

## Trial Description

### Title

**Diacerein for the treatment of epidermolysis bullosa simplex**

### Trial Acronym

**Diacerein for EBS-DM**

### URL of the trial

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### Brief Summary in Lay Language

**Epidermolysis bullosa simplex is a genetic disease affecting mainly the skin and mucous membranes. Due to the absence or the misfolding of a protein, skin layers don't stick together properly. This leads to blistering to the skin even upon minor trauma. In the case of Epidermolysis bullosa simplex it was seen that also inflammatory components (like interleukin-1beta) are active, which aggravate the disease. The aim of this study is to block interleukin-1beta, thereby rendering more stability to the skin. In the laboratory the active agent "Diacerein" was tested and which showed promising results in terms of increasing cellular stability. Based on these results a pilot study was conducted, also giving promising results, which shall be confirmed in the present study. There, patients will apply a diacerein cream every day for four weeks. A second group of patients will receive placebo. In the following year, the groups will be crossed-over. During the four weeks of application, blisters will be counted and recorded, to see if blister numbers go down. In the following three month blisters will be counted in the absence of the cream, to see when blister numbers start increasing.**

### Brief Summary in Scientific Language

**Epidermolysis bullosa simplex type Dowling-Meara (EBS-DM) is a rare condition of the skin and mucous membranes, affecting 1 in about 50.000 people. Up to date, no causal therapy is available and treatment is restricted to the amelioration of symptoms like pruritus and pain. Dominant mutations in keratins of basal keratinocytes lead to a conformational change of these intermediate filament (IF) components, their aggregation in the cytoplasm upon minor mechanical trauma and subsequently to a collapse of the IF network and the cytolysis of basal keratinocytes. For K14 based EBS-DM we found, that the inflammatory cytokine interleukin 1 beta (IL-1 $\beta$ ) is constitutively activated in patient keratinocytes. In a positive feedback loop, it leads to the activation of the c-jun N-terminal kinase pathway and the**

**overexpression of K14 and IL-1 $\beta$  itself. However, when treating patient keratinocytes with IL-1 $\beta$  antibody or the small molecule diacerein, expression approximated wildtype levels and keratinocytes were less susceptible to stress. These results led to a pilot study, in which five EBS-DM patients were treated with a 1% diacerein cream. The study consisted of an open phase, during which all patients received 1% diacerein cream to apply underneath both armpits, and a placebo-controlled phase, where armpits were randomized and patients received 1% diacerein cream for one armpit and placebo for the other. The outcome of this study was a statistically significant reduction of blisters during the open phase. During the double-blinded controlled phase, only one time interval showed a significant difference between placebo and diacerein. Overall, data analysis was challenging because only three out of five patients finished the controlled phase per protocol. However, the promising results during the open phase are very much encouraging the present application. Here, we suggest a placebo-controlled, randomized, double-blinded trial, including 15 EBS-DM patients (aged 4-19 years). The study design comprises a placebo and an intervention group of patients and consists of a 4-weeks part for efficiency analysis with the primary endpoint being a reduction of blister numbers by 40%, and a follow-up, with the secondary endpoint being the time until the achievement of the initial blister number. Patients will be monitored at their local centers by a study nurse. This procedure will be done in two subsequent years, with a cross-over of patient groups. This allows the exclusion of temperature effects, which are known to influence blistering, and differences in blister numbers between patients are excluded to influence the result.**

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

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**Description IPD sharing plan**

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## Organizational Data

■ DRKS-ID: **DRKS00005412**

■ Date of Registration in DRKS: **2013/11/06**

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Date of Registration in DRKS: **2013/11/06**

- 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.: **415-E/1619/10-2013 , Ethikkommission des Landes Salzburg**

## Secondary IDs

- EudraCT-No.  
(for studies acc. to Drug Law): **2013-002034-21**

## Health condition or Problem studied

- ICD10: **Q81.0 - Epidermolysis bullosa simplex**

## Interventions/Observational Groups

- Arm 1: **1% diacerien cream**  
**Active agent: diacerein**  
**Application: once daily, topically**
- Arm 2: **placebo**

## Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: [---]\*
- Allocation: **Randomized controlled trial**
- Blinding: [---]\*
- Who is blinded: **patient/subject, investigator/therapist, caregiver, assessor, data analyst**
- Control: **Placebo**
- Purpose: **Supportive care**
- Assignment: **Crossover**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **Yes**

### Primary Outcome

**Reduction of blisters within four weeks by 40% in the verum group, in comparison to the placebo group.**

### Secondary Outcome

**Time span until the reaching of the initial blister number (+/-10%) during the follow-up.**

## Countries of recruitment

- **AT Austria**

## Locations of Recruitment

- **University Medical Center Division of Experimental Dermatology and EB House Austria, Salzburg**

## Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2014/05/01**
- Target Sample Size: **15**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

### Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **4 Years**
- Maximum Age: **19 Years**

### Additional Inclusion Criteria

- **An age between 4 and 19 years**
- **Diagnosis of EBS-DM.**
- **Mutations in the keratin 5 or keratin 14 gene**
- **signed consent form**

### Exclusion criteria

- **other types of EB with mutations in the keratin 5 or keratin 14 gene.**
- **lack of mutation analysis**

- **Known or expected intolerance to diacerein a component of the cream (e.g. tartrazin) or substances with a similar structure**
- **Pregnancy or lactation**
- **Contemporaneous participation in another clinical trial.**
- **Patients with hepatic dysfunction**
- **Relevant other diseases (e.g. acute infections, ...)**

## Addresses

### ■ Primary Sponsor

**Division of Experimental Dermatology and EB House Austria**  
**Department of Dermatology**  
**University Hospital Salzburg**  
**Paracelsus Medical University**  
**University Hospital for Dermatology**  
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### ■ Contact for Scientific Queries

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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.)**

**Fonds zur Förderung der wissenschaftlichen Forschung (FWF)**

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E-mail: **office at fwf.ac.at**

URL: **www.fwf.ac.at**

- **Private sponsorship (foundations, study societies, etc.)**

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**Austria**

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Fax: [---]\*

E-mail: [---]\*

URL: [---]\*

## Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2015/10/17**

## Trial Publications, Results and other documents

*Please note:*

*There are additional attributes available concerning this trial. To open an extended view please [click here](#).*