EB Research Network

Aiming for a world where EB is curable

Annual Report #2022

Prepared by Sandra Eder EB Resnet Coordinator

May 2023

eb Research Network.

CONTENT

1. Summary

Finally, the pandemic has receded, and EB research could continue as usual in 2022. Laboratories do not have to restrict their work further, and researchers can pursue their studies on essential EB research projects.
In 2022, EB Research Network (EB Resnet) organized and conducted two online research funding rounds efficiently and with the usual quality. Digitization helps, and some aspects of the reviewing process were improved through the online format. Nevertheless, we realize how critical face-to-face meetings of the EB community are. Therefore, we look forward to an expert meeting and prioritization workshop in person for this year's CIF (chronic inflammation & fibrosis) / repurposing call jointly organized with our strategic partner LifeArc.

A milestone in 2022 was the approval of the first EB drug worldwide - Filsuvez® can already be prescribed in some European countries. What a big step for EB research! Amryt Pharma has proven that getting a drug for EB approved and even on the market is possible. In some countries, the gel can already be officially ordered through pharmacies and can even be reimbursed in Germany and Austria. The Black Pearl Award deservedly went to Amryt Pharma for their professional cooperation with DEBRA groups and other EB patient organizations. The input of European DEBRA groups provided the impetus for approval at the EMA. This clearly shows how important it is for patient groups to be heard and actively involved in the approval process.
The submission for approval of Krystal's VYJUVEK (also known as B-VEC) gel in the USA is another milestone. In 2023 approval is expected in the USA, and in 2024, also in Europe. The gene therapy gel is a promising new form of therapy - even if it does not lead to a permanent cure. One problem is undoubtedly still the administration - since it is a gene therapy product, it will probably have to be administered in the clinic. Working together as united EB patient organizations in the approval process will be essential.

We welcome a new ordinary member: DEBRA Switzerland joined the EB Resnet Network in December 2022! Learn more about our network and partners, mission, and strategic goals in our first report section, "**EB Research Network. "**

With the extensive project database on the EB Resnet website, we aim to bundle current and completed EB research. There are not only projects from the official funding rounds listed but also nationally funded EB research projects of our members. Our project database has 135 EB research projects –active, completed, and publicly available to all. It is remarkable that, since 2007, more than 17 million euros have been invested into EB research only through the international funding rounds of DEBRA groups. National EB patient groups provided additional funding and trusts worldwide. You will find more about the projects listed on EB Resnet under "**Projects**."

The first approval and other products in the approval process show how dynamic EB therapy development has become. Currently, more than 40 clinical trials for EB are registered in various registries throughout the world. To facilitate an overview, EB Resnet developed a new online tool last year and now makes it available on the

website. The idea is to map all EB relevant studies and to facilitate the search for specific topics with a filter and search function. See more about clinical trials, an update about some ongoing trials, and the new database under the **"Clinical trials"** section.

At the funding level, 2022 closed with three committed projects to the two funding calls (AP Call 2022 and Special Ad-hoc Call Repurposing). In the AP Call 2022, two projects in the preclinical area convinced the reviewers as well as the expert panel. One project was approved in the special Ad-hoc Repurposing Call. Additionally, one project was resubmitted from the AP 2021 call and was reviewed positively. This EB Resnet report 2022 gives an insight into the statistics of the funding rounds since 2007. You can learn more about the funding round and the recommended projects in the **"Research funding"** section.

The challenge remains – we need a way forward to translate these results as quickly as possible. Even though there are many active clinical trials, there is also a need for targeted coordination with patient organizations, pharmaceutical companies, clinicians, healthcare providers, and regulatory authorities.

Outlook 2023

Thematically, EB Resnet remains true to its established priorities for therapy development. However, we will focus on unmet clinical needs in chronic inflammation and fibrosis. In May 2023, EB Resnet member DEBRA Austria will organize a prioritization workshop with our strategic partner LifeArc. LifeArc has a long-term relationship with DEBRA Austria and is willing to put additional funds into EB research. We anticipate holding a joint special call that opens in July 2023. The funding round will be organized in a two-stage application process, with an expression of interest (EOI) submission in the summer and submission of the complete application in autumn/winter 2023.

Sandra Eder

EB Resnet Coordinator

2. EB Research Network

THE EB RESEARCH NETWORK IS AN ALLIANCE OF PATIENT ORGANISATIONS WORKING TOGETHER AND IN COOPERATION WITH PARTNERS TO DEVELOP AND DELIVER EFFECTIVE THERAPIES FOR ALL PEOPLE LIVING WITH EPIDERMOLYSIS BULLOSA (EB).

EB Resnet aims to show the current state of EB research, its challenges – including gaps in knowledge or technology that hinder progress - and opportunities to develop therapies and advance their introduction into the clinic. Researchers, clinicians, patients, and industry partners all have an essential role.

The EB Resnet website provides information on current EB research projects worldwide and highlights cooperation opportunities with and for the industry. In addition, international funding rounds for EB research are announced and processed via EB Resnet's website.

