bullosa and revertant mosaicism

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1. To determine if auto-antibodies against the re-expressed protein exist in the peripheral circulation in patients with EB and revertant mosaicism and compare this incidence to the group of patients with EB and without revertant mosaicism. 2. To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin and subcutaneous tissue disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON38779

Source
ToetsingOnline

Brief title
Auto-antibodies in epidermolysis bullosa and revertant mosaicism

Condition

- Skin and subcutaneous tissue disorders congenital

Synonym
genetic skin condition, Inherited blistering disease - epidermolysis bullosa

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Auto-immunity, Epidermolysis bullosa, Revertant mosaicism

Outcome measures

Primary outcome

1. Number and percentage of patients in which circulating auto-antibodies are found. Corresponding subgroups of study group and control group as well as the whole study group and control group are compared.

Secondary outcome

1. Number and percentage of patients in which auto-antibodies are found to bind to their skin.

2. Presence of epitopes within detected auto-antibodies that correspond to epitopes known to cause auto-immune blistering disease.

Study description

Background summary

Revertant mosaicism refers to the co-existence of cells, within an individual, carrying disease-causing mutations with cells in which the inherited mutation is genetically corrected by a spontaneous event. This phenomenon exists in patients with epidermolysis bullosa (EB). This group of hereditary blistering diseases can be caused by mutations in at least 18 different genes. Clinically, EB patients with revertant mosaicism have patches of fragile skin that blister due to lack or aberrant expression of one of the proteins important for the adhesion of the epidermis to the dermis (mutant skin), and patches of clinically healthy skin with re-expression of this protein (revertant skin).

As a form of natural gene therapy, revertant mosaicism presents a possibility of using autologous revertant cells to treat EB with grafting of cultured skin equivalents or systemic treatment with induced pluripotent stem cells. However, the presence of two cell populations within an individual could result in an

auto-immune reaction against the re-expressed protein. The same proteins that are re-expressed in revertant skin, are also known to be targeted by pathogenic auto-antibodies in auto-immune blistering skin diseases.

The presence of pathogenic auto-antibodies could potentially preclude successful application of revertant cell therapy in patients with EB and revertant mosaicism as well as other therapies in patients with EB without revertant mosaicism, which similarly aim to restore the affected protein. Alternative approaches to therapy or adjunctive measures, like immunosuppression, may be required.

Study objective

1. To determine if auto-antibodies against the re-expressed protein exist in the peripheral circulation in patients with EB and revertant mosaicism and compare this incidence to the group of patients with EB and without revertant mosaicism.

2. To correlate the presence of circulating auto-antibodies with auto-antibody deposition in the revertant or mutant skin.

3. To assess possible pathogenicity of these auto-antibodies by epitope mapping

Study design

Pilot study.

Intervention will consist of venepuncture to obtain a single blood sample (10ml per patient), which is subjected to analysis by immunoblotting, immunoprecipitation, enzyme-linked immunosorbent assay and immunofluorescence assay analysis for antibody detection.

Patients* archived skin biopsy specimens of mutant and/or revertant skin will be studied for deposition of antibodies by immunofluorescence.

Study burden and risks

Risk associated in this study is negligible.

Knowledge of the presence and nature of auto-antibodies in EB patients with revertant mosaicism is, however, essential to direct future therapeutic interventions.

In view of the rarity of EB and the small sizes of the study groups, this research though non-therapeutic, is considered to be group-related.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

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

The patients are selected from the EB-database of the Department of Dermatology, UMCG, Groningen. ;In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Diagnosis: EB due to mutation in one of the following genes: COL17A1, LAMB3 and COL7A1.
- > 10 years of age.
- Informed consent acquired.
- Archived biopsy specimen present.

Exclusion criteria

Contraindication to venepuncture.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-06-2013
Enrollment:	28
Type:	Actual

Ethics review

Approved WMO Date:	23-10-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-11-2013
Application type:	Amendment
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	NL45721.042.13