Trial Description

Title

IL-10-dependent immune suppression after trauma - regulation of monocytes and T-cells-controlled immune defense

Trial Acronym

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URL of the trial

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Brief Summary in Lay Language

In trauma patients immunologic dysfunction often results in infectious complications, sepsis, organ failure, and mortality. First phase of the inflammatory reaction - early after trauma, and a second phase - days after trauma, are already described. Complications often develop in the second phase and are closely associated with reduced immune response. The aim of the present study is to characterize this immunologic dysfunction before the onset of post-traumatic complications. Trauma patients (fulfilling including criteria) who develop complications after trauma and those without complications after trauma as well as healthy volunteers will be included in this study. The study may deliver data about optional therapeutic approaches.

Brief Summary in Scientific Language

In trauma patients immunologic dysfunction often results in infectious complications, sepsis, organ failure, and mortality. First phase of the inflammatory reaction - early after trauma, and a second phase - days after trauma, are already described. Complications often develop in the second phase and are closely associated with reduced immune response. The aim of the present study is to characterize this immunologic dysfunction before the onset of post-traumatic complications. Therefore, two hypothesis will be tested in a time-course of 10 days after trauma. 1. The expression of Pattern-Recognition Receptors on monocytes and their function are modulated by alterated cytokine levels after trauma. Subsequently, Damage-Associated Molecular Pattern (DAMPs)-Signals can not be recognized and transduced. 2. T-regulatory cells (T-regs) are induced by enhanced IL-10 expression. T-Regs recognize DAMPs and induce immune suppression possibly resulting in post-traumatic complications.

Organizational Data

- DRKS-ID: **DRKS00003318**
- Date of Registration in DRKS: **2011/10/31**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**

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Investigator Sponsored/Initiated Trial (IST/IIT): **yes**

- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **312/10 , Ethikkommission des Fachbereichs Humanmedizin der Johann-Wolfgang-Goethe-Universität Frankfurt am Main**

Secondary IDs

Health condition or Problem studied

- ICD10: **A41 - Other septicaemia**
- ICD10: **A41.0 - Septicaemia due to Staphylococcus aureus**
- ICD10: **A41.9 - Septicaemia, unspecified**
- ICD10: **J80 - Adult respiratory distress syndrome**
- ICD10: **N17 - Acute renal failure**
- ICD10: **K72.0 - Acute and subacute hepatic failure**

Interventions/Observational Groups

- Arm 1: **Healthy volunteers (to gain a normal serum pool and determine normal ranges of cytokines as well as functionality of monocytes and Tregs a group of healthy volunteers will be analyzed)**
- Arm 2: **Traumatized patients without complications (a group of trauma patients who do not develop complications during 10 in-hospital days after trauma will be analyzed daily in order to determine the cytokine pattern and functionality of monocytes and Tregs in dependence of injury severity).**
- Arm 3: **Traumatized patients with complications (a group of trauma patients who develop complications during 10 in-hospital days after trauma will be analyzed daily in order to determine the cytokine pattern and functionality of monocytes and Tregs in dependence of complication developed).**

Characteristics

- Study Type: **Non-interventional**
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Study Type Non-Interventional: **Other**

- Allocation: **Non-randomized controlled trial**
- Blinding: **Open (masking not used)**
- Who is blinded: **[---]***
- Control: **Other**
- Purpose: **Basic research/physiological study**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

Clinical: Diagnosed complication after trauma (sepsis, septic shock, organ failure, multiple organ failure, death)
Experimental: analysis of monocyte and regulatory t-cells function, daily in a time course of 10 days after trauma + determination of the cytokine profile in serum.

Monocytic functionality is evaluated by whole blood stimulation with lipopolysaccharide and subsequent detemination of cytokines in the supernatant (TNF-α, IL-1β and IL-10) by ELISA method. Phagocytosis-activity of monocytes is determined by incubation of blood samples with FITC-stained E.coli (opsonized)-solution and subsequent flow cytometric analysis.
Determinatio of T-cell function is performed by stimulation with ConA and subsequent measurement of cytokines (IFN-γ, IL-2, IL-4 und IL-10) in the supernatant.

Secondary Outcome

Clinical: Diagnosed complication after trauma (sepsis, septic shock, organ failure, multiple organ failure, death)
Experimental: analysis of the regulatory activity of t-regulatory cells.

1. Culture flasks are pre-coated with monoclonal anti-CD3 antibody. One part of CD4+ cells contains Tregs, another part of CD4+ cells is depleted from Tregs (CD4+ und CD4+CD25+CD127dim/-) by using microbeads. Both samples + soluble monoclonal anti-CD28 are added to the pre-coated or uncoated control plates. Experiments with control antibodies are also performed. After 3 days, the supernatant is collected and the cytokine profile will be analyzed (IFN-γ, IL-2, IL-4 und IL-10). Here, we analyze the contribution of Tregs to the induction of T-helper cells (type 2, Th2) in dependence on complication development after trauma.

2.By using neutralizing anti-Human IL-10-antibody, on the one hand the IL-10-dependent maturation of Tregs will be analyzed and on the other hand Tregs-produced IL-10 neutralized. Thereby, the IL-10-driven Th2-induction can be inhibited. For this analysis, the identical experiment design as described above will be used and IL-10 antibody as well as control antibody will be added to the

samples in different flasks. The same parameter as described above will be evaluated. Here, the role of IL-10 in Tregs-induction and subsequent Th2 induction will be clarified.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

Recruitment

- Planned/Actual: **Planned**
- (Anticipated or Actual) Date of First Enrollment: **2012/02/01**
- Target Sample Size: **140**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **80 Years**

Additional Inclusion Criteria

all patients with an Injury Severity Score (ISS) between ≥ 16 and ISS < 42, primary allocation after accident, preclinical time < 120 min, regular completion of the first treatment in the emergency room, signed informed consent

Exclusion criteria

all patients with an ISS < 16 and ISS > 42, very poor prognosis/unfavourable prognosis (infaust prognosis) within first 24h after trauma, dementia or lacking cognitive abilities to participate the study (before trauma), patients with severe burn injuries, acute myocardial infarction, coronary bypass surgery, patients who are not primary allocated to the intensive care unit of the study center, tumor patients (chemotherapy,irradiation, HIV, Hepatitis A, B, C, HCV, CMV, immune suppressive drug medication

Addresses

■ **Primary Sponsor**

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■ **Contact for Scientific Queries**

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Sources of Monetary or Material Support

■ **Institutional budget , no external funding (budget of sponsor/PI)**

Klinik für Unfall-, Hand- und Wiederherstellungschirurgie
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URL: **[---]***

Status

- Recruitment Status: **Recruiting planned**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*