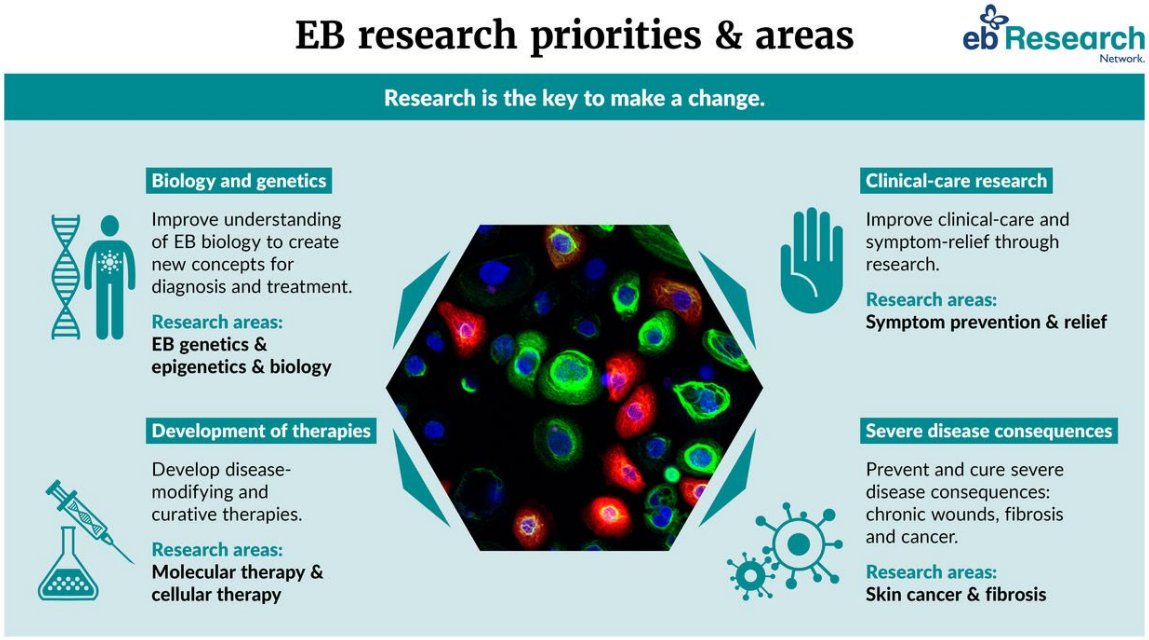
Our Mission

Translating successful research into patient benefit.

Strategic goals

In the current EB Resnet strategy (2020-2024), three strategic aims are defined:

1. **To support research to develop effective and safe treatments**
2. **To develop partnerships to expand research**
3. **To drive clinical translation and the adoption of treatments internationally**



Current research priorities and areas (EB Resnet 2023)

EB Resnet Members & Partners

We warmly welcome DEBRA Switzerland as a new ordinary member. DEBRA Spain will fund its first research grant in 2023 and change its member status from ordinary to funding member beginning of 2023.

EB Resnet member organizations

Funding members

DEBRA Austria, DEBRA UK, DEBRA Ireland, DEBRA Spain, DEBRA France

Ordinary members

EB-LOPPET, DEBRA Australia, DEBRA Switzerland

Partners & Strategic Partners

DEBRA International, EB Clinet, EB House Austria, LifeArc

If you are interested in supporting EB Resnet or have any particular questions about the report or about EB Resnet please contact office@eb-researchnetwork.org !

3. Research Funding

EB RESNET SUPPORTS AND COORDINATES RESEARCH FUNDING ON BEHALF OF ITS MEMBER ORGANISATIONS AND PARTNERS. IT CURRENTLY OFFERS THREE FUNDING SCHEMES: RESEARCH GRANTS THROUGH SCHEDULED CALLS FOR PROPOSALS, AD-HOC GRANTS (OUR FLEXIBLE FUNDING SCHEME TO ACCOMMODATE CO-FUNDING OPPORTUNITIES WITH OTHER FUNDERS), AND CO-FUNDING FOR INDUSTRY-PARTNERING PROJECTS.

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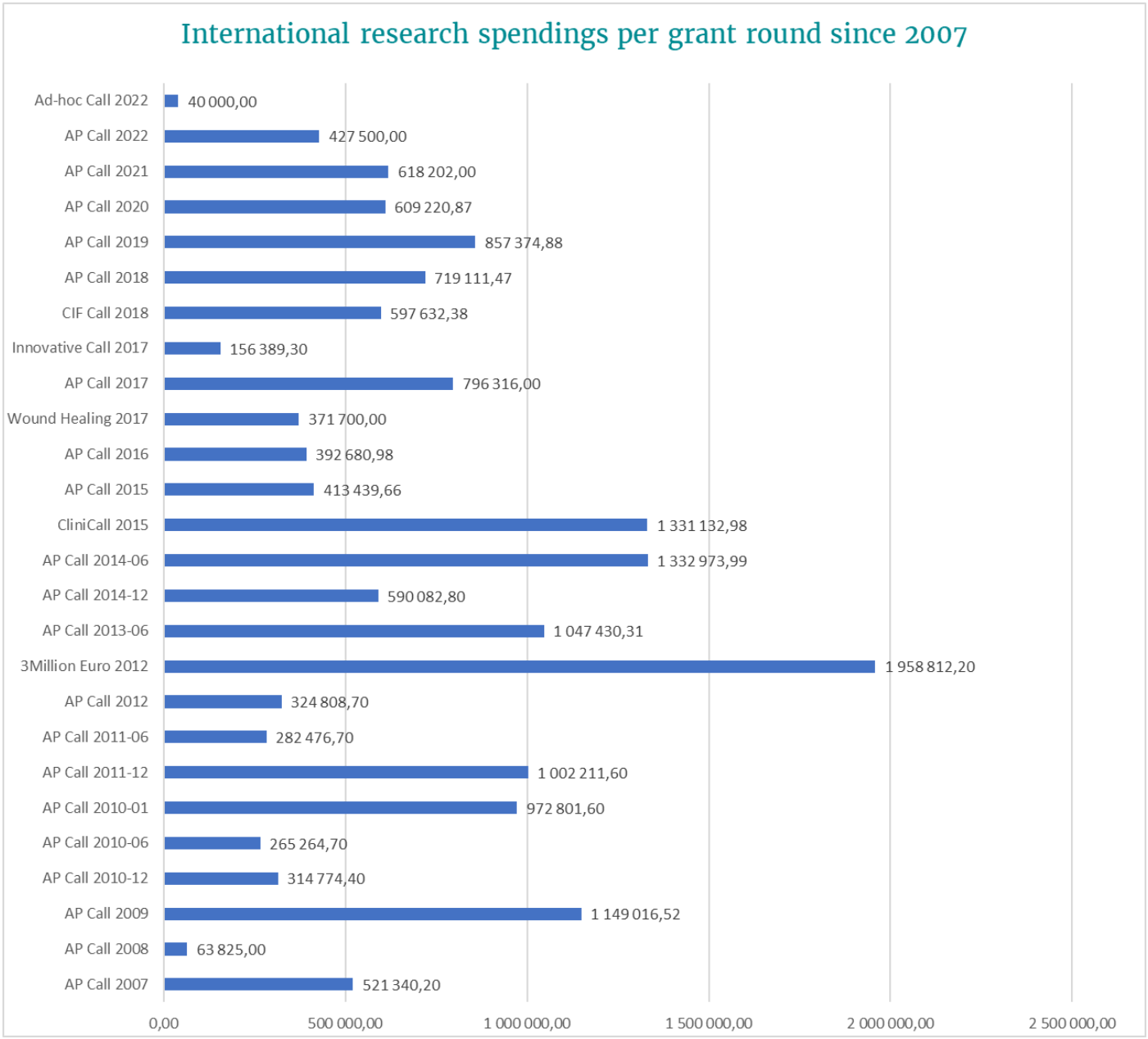
EB Resnet welcomes proposals for innovative research and clinical development of treatments or diagnostics. All submissions are evaluated for scientific excellence, feasibility, value for money, and whether they address the priority needs of people with EB. We undertake peer review to ensure that only the best research is funded.

