Trial Description

Title

ACE inhibitor for lung protection during mechanical Ventilation for acute lung injury - pilot trial

Trial Acronym

ACEmeVENT-Pilot

URL of the trial

[---]*

Brief Summary in Lay Language

Artificial mechanical ventilation represents the life-supporting treatment in patients with acute respiratory failure. Mechanical ventilation, however, cause mechanical alterations of pulmonary cells and may induce additional lung injury and aggravate respiratory failure. ACE-inhibitors are pharmacological compounds that are broadly used in vascular and cardiac medicine and have been proven to protect the heart and kidneys. There are experimental studies that demonstrate a beneficial and protective effect of ACE inhibitors on lung cells. This study investigates, whether the administration of an ACE inhibitor is a safe intervention in ventilated patients with respiratory failure.

The following changes were reported with the amendment from 9.10.2013:
- inclusion criteria "...onset of ventilation not longer than 48h ago" increased to "...onset of ventilation not longer than 60h ago"
- inclusion criteria "age 18-80 years" changed into " age not less than18 years"
- exclusion criteria: "Patients after bone marrow- or stem cell transplant limited to "...during the last 12 months"

The following changes were reported with the amendment from 05.02.2015:
- projected sample size of 210 patients reduced to 60 patients in consultation with the data monitoring committee (DMC) due to delay of recruitment.
- further secondary endpoint: change of kidney function until day 28 based on serum creatinine

Brief Summary in Scientific Language

Alveolar overdistension is an important pathogenetic mechanism in ventilator induced lung injury leading to alveolar epithelial cell apoptosis and aggravating acute lung injury (ALI). Protective ventilatory strategies (low tidal volume) have improved the outcome of ALI/acute respiratory distress syndrome (ARDS). However, it remains a problem that in ALI/ARDS unknown proportions of the lung exhibit low compliance (baby lung effect). Thus, alveolar overdistension may occur, despite the use of low tidal volume ventilation. So far, there is no established pharmacological treatment of ALI/ARDS. No pharmacological intervention that increases the tolerance of pulmonary parenchyma to overdistension exists. Angiotensin Converting Enzyme (ACE) inhibitors prevent alveolar epithelial cell apoptosis in several models including mechanical stretch-induced apoptosis. A polymorphism of the ACE gene resulting in increased ACE activity correlates with an increased incidence and a poor prognosis of ALI/ARDS.
The ACEmeVENT-Pilot is a randomised, double blind, placebo controlled, multi-centre study that will investigate treatment with ACE inhibition in ventilated patients with ALI/ARDS. A total of 210 patients will be randomised to continuous i.v. administration of the ACE inhibitor Enalaprilat with a maximum dose of 10 mg/d or placebo in addition to standard treatment. The trial will contribute to the question if ACE inhibition is a safe intervention in ventilated ALI/ARDS, and will investigate trends in efficacy indicating the need for a larger phase III trial.

Do you plan to share individual participant data with other researchers?

[---]*

Description IPD sharing plan

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Organizational Data

- DRKS-ID: DRKS00000156
- Date of Registration in DRKS: 2011/10/24
- Date of Registration in Partner Registry or other Primary Registry: [---]*
- Investigator Sponsored/Initiated Trial (IST/IIT): yes
- Ethics Approval/Approval of the Ethics Committee: Approved
- (leading) Ethics Committee Nr.: 237-11-11072011, Ethikkommission an der Medizinischen Fakultät der Universität Leipzig

Secondary IDs

- EudraCT-No. (for studies acc. to Drug Law): 2010-020403-75
- BfArM-No.: 4037413

Health condition or Problem studied

- ICD10: J80 - Adult respiratory distress syndrome

Interventions/Observational Groups

- Arm 1: Administration of Enalapril i.v. (10 mg per day) during mechanical ventilation in addition to standard treatment of acute lung injury/ARDS
- Arm 2: Administration of placebo i.v. (NaCl, 10 mg per day) during mechanical ventilation in addition to standard treatment of acute lung injury/ARDS
Characteristics

