

## 4<sup>th</sup> Conference of 'EB-CLINET – Clinical Network of EB Centres and Experts' 26 - 27 September 2017 – Salzburg, Austria

### EB-CLINET CONFERENCE REPORT

The 4<sup>th</sup> conference of EB-CLINET took place at the Crowne Plaza Hotel in Salzburg from 26-27 September 2017. This new location offered plenty of room for the main sessions as well as for various parallel sessions, and regular breaks facilitated a good and fruitful exchange between the participants within the pleasant atmosphere of the venue.

For the first time, the EB-CLINET conference was held together with the EB2017 – 5<sup>th</sup> World Conference of EB Research. Both meetings provided an update on EB research and its translation to clinical benefit for patients – 'from lab-bench to bedside'. One shared day of the programme gave an opportunity to bring together scientists and clinicians, and therefore allowed a lively exchange of EB professionals. Most participants took the opportunity to visit both conferences. Altogether, 300 experts from 36 countries attended the combined meetings set in beautiful Salzburg.

In addition to the main sessions, eleven parallel sessions were held as closed meetings. Expert panels took the opportunity to further develop six different Clinical Practice Guidelines on the themes of hand surgery, anaemia, diagnostics, psychosocial care, physiotherapy, and occupational therapy. Furthermore, an Industry Partnering Panel was held, as well as a meeting of the EB sub-thematic group of the ERN-Skin, and a meeting about the development of an international EB registry.

Funding for both conferences was kindly provided by DEBRA Austria with additional sponsorship from Castle Creek Pharmaceuticals, Amryt Pharma, Amicus Therapeutics, Chiesi Farmaceutici, Factor Bioscience, Fibrocell, PolyMem, Mölnlycke Health Care, Beckman Coulter, ProQR Therapeutics and Interspar. CAP Partner generously supported the meetings with the management of the registration process.

On the morning of the shared day, Tuesday 26 September, the EB-CLINET part was officially opened with a warm welcome by the host of the conference, **Gabriela Pohla-Gubo** (EB House Austria), who also spanned the bridge between the two meetings and highlighted the importance of collaboration between scientists and clinicians.

The first two sessions on current clinical trials dealt with gene-cell therapies and symptom relief treatments. Detailed information will be provided in the EB2017 conference report which is planned to be published in the JID.

Miscellaneous themes were presented during the next session.

In his talk **Rainer Riedl** (DEBRA Austria) presented the patients' view on clinical research and clinical studies. As Mike Jaega (DEBRA International, UK) and Avril Kennan (DEBRA Ireland) could not participate in the conference, their statements were shown in a video message. Rainer Riedl presented Avril's work and her initiative to set up a patient panel as part of DEBRA International's peer review process for EB research grants. He pointed out that patient involvement and patient advocacy is regarded as highly important and should be expanded in the future. He concluded with his thoughts as a father of a butterfly child and emphasized the need for a transparent communication with and efficient medical and psycho-social care of patients included in clinical studies.

**Jouni Uitto** (Thomas Jefferson University, USA) reported about new technologies for improving diagnostic accuracy in EB. He concluded that homozygosity mapping is an effective screening method for the molecular diagnosis of EB in consanguineous populations. Further, he pointed out that a COL7A1-targeted NGS panel efficiently identifies mutations in families affected with DEB. Moreover, the use of a 21 EB-related gene NGS panel is an effective method to diagnose EB of largely unknown subtypes.

**Martin Laimer** (University Clinic of Dermatology Salzburg, EB House Austria) and **Dimitra Kiritsi** (University Clinic Freiburg, Germany) presented treatment options for advanced squamous cell carcinoma (SCC). Martin Laimer talked about Nivolumab, an anti-PD1 monoclonal antibody. A phase II study of Nivolumab in patients with previously-treated locally advanced / metastatic SCC of the skin, is conducted in several centres in Austria. Dimitra Kiritsi explained how Cetuximab, which inhibits signalling through the epidermal growth factor receptor, extended the lives of DEB patients with metastasized cutaneous SCC.