The actual funding contribution can vary widely from year to year owing to several factors: first, the number of funding rounds held in any year varies (while usually two, it has varied from one to three, depending on funding availability from contributing DEBRAs or other funders, and other commitments); second, the number of research grant applications to any call has varied, usually in the range of 12-25; and third, as EB Expert Panel recommendations for funding, are based solely on research quality and importance for patient benefit, the proportion of project applications funded has ranged from ~10% - 50%, with an average of around 25%.

Research Grants Statistics

Facts and figures since 2007

The International EB Research funding rounds include the All Priorities Calls (AP Calls) and the Special Calls. AP Call means that project topics must fit one or more of EB Resnet's four strategic research priorities (see page 3). Alternatively, a Special Call may be issued to solicit proposals for important unresolved research questions, technology needs, or clinical consequences of EB (e.g., chronic inflammation and fibrosis). Since 2007, 20 AP Calls and 5 Special Calls have been organized, and approximately 17.2 million Euro has been invested in international EB research in the form of Research Grants. These funds have been raised primarily by national DEBRA groups and occasionally other EB patient organization funding partners.

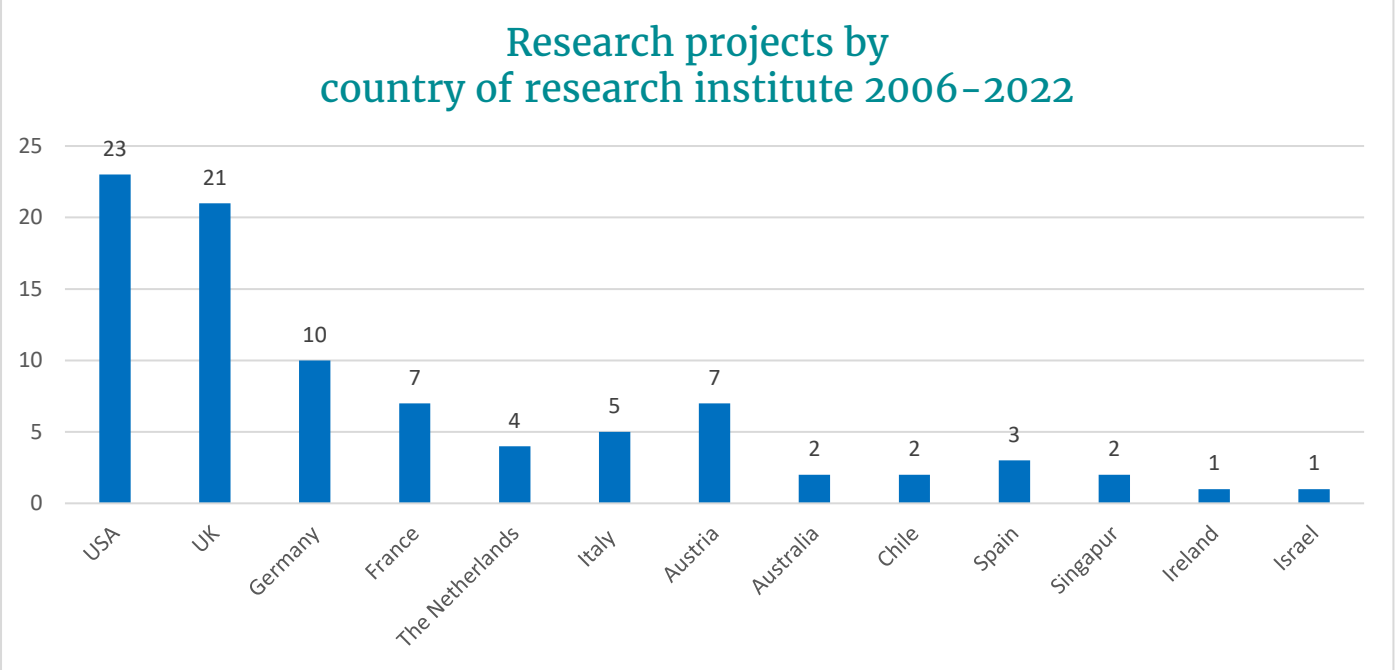


Research grants approved in Euros by research funding round since 2007.

