ISRCTN27114642 https://doi.org/10.1186/ISRCTN27114642

A study comparing granulocyte macrophage-colony stimulating factor (GM-CSF), vaccination and placebo in patients who suffer from immune depression after resection of either pancreas or oesophagus

Submission date
05/12/2008

Registration date
27/02/2009

Last Edited
08/12/2015

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Haematological Disorders

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Claudia Spies

Contact details
Augustenburger Platz 1
Berlin
Germany
13353
+49 (0)30 450 551001
claudia.spies@charite.de

Additional identifiers

Study information

Scientific Title

Influence of post-operative influenza vaccination versus granulocyte macrophage-colony stimulating factor (GM-CSF) in immune-compromised patients undergoing pancreatic or oesophageal resection on the course of immunosuppression and the post-operative infection rate: a prospective, randomised, double-blinded, double-dummy, placebo-controlled, monocentre pilot study

Acronym
ART VI

Study objectives
The post-operative vaccination or the post-operative treatment with granulocyte macrophage-colony stimulating factor (GM-CSF) produces a higher sufficiency of immune reactivity shown through a normalisation of monocyte human leukocyte antigen-DR (HLA-DR) expression while avoiding immune paralysis in patients suffering from severe immune suppression.

On 22/10/10 this record was updated to include an extended overall trial end date, from 31/3 /2010 to 31/03/2011, due to the yearly unavailability of study vaccine for several months. The secondary outcomes have also been updated and more details may be found in the relevant field with the above update date.

On 09/06/2015 the following changes were made to the trial record:
1. The overall trial start date was changed from 26/10/2008 to 13/05/2008.
2. The overall trial end date was changed from 31/03/2011 to 16/04/2011.
3. The target number of participants was changed from 60 to 63.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The local ethics committee (Ethics board committee Berlin, Landesamt fur Gesundheit und Soziales [LaGeSo], Berlin) was informed throughout and gave permission for the performance of this clinical trial on the 01/09/2008 (ref : ZS EK 15 287/08)

Primary study design
Interventional

Study design
Prospective randomised double-blinded double-dummy placebo-controlled monocentre pilot study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Post-operative immunological stimulation in severe immune suppression

Interventions
In this study the potential of post-operative immunological stimulation in patients with immune suppression is compared to placebo:
1. 0.5 ml Mutagrip® 2008/2009

2. 250 µg/m^2 body surface Sargramostim
3. Physiological saline

Duration of the treatment: minimal 24 hours, maximum 72 hours
Frequency: daily subcutaneous injection and daily 24 hour perfusion for a maximum of 3 days
Follow up: 9 post-operative days as well as safety

Intervention Type
Biological/Vaccine

Primary outcome(s)
HLA-DR expression of monocytes on the first 5 post-operative days

Key secondary outcome(s)
Current information as of 22/10/10:
1. For all 60 study patients:
1.1. Post-operative infection rate and infection days on the first 9 post-operative days
1.2. Post-operative incidence of delirium and delirium days (CAM-ICU, NuDesc, DDS) on the first 9 post-operative days
1.3. Ventilation time, intensive care unit (ICU) stay, length of stay, APACHE II score, SAPS II score, SOFA score, TISS-28 score (ventilation time and scores on the first 9 post-operative days)

2. For the first 33 study patients:
2.1. Cytokines in serum, Th1/ Th2-ratio, Th17/ Treg-ratio, further parameters of immune function on the first 5 post-operative days
2.2. Quantitative expression of transcription factors (T-bet, Eomesodermin, Gata-3, Foxp3, ROR-gamma t, PU.1, STAT-1, STAT-3, STAT-5, NF kappa B) and proteins (SOCS-3, SOCS-1, SOCS-5, TGF-beta, IL-17, IL-6, IL-10, IFN-?, TNF-a, IL-23, IL-10) as well as the synthesis of the corresponding effector proteins on the first 5 post-operative days

Initial information at time of registration:
1. Cytokines in serum, Th1/ Th2-ratio, Th17/ Treg-ratio, further parameters of immune function on the first 5 post-operative days
2. Quantitative expression of transcription factors (T-bet, Eomesodermin, Gata-3, Foxp3, ROR-gamma t, PU.1, STAT-1, STAT-3, STAT-5, NF kappa B) and proteins (SOCS-3, SOCS-1, SOCS-5, TGF-beta, IL-17, IL-6, IL-10, IFN-?, TNF-a, IL-23, IL-10) as well as the synthesis of the corresponding effector proteins on the first 5 post-operative days
3. Post-operative infection rate on the first 9 post-operative days
4. Post-operative incidence of delir (CAM-ICU, NuDesc, DDS) on the first 9 post-operative days
5. Ventilation time, intensive care unit (ICU) stay, length of stay, APACHE II score, SAPS II score, SOFA score, TISS-28 score (ventilation time and scores on the first 9 post-operative days)

Completion date
16/04/2011

Eligibility

Key inclusion criteria
1. Tumour resection of the upper aero-digestive tract
2. Informed consent
3. Adulthood (aged greater than or equal to 18 years, either sex)

4. Negative pregnancy test
5. Highly effective contraception in premenopausal women
6. No participation in any other pharmaceutical study during the course of the study
7. Monocyte HLA-DR expression below 10.000 antigens/surface on the first post-operative day

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Lack of willingness to accept the storage and transfer of pseudonymous data
2. Incapacitation
3. Staff member of the Charité Berlin
4. Pregnancy
5. Lactation
6. Congenital or acquired blood disorder
7. Chemotherapy or radiotherapy within the last 28 days
8. Leukaemia
9. Emergency operation
10. Proven infection within the last 7 days
11. Known infection of hepatitis B, hepatitis C, human immunodeficiency virus (HIV) or positive result during pre-operative screening
12. Allergy against any ingredients of the trial drug
13. Autoimmune diseases
14. Intake of immunosuppressive drugs up to 4 weeks before surgery
15. Cardiac arrhythmia without adequate therapy
16. Unstable angina pectoris
17. Symptomatic congenital heart defect
18. History of thrombosis or thromboembolic incidents
19. Body weight below 50 kg
20. Thrombocytes below or equal to 100,000/µl on the day before surgery
21. Neutrophils below or equal to 1,500/µl on the day before surgery
22. Haemoglobin below or equal to 8 g/dl on the day before surgery
23. Bilirubin above 2 g/dl on the day before surgery
24. Creatinine above 1.5 g/dl on the day before surgery
25. Aspartate aminotransferase (AST)/alanine aminotransferase (ALT) above 90 U/l on the day before surgery

Date of first enrolment
26/10/2008

Date of final enrolment
16/04/2011

Locations

Countries of recruitment
Germany

Study participating centre
Charité - Universitätsmedizin Berlin
Berlin
Germany
13353

Sponsor information

Organisation
Charité - University Medicine Berlin (Charité - Universitätsmedizin Berlin) (Germany)

ROR
https://ror.org/001w7jn25

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Charité Universitätsmedizin Berlin

Alternative Name(s)
Medical School - Charité - University Medicine Berlin

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	07/12/2015		Yes	No