The last session of the first EB-CLINET day covered the topic 'How to define outcomes in EB'.

**Helmut Hintner** (University Clinic of Dermatology, EB House Austria) talked about how to evaluate success in EB treatment and stated that it always depends on the subjective perception of each individual. Different questionnaires to measure the quality of life are currently used, but much effort is needed to define more objective criteria to measure the outcome of treatments.

**Jemima Mellerio** (Guy's and St Thomas' NHS Foundation Trust, UK) reported news about the PEBLES study on the natural history of EB. It has already included 55 patients and will help to find meaningful endpoints in future clinical trials.

**Daniel Solis** (Stanford University School of Medicine, USA) talked about a cross-sectional study on the natural history of wounds in RDEB and stated that this study sets a baseline for the design of future studies. He also informed the audience about a prospective wound study which uses a tissue analytics mobile phone software programme to quantify the dynamic wound healing process.

In the last talk of the day, **Agnes Schwieger-Briehl** (University Children's Hospital Zürich, Switzerland) presented data about different types of EBS with different inheritance patterns. She pointed out that different outcomes in different subtypes depend not only on the affected gene or the type of mutation, but also on the influence of epigenetic factors or the quality of treatments.

In the evening, delegates of both conferences had the opportunity to join a guided tour through the Fortress "Hohensalzburg" and breathe the medieval air between the old walls of the castle. The tour was followed by a joyful dinner in the Heraldry Hall.

The second EB-CLINET day was dedicated to hot topics in EB care.

Firstly, **Rainer Riedl**, showed the different roles in which DEBRA has already and will also in future facilitate basic research, and clinical studies, as well as medical and psycho-social care for EB patients: DEBRA groups around the globe offer their knowledge and their experience with the disease but they also provide substantial financial support. Thus DEBRA plays an important role in bringing together all relevant stakeholders and pushing forward EB research and medical care. To date, approximately 30 million Euro have been raised by DEBRA and spent especially for EB research. Rainer Riedl pointed out that DEBRA could be looked at as a “catalyst” or as “glue” between the different stakeholders and partners like patients, clinicians, scientist, sponsors, pharma companies, regulators and payers.

In her talk about osteoporosis and osteopenia in RDEB, **Anna Martinez** (Great Ormond Street Hospital, UK) pointed out that optimization of nutrition, wound care, and mobility is important to prevent fractures. She emphasized the need for good longitudinal studies of bone health as well as trials of non-pharmacological interventions such as vibration platforms. Furthermore, she stressed that reaching puberty is critical to bank more bone mass and reduce fracture risk. In addition, new medicines for osteoporosis have to be considered (such as Denosumab - anti-RANKL).

**Margarita Calvo** (Pontificia Universidad Catolica, Chile) presented the results of her study on neuropathic pain in EB. She found out that RDEB patients are at high risk to develop neuropathic pain and could show through biopsies that small nerve fibers (C-fibers) are reduced in RDEB skin. Testing of RDEB patients on neuropathic pain using the DN4 questionnaire (Bouhassira et al., 2005) is recommended.

**Roger Cornwall** (Cincinnati Children's Hospital, USA) reported about his experiences on patient-driven treatment of hand contractures in EB and emphasized the importance of listening to the patients' needs. An important goal is to identify the factors that drive contracture formation and the wound healing .

**Kattya Mayre-Chilton** (DEBRA International, UK) talked about the different steps and tools needed to develop a Clinical Practice Guideline (CPG). The CPGs support health care professionals in their treatment of EB patients by providing internationally approved recommendations. She encouraged everyone who would like to share his/her experience to join one of the following panels: Women health & child birth, sexuality, anaesthetics & clinical procedure, gastrostomy, bone, eye care, renal. Please contact Kattya directly ([kattya\\_chilton@hotmail.com](mailto:kattya_chilton@hotmail.com)).