Not all data are known of the early funding rounds from the early 1990s, as some paper records were lost to flooding in storage by the funding member.

Since 2007, EB Resnet has kept reasonably good statistics with committed funding.

The number of International Research Grants approved per year since 2007.



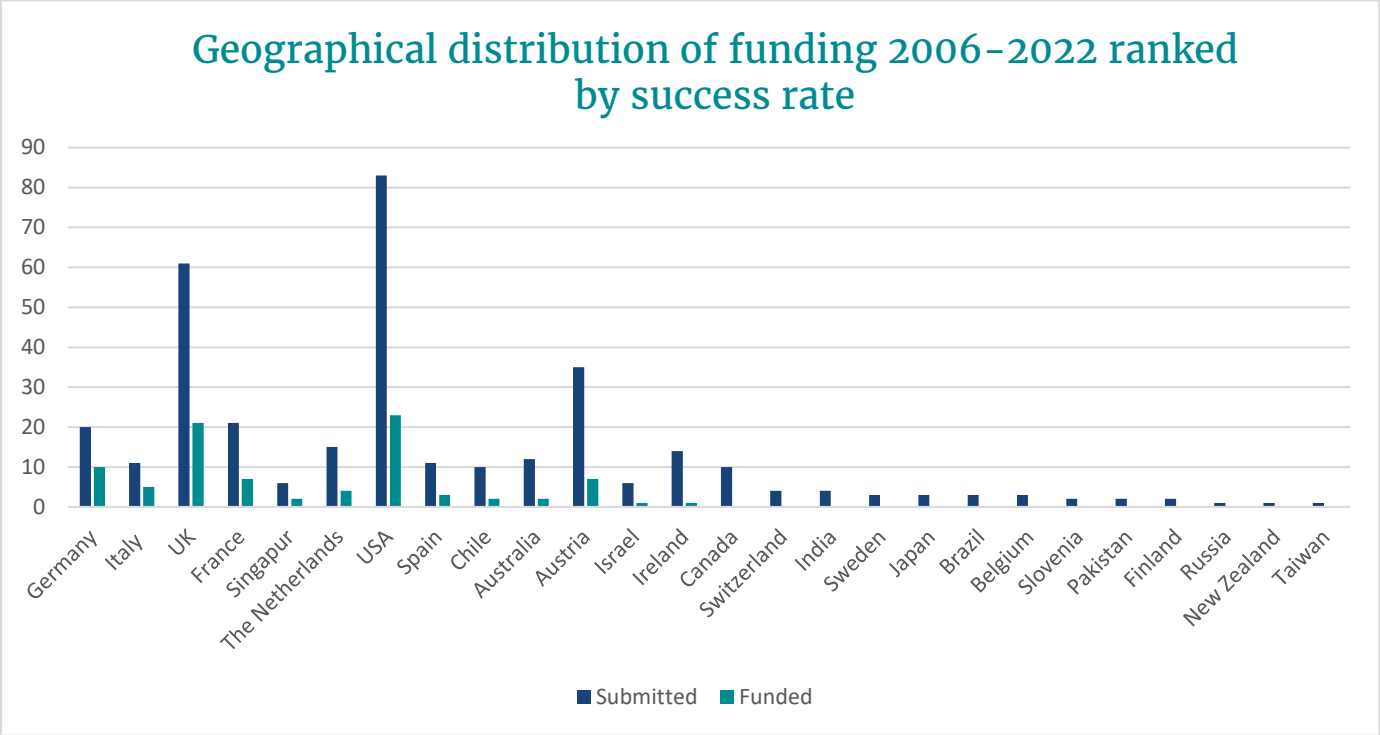
The number of international research grants approved per country of the research institution since 2007.

With 23 projects, the USA still ranks top among the countries that have received the most project funding, followed by the UK and Germany. Researchers from other European countries, Australia, South America, and Asia, have also received funding. In principle, the approved projects reflect those countries with influential EB research and clinical groups with a long track record and countries with the greatest number of grant application submissions. The majority of grant applications came from the USA and the UK – where it is notable that many of the established groups are led by researchers and clinicians supported by DEBRA at early stages of their careers in the period from the late 1980s – the turn of the Millenium.

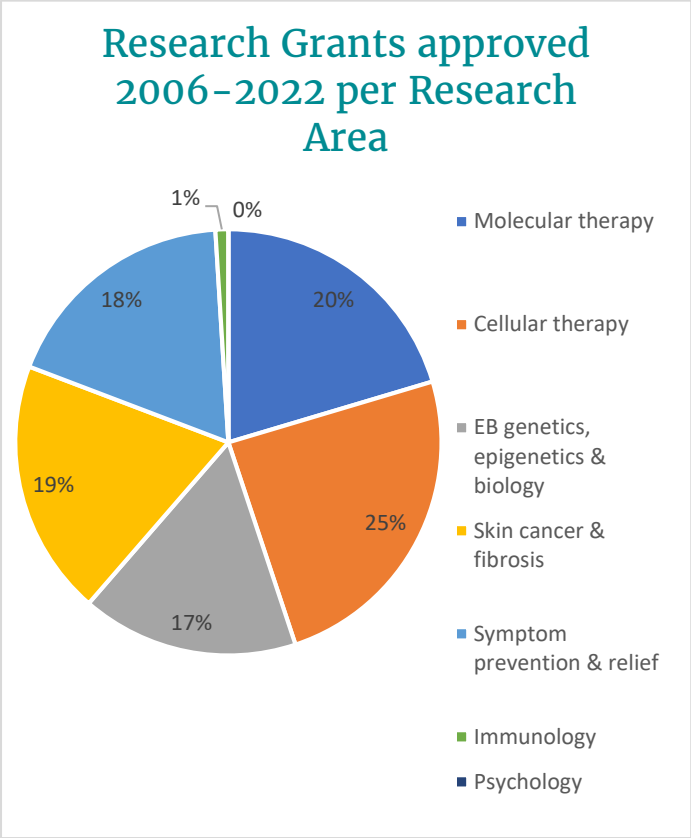
Germany is the most successful country (as measured by successful grant applications compared to the number of submitted grant applications), with 20 submissions and ten approved projects.

