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Using nitrogen-washout to detect lung disease after donor-stem cell transplantation

Submission date
27/09/2018

Recruitment status
No longer recruiting

Registration date
29/11/2018

Overall study status
Completed

Last Edited
16/12/2020

Condition category
Respiratory

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Bronchiolitis obliterans (BO) and its clinical equivalent, bronchiolitis obliterans syndrome (BOS), is a severe lung complication in patients who have received a stem cell transplantation. It has many complications and a high rate of death. BO affects the small airways in the lung and is defined as the development of a new fixed airways obstruction. The obstruction usually occurs within the first two years after stem cell-transplantation but may develop as late as 5 years later. Current estimates suggest that about 2% - 5% of all patients who have received donor stem cell transplantation, and about 14% of patients in whom the body rejects the donated stem cells, are affected. Unfortunately, the survival and treatment of BOS over the last 20 years has not improved, with an overall survival of about 15% at 5 years. Patients present with dyspnoea (breathlessness) by exertion, dry cough, wheezing and dry crackles on lung auscultation (stethoscope). However, in early disease, patients may have no respiratory symptoms and lung function tests could be normal, before the criteria for BOS are met. Symptoms and signs of airflow obstruction on spirometry (lung test) do not occur until the disease of the small airways is widespread and lesions are more likely to be irreversible. The gold standard for diagnosing BOS still requires transbronchial, thoracoscopic or open lung biopsy (tissue sample), which are all invasive methods and several studies have noted mortality rates of 30% to 60%. Therefore, more sensitive and reproducable measurements are needed to detect the disease earlier. The aim of this study is to find out whether a test called nitrogen (N2)-washout can be used for the early detection of BO after stem cell transplantation.

Who can participate?
Patients aged 18 and older undergoing stem cell transplantation

What does the study involve?
All participants undergo lung function tests and complete a questionnaire on breathing symptoms and medication. All the measurements take about 40-50 minutes per patient and are carried out once before transplantation, monthly for the first year after transplantation, and every three months in the second year after transplantation.

What are the possible benefits and risks of participating?
The possible benefit of the study outweighs the risks in that an earlier identification of BO may

lead to improved clinical outcomes. Lung function tests may lead to coughing, dizziness or acute hyperventilation (fast breathing) caused by repeated deep expirations and inspirations (breathing out and in). These are temporary in nature.

Where is the study run from?
University Hospital Basel (Switzerland)

When is the study starting and how long is it expected to run for?
December 2015 to December 2020

Who is funding the study?
University Hospital Basel (Switzerland)

Who is the main contact?
Dr Desiree Schumann

Contact information

Type(s)
Public

Contact name
Dr Leander Gonzalez

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4051

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
EKNZ 340/13

Study information

Scientific Title
The use of N2-washout for the early detection of bronchiolitis obliterans after allogenic stem cell transplantation

Acronym
Adorable Study

Study objectives
The trialists hypothesise that an abnormal phase III-slope (SBW) or an increased LCI (MBW) in patients with stable lung function after hematopoietic stem cell transplantation, can detect early changes in small airways (i.e. bronchiolitis obliterans) before clinical symptoms occur.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethikkommission Nordwest und Zentralschweiz, 26/09/2014, ref: EKNZ 340/13

Study design
Single-center longitudinal observational study

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet

Health condition(s) or problem(s) studied
Bronchiolitis obliterans in allogenic stem cell transplantation patients

Interventions
All measurement methods, principally N2-MBW, DTG-SBW and, depending on the clinical picture, FeNO, DLCO, FOT, spirometry and body plethysmography, will be carried out by the researchers in accordance with international guidelines once before transplantation, monthly for the first year after transplantation and every three months in the second year after transplantation. A validated measurement system will be used for the washout measurements and the evaluation will be performed in accordance with the recommended standard. For this, either the measuring systems' software (Eco Medics AG) or an external software, Lungsim im Matlab R 2006a (The MathWorks, Inc, Version 7.2), will be used. The latter was specifically developed for the advanced offline analysis of washout measurements.

Changes in LCI, Scon and Sacin, microbiological parameters such as colonization, infection and dysbiosis, and serum biomarkers of inflammation or extracellular matrix turnover such as collagen formation and degradation molecules, are measured over time following allogenic stem cell transplantation in:
1. Patients without pulmonary symptoms and low or high GvHD risk according to the GvHD risk score

2. Patients with pulmonary symptoms and lung function criteria for bronchiolitis obliterans
3. Patients with pulmonary symptoms, lung function criteria for BO and histological confirmation of either lymphoproliferative or constrictive BO

Intervention Type
Procedure/Surgery

Primary outcome measure
Lung clearance index (LCI) is measured with the multiple breath washout technique (N2-MBW) before transplantation, monthly for the first year after transplantation and every three months in the second year after transplantation

Secondary outcome measures
Measured before transplantation, monthly for the first year after transplantation and every three months in the second year after transplantation:
1. Scon and Sacin are measured using single-breath washout measurements
2. Microbiological parameters such as colonization, infection and dysbiosis, measured using oropharyngeal swabs
3. Serum biomarkers of inflammation or extracellular matrix turnover such as collagen formation and degradation molecules, measured using blood samples

Overall study start date
01/12/2015

Completion date
31/12/2020

Eligibility

Key inclusion criteria
1. 18 years and older
2. Patients undergoing allogenic stem cell transplantation

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
200

Total final enrolment
181

Key exclusion criteria
1. Failure to provide informed consent
2. Patients too ill or unfit to undergo a lung function test
3. Patients who have undergone stem cell transplantation before inclusion

Date of first enrolment
01/01/2016

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
Switzerland

Study participating centre
University Hospital Basel
Clinic of Pneumology
Petersgraben 4
Basel
Switzerland
4051

Sponsor information

Organisation
University Hospital Basel

Sponsor details
Petersgraben 4
Basel
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4051

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04k51q396

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University Hospital Basel

Results and Publications

Publication and dissemination plan
The trialists strive to publish all data at conferences and/or in peer-reviewed journals. Additional documents will be available on request.

Intention to publish date
31/12/2021

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date