Constipation in children and adults with EB was the topic of **Lynne Hubbards** talk (Guy's and St Thomas' NHS Foundation Trust, UK). It is very common in EB and is often a cause of pain and distress. Lynne Hubbard pointed out that an adequate intake of fluid as well as fibre is crucial in preventing and treating constipation.

**Elena Pope** (The Hospital for Sick Children, Canada) reported that risk factors of oesophageal strictures depend on the age of the patient and EB subtype. These strictures often need intervention, however, there is no consensus on the best approach for a dilatation: it can be done ante- or retrograde, by endoscopy or fluoroscopy. Furthermore, there is no evidence that medical treatment may prevent strictures, though she suggested that the use of budesonide slurry should be further explored.

**Anne Lucky** (Cincinnati Children's Hospital, USA) talked about anaemia, which can be a severe and even life-threatening complication in EB. It is caused both by iron deficiency and chronic inflammation. She recommended regular monitoring after the age of two, so that iron deficiency can be treated early on

enterally, intravenously, or by transfusion. Prevention and treatment of anaemia help to maintain a good quality of life.

The medical use of Cannabis for EB patients was the topic of both, **Nicholas Schröder** (University Medical Center Groningen, Netherlands) and **Anja Diem** (EB House Austria). Patients with EB already use cannabis and it seems to alleviate pain and itch. Anja Diem stressed that an open and fact-based discussion about the possibilities of the medical use of cannabis in EB is needed and that the patients' input and experience should be heard. The ratio and interplay of the substances THC and CBD are important and that "CBD-only" products might be an option for some indications.

Nicholas Schröder claimed that according to his research there are no severe side effects in the use of cannabis and that a standardization of the substances included in the medical cannabis is essential to objectify patient-perceived results. He reported that the combination of cannabinoids is more effective than a single cannabinoid and concluded that the therapeutic use of cannabinoids has to be optimized.

The results of the ESSENCE study, a Phase 3, double-blind, vehicle-controlled trial of the topical investigational drug SD-101 in patients with EB, were presented by **Amy Paller** (Northwestern University Skin Disease Research Center, USA). She showed that although in the ITT (intention-to-treat) population there was no difference in time to wound closure between SD 101 and placebo, there were encouraging trends in certain subpopulations. As this was the largest registration directed study in EB, lots of data could be collected and analysis is still going on.

A case study of a patient with RDEB and Marfan syndrome was presented by **Chiara Fiorentini** (University of Modena and Reggio Emilia, Italy), who reported about the difficulties of managing these two pathologies, their complications, and the vital need for a multidisciplinary approach.

Wound care as a source of stress was the topic of a study conducted by **Petra de Graaf-Mauritz** (University Medical Centre Groningen, Netherlands). The first part of the study, a qualitative research based on interviews with patients and their parents, is already finished. The second part, a quantitative research based on objective questionnaires is still ongoing and results will be published soon.

**Vamsi Yenamandra** (University Medical Centre Groningen, Netherlands) presented a practical clinical diagnostic tool for subtyping EB which is especially useful in poor settings. This so-called "Epidermolysis Bullosa Clinical Diagnostic Matrix" appeared acceptably accurate in classifying the type and subtype of EB, although it was less accurate in infants and children younger than six months. As this tool necessitates full documentation of clinical features, it facilitates phenotype genotype correlations. An electronic application was developed to simplify usage and is available for free on the EB-CLINET website.

**Gabriela Pohla-Gubo** closed the conference with a short recap of the development and role of EB-CLINET as a platform for connection, communication and collaboration. She finished with expressing the hope that the next EB-CLINET conference will again be held together with the EB research conference, most probably in London in 2019 (to be confirmed).

For further information please contact [office@eb-clinet.org](mailto:office@eb-clinet.org) or visit the EB-CLINET website [www.eb-clinet.org](http://www.eb-clinet.org).

*Text by Katharina Ude-Schoder and the EB-CLINET Team*