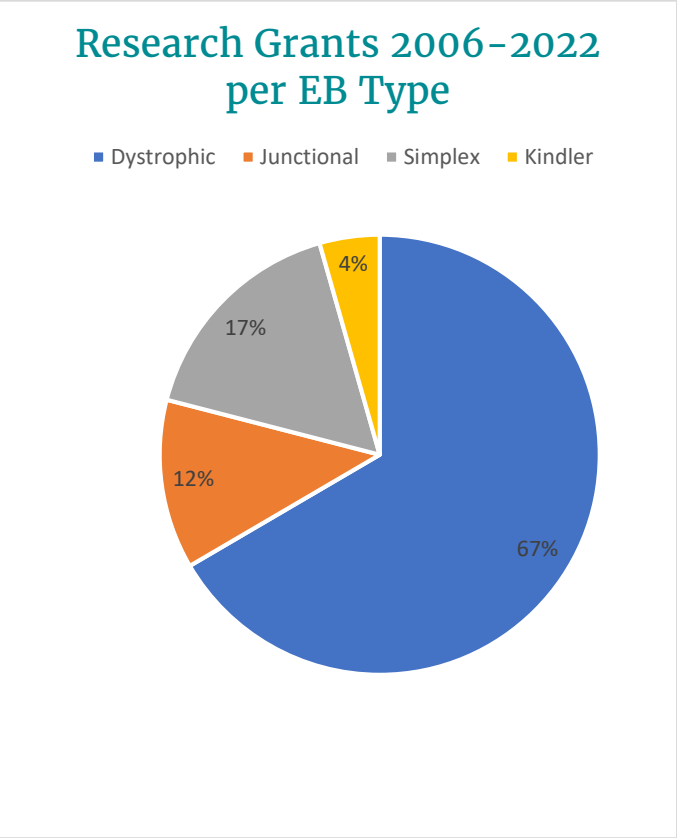
It is important to emphasize that EB research supported via national DEBRA groups and EB Resnet has never been geographically restricted. The data show that there are excellent EB researchers worldwide. In taking forward research into the clinic, partnerships with companies will be increasingly required, and in EB – just as in the wider biopharma and healthcare industries - there is a preponderance of such companies in the USA, which will require increased international thinking.

More than 330 project submissions have been reviewed by international expert panels since 2007.



The number of submitted and approved international research projects (2007-2022) by country of research institution, ranked by the success rate of submissions. Only submissions from DEBRA International / EB Resnet funding rounds are included.





Research Grants approved were analyzed per research area and EB type (2007-2022).

The research areas of the 87 research projects studied are quite diverse and evenly distributed. Molecular and cellular approaches together account for almost half of the projects. Often, projects cannot be assigned to just one area - there are overlaps – especially in these two areas. The general understanding of the disease and the background of EB is addressed in EB genetics, epigenetics, and biology, which accounts for 17 %. Equally important is the area of cancer research and fibrosis, which with 19 %, has a similar share as the no less essential research areas of symptom control and relief.

Looking at the expenditure in relation to the EB types, we see an evident dominance in RDEB among research projects. This reflects the focus on patients with RDEB as the most severely affected. The nature of the biology of RDEB and the status of research creates opportunities for therapy development. This is in contrast to, for example, severe (Herlitz) JEB, where the nature of the disease and the extreme fragility of children have hindered the investigation of therapeutic approaches developed to date. More recent, less invasive technologies may enable the treatment of such highly fragile patient groups in the future.

Research Funding: Calls for Proposals 2022

AP Call 2022 & Ad-hoc Special Call Repurposing 2022

The 2022 funding rounds were opened at the beginning of June 2021 and were accessed via the EB Research Network website and handled via Grant Tracker (online Grant Management Software). We could not organize an in-person Expert panel meeting owing to the COVID-19 pandemic. To allow focused discussion of the most promising proposals during the online meeting of our Experts on December 14, we again introduced a triage step following external peer review, as in 2020 and 2021, to shortlist proposals. For this triage, EB Expert Panel (EBEP) members were grouped according to their areas of expertise, with each group assigned 4-6 proposals together with the associated external reviews for consideration. The process was conducted via anonymous voting in Grant Tracker.

AP Call 2022

A total of 13 project proposals were submitted. Four projects were excluded due to severe deficiencies (consensus decision by EBEP). Two projects reached the 'international importance' standard for funding and two the 'national importance' standard. Owing to the limited budget, only the first two projects will be funded.

Special Ad-hoc Repurposing Call 2022

In total, 8 projects were submitted to this special call. The three remaining reviewed projects resulted in only one recommendation from the reviewers and our internal experts.

The projects are currently under negotiation, and we hope to sign the contracts soon. Below you can find more about the funded/recommended projects 2022.

Research Grants recommended for funding and covered by budget 2023

Garcia-Diez 1: In vivo correction of Recessive Dystrophic Epidermolysis Bullosa by gene editing mediated by adenoviral vectors.

Institution: University Carlos III de Madrid

Funding Round: AP Call 2022 (recommended on international level), funded by DEBRA Spain and DEBRA Austria

Main targeted unmet medical need: Mutation correction and Wound healing

This project targets one of the most severe complications of EB: fibrosis - pathological skin thickening and scarring that occurs mainly in patients with recessive dystrophic EB (RDEB) and contributes to developing aggressive skin cancer.

The proposed research approach is particularly exciting because it is already being tested for another indication in phase 2/3 clinical trial. Initial data from the research group also indicate an effective reduction of fibrosis in RDEB mouse models. The project relies on a repurposing model of an already-known molecule and could move relatively quickly into clinical implementation if the results are positive.

Link to Project description.

Condorelli 1: Notch signalling by the gamma-secretase inhibitor PF-03084014 to counteract fibrosis progression in recessive dystrophic epidermolysis bullosa

PI: Dr Angelo Condorelli

Institution: Bambino Gesù Children's Hospital, Rome, Italy

Funding Round: AP Call 2022 (recommended on international level)

Funding Body: funded by DEBRA Austria

Main targeted unmet medical need: Chronic inflammation and Fibrosis

This project comes from gene therapy and is based on CRISPR/Cas9 technology. The research team proposes the development of an *in vivo* (directly on the skin) gene therapy in the form of a skin gel for RDEB patients. Correction of a prevalent mutation in the collagen 7 (COL7A1) gene could be achieved with a specific adenoviral vector. The aim is to develop a drug for treating chronic wounds, which could also be effective in the digestive tract of EB patients.

Link to Project description (not yet available).

Hovnanian 8: EGFR pathway in generalized severe Epidermolysis Bullosa simplex and effects of the EGFR inhibitor erlotinib.

PI: Prof Alain Hovnanian

Institution: INSERM, Paris, France

Funding Round: Special Ad-hoc Call Repurposing 2022

Funding Body: funded by DEBRA France, administrated by DEBRA Austria

Main targeted unmet medical need: Itch

Individuals with epidermolysis bullosa simplex (EBS) suffer from painful blistering of their skin after minor trauma. They also develop painful calluses of palms and soles in the severe forms of the disease. Recently a new biological pathway was identified in similar skin conditions which were very efficiently improved by pharmacological inhibition of this pathway. There is preliminary evidence for activation of the same pathway in patients with EBS. This project aims at investigating the role of this pathway in severe EBS and to test at the preclinical level whether its pharmacological inhibition can improve the disease phenotype.

Link to Project description (not yet available).

Overview Research Grants since 2006

Research Funding: Ad-hoc Grants 2022

The Ad-hoc funding channel enables small funding grants to be awarded quickly and flexibly. The aim is to allow, for example, co-financing opportunities, new project ideas or proof-of-concept projects. Of course, all ad hoc project proposals undergo rigorous review. Academic researchers, clinicians, and the industry can contact us outside the official funding rounds to submit research proposals.

In 2022 we used the Ad-hoc Channel to open the above-mentioned Special Ad-Hoc Call 2022 - Repurposing drugs for EB. In addition, one project was granted funding as resubmitted (initially handed in to AP Call 2021) to the standard Ad-hoc funding channel.

Ad-hoc Projects recommended for funding

Connelly 1: Investigating the impact of EBS-causing keratin mutations on epigenetic gene regulation.

PI: Prof John Connelly

Institution Queen Mary University of London

Funding Round: Ad-hoc Project (Resubmission from AP Call 2021)

Funding Body: funded by DEBRA Austria

Main targeted unmet medical need: Wound healing

Epidermolysis bullosa simplex (EBS) is caused by mutations in keratins that are essential for skin strength and resiliency. Recent studies by the research team have discovered that keratin defects also cause dramatic changes in the structural properties of the nucleus of skin cells. As the nucleus is a central point for regulating gene expression, the group hypothesizes that these structural changes in the nucleus also influence the organization of DNA (also known as the epigenetic state) and the expression of genes. The proposed project will therefore investigate how EBS mutations influence the cell's epigenetic state. The team will profile the global changes in key epigenetic markers in healthy and patient-derived keratinocytes and skin samples. The findings will provide new and fundamental insights into EBS pathology, specifically the epigenetic state, which is a powerful regulator of cell function but currently unknown in EBS.

Link to Project description.

Overview Ad-hoc Grants

Research Funding 2023 - Outlook

EB Resnet member DEBRA Austria is planning a Special Call 2023 with itspartner LifeArc. Preparation work started already in 2022. The starting point will be a survey among experts to consider additional druggable disease targets in EB and other inflammatory and/or fibrotic conditions that may point to novel treatments for EB. Similar to the Chronic Inflammation & Fibrosis Calls, we would like to start the discussion with experts and ask specifically about conditions, pathways, and molecules worth further investigating. A structured questionnaire circulated among experts will help gather crucial information for discussion at a hybrid round table in May 2023 in London.

Identifying drugs already marketed for other conditions but with evidence of possible value to EB may be the first step to approaching the industry or publishing a targeted proposal call (Repurposing Call 2023).

More information on EB Resnet.

DEBRA UK launched an international funding round beginning of 2023. All recommended national EB projects funded by DEBRA UK (or other national DEBRA groups) are also displayed on EB Resnet's project database. More information on the UK call on DEBRA UK's website.

EB Expert Panel (EBEP)

Its members are senior EB researchers and clinicians who jointly reflect the breadth of EB research. For Special Calls for research proposals, which may focus on a particular unmet research need or novel technology, we convene Expert Panels with expertise specifically relevant to the topic of the call, which can involve selected steady EBEP members and additional experts chosen for their specific area of knowledge. Members of our Expert Panels work to act as a guardian of scientific quality and relevance to people with EB of the research that EB Resnet funds. Its members review both proposals and progress of research funded by EB Resnet members: this peer-review process is central to maintaining our reputation as a research funder among the academic and clinical research community, bioindustry, and research sponsors and donors.

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Jouni Uitto: Passing of a pioneer of EB research (1943 - 2022)

© Thomas Jefferson University

We are deeply saddened by the passing of Jouni Uitto, one of the pioneers of EB research.

He was a long-standing member of DEBRA's Medical and Scientific Advisory Panel (MSAP) and the EB Expert Panel (EBEP). His contribution to DEBRA and the entire EB community, especially to EB patients, was immense over many years.