- Study Type: Interventional
- Study Type Non-Interventional: [---]*
- Allocation: Randomized controlled trial
- Blinding: [---]*
- Who is blinded: patient/subject, investigator/therapist, caregiver
- Control: Placebo
- Purpose: Treatment
- Assignment: Parallel
- Phase: IIb
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): Yes

Primary Outcome

Number of days alive and off ventilator until 28 days after randomisation (VFD)

Secondary Outcome

Renal function: (a) days alive and off renal replacement therapy until day 28, (b) chronic renal failure leading to renal replacement therapy in survivors at day 60 (c) mean daily fluid balance for day 0 to 5 (d) change of kidney function until day 28 based on serum creatinine || Cardiovascular function: (a) days alive without vaso-active drugs until day 28 (VAS) (b) maximum and mean SOFA-subscore for the cardiovascular system for day 0 to day 28 (c) maximum vasopressor dose || Survival at day 28 and day 60 (SV) || Breathing without assistance at day 28 (%) || Organ failure free days, except lung until 28 days after randomisation || Highest Sequential Organ Failure Assessment score until 28 days after randomisation || Days alive and outside ICU until 28 days after randomisation || Change in PaO2/FiO2

Countries of recruitment

- DE Germany

Locations of Recruitment

Recruitment

- Planned/Actual: Actual
Planned/Actual: **Actual**

- (Anticipated or Actual) Date of First Enrollment: **2012/05/10**
- Target Sample Size: **60**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

### Inclusion Criteria

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

### Additional Inclusion Criteria

1. intubated patients on mechanical ventilation and onset of ventilation not longer than 60h ago
2. Present (acute lung injury (ALI) / acute respiratory distress syndrome (ARDS)) defined by:
   a. sudden onset
   AND
   b. PaO₂/FiO₂ ≤ 300 mmHg (ARDS: PaO₂/FiO₂ ≤ 200 mmHg)
   AND
   c. bilateral pulmonary infiltrates on a chest radiograph consistent with the presence of edema,
   AND
   d. no clinical evidence of left atrial hypertension (e.g. as in heart failure); if measured, pulmonary-capillary wedge pressure of 18 mm Hg or less.
3. Age not less than 18 years
4. Written informed consent of patient, person in charge or legal representative or acknowledgement of emergency situation by medical consultant

### Exclusion criteria

1. positive pregnancy test in women with childbearing potential
2. nursing women
3. unsuggestive of elevated intracranial pressure
4. unsuggestive of neuromuscular diseases, if they are likely to affect spontaneous breathing
5. known sickle cell anaemia
6. severe chronic respiratory insufficiency in pre-existing pulmonary disease
7. severe adiposity > 45 kg/m²
8. burns of more than 30% of the body surface area
9. other medical conditions with an expected 6-months mortality >50%
10. **Patients**
   a. after bone marrow- or stem cell transplant during the last 12 months
   b. after lung transplant
   11. liver cirrhosis Child Pugh C
   12. contraindications following the SmPC
   13. Participation in another interventional clinical trials in the last 30 days
14. advanced relations to investigator
15. known nephrotic syndrome with proteinuria of >1g/day
16. clinical relevant electrolyte disorder in the assessment of the investigator
17. known immn order or collagen disease (i.e. lupus erythematoses, sklerodermia)
18. concomitant systemic therapy with immunsuppressives (i.e. corticosteroids, cytostatic agents, antimetabolite, allopurinol, procainamid or lithium) expect treatments of preexisting diseases or sepsis with glucokortikoids according to the respective guidelines.

Addresses

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Sources of Monetary or Material Support

- Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)
  
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Status

- Recruitment Status: Recruiting complete, follow-up complete  
- Study Closing (LPLV): 2016/01/18

Trial Publications, Results and other documents

- Trial results Ergebnisbericht