Jouni's huge contribution to research to unravel the causes and complications of EB have driven forward the hope for better diagnostics, prognostics and effective treatments for people with EB. On their behalf, we say 'thank you' for a lifetime dedicated to improving their lives and offering the prospect of a brighter future. His scientific publications and invitations to lead major conferences attest to Jouni's contributions to the EB community. For DEBRA, he has chaired every biennial international research conference organized since 2006 and participated in Expert Panels convened to discuss medical and research priorities for EB patients.

The whole EB community will remember his winning smile and sense of humor and his outstanding commitment to EB research, to which he gave much weight during his career. Our thoughts are with his family.

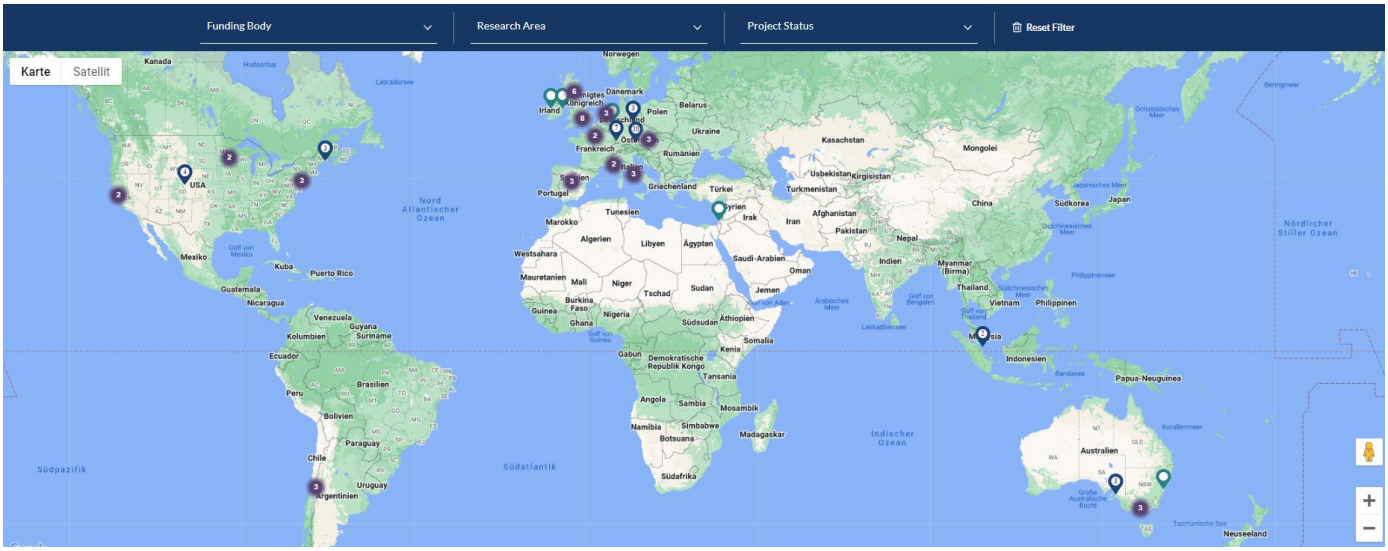
Jouni was a Professor and Chair of Dermatology and Cutaneous Biology at Thomas Jefferson University in Philadelphia.

Useful links

- EB Expert Panel Members
- Review-Process

4. Project Overview

THE EB RESNET PROJECT DATABASE RANGES FROM NATIONAL PROJECTS IN THE NATIONAL MEMBER GROUP STATES TO INTERNATIONALLY FUNDED PROJECTS IN OVER 60 RESEARCH INSTITUTIONS WORLDWIDE. THE PROJECTS COVER ALL CURRENT RESEARCH PRIORITIES AND ALL EB TYPES.



EB Resnet Project Map shows current and completed projects worldwide.

Project types

EB Resnet shows different EB research projects on its website. Those projects funded through EB Resnet research funding rounds (formerly through DEBRA research funding calls) are called Research Grants. The Research Grants are reviewed and evaluated through the international peer review process with the EB Resnet EB Expert Panel (EBEP). The selection process for these projects is subject to a rigorous scientific expert analysis. Those projects selected by local members through their national funding streams and own review process are called national research projects.

Project Database & Project Map

There are 135 projects in the EB Resnet project database. 35 projects in the database are ongoing and being conducted at 27 different research institutions worldwide. Again, 15 of these are active Research Grants.

EB Resnet members and partners fund research projects, either jointly or individually.

The Google Map on the EB Resnet website shows the geographic location of all projects. Our database provides a lay summary, a short scientific summary, the strategic relevance for EB, related publications, and a short impact report for each completed project.

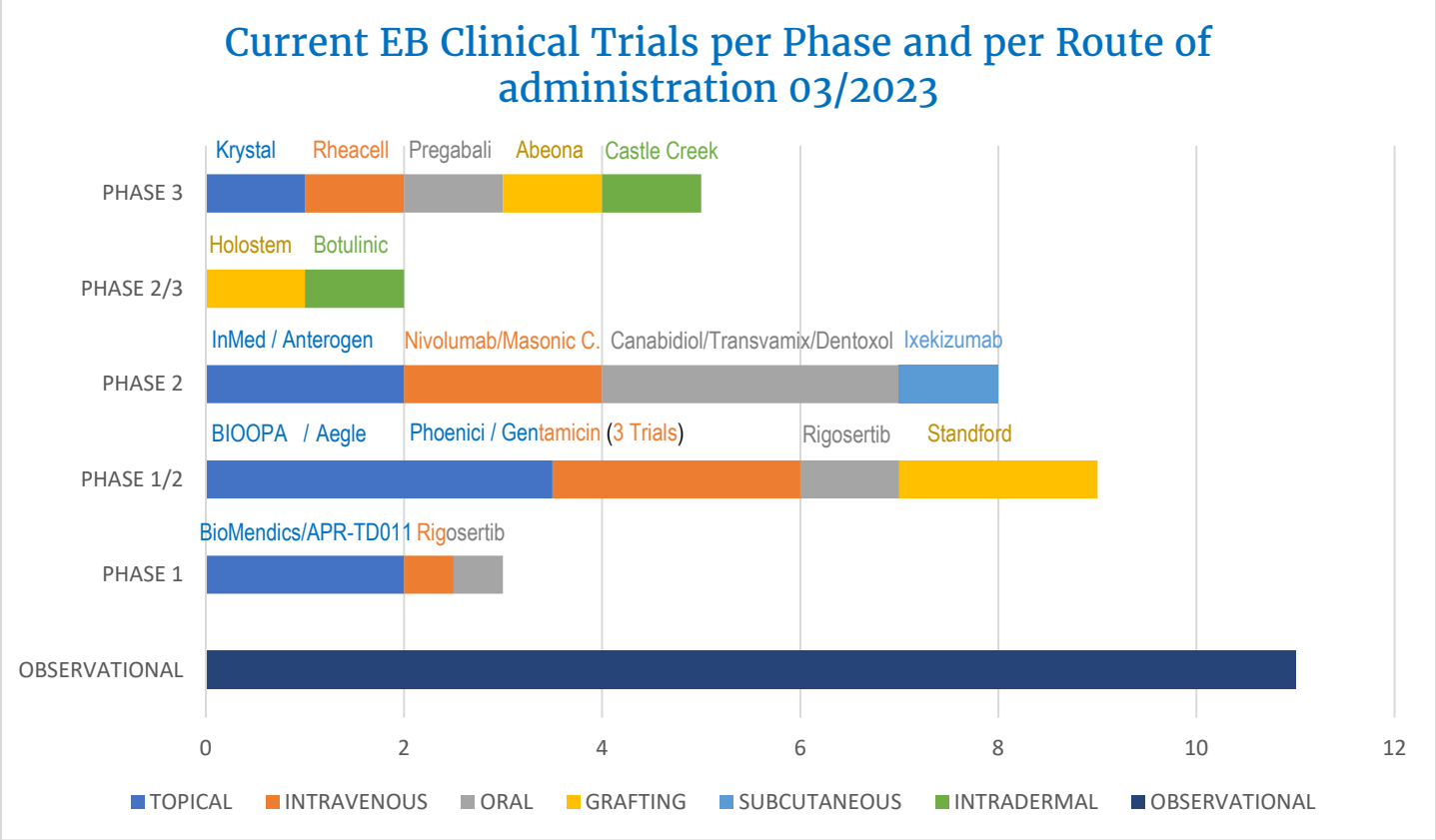
Search our database or Search our Google map

5. Clinical trials for EB

THE APPROVAL OF AMRYT PHARMA'S FILSUVEZ - THE WORLD'S FIRST EB DRUG - IN 2022 BOOSTS OTHER CLINICAL TRIALS FOR EB. THE INTERNATIONAL TRIAL REGISTRIES SHOW OVER 40 ACTIVE CLINICAL TRIALS FOR EB WORLDWIDE. WE HAVE CREATED A NEW DATABASE OR ONLINE TOOL TO MAKE IT EASIER TO KEEP TRACK OF THEM.

Current clinical trials for EB

Currently, five phase 3 clinical trials for EB are ongoing worldwide. Twenty-five additional studies are active or recruiting patients. As clinical trials are dynamic, with new trials being registered, completed, or withdrawn or protocols modified, we can only provide a snapshot at a particular time. We have listed those interventional studies that are currently enrolling patients or, to our knowledge, will start/continue soon (01/2023).



The number of active clinical trials by phase and type of application. Status 03/2023.

New clinical trials database on EB Resnet's website

New EB Resnet clinical trials' online tool goes live

© Dmytro Sheremeta

The main aim of the tool is to provide a pooled overview of all studies relevant to EB. It combines studies from the following registries: Clinicaltrials.gov, the EU Clinical Trials Registry, the International Clinical Trials Registry Platform (ICTRP), and the UMIN Clinical Trials Registry.
It is available on EB Resnet's website since spring 2023. All registered ongoing and completed interventional and observational studies for EB will be found. The EB Resnet team and the EB Clinet team will take care of the constant updating of the international database.
The database assigns the studies to the respective therapeutic approach, contains a brief description, and offers further information at a glance, such as the route, the EB subtype, the study phase, and the status. The database's filter functions help you refine your search by therapeutic approach, EB subtype, or study phase. In addition, a search function allows you to search specifically by keyword or, for example, by the sponsor.
You can click on the links to the respective study register and the study sponsor to obtain more detailed information. If you have specific questions about the studies, please get in touch with the respective study centre directly.
We hope the new tool will be helpful and would be very happy to communicate this to the EB community.

Please note that DEBRA cannot guarantee the completeness of the lists, even though they are updated regularly. We are happy to support the maintenance of the database - information about missing studies or updates is very welcome. Thank you very much for your support.

Link to the new clinical trial online tool:
https://www.eb-researchnetwork .org/clinical-translation/clinical-trials-database/

The new clinical trials tool enables you to distract easily a nice graphic by using different filter options. One example is shown below for all ongoing gene- and combined gene/cell therapies.

Trial description	Route	EB subtype	Study phase	ID number	Sponsor
			PHASE 1 PHASE 2 PHASE 3 PHASE 4		
Topical application of Beremagene Geperpavec (B-VEC) expressing collagen VII protein	Topical	DEB	Phase 3	NCT04917874	Krystal Biotech, Inc.
Grafting of epidermal sheets containing kertinocytes (EB-101) corrected with a gamma-retroviral vector carrying COL7A1 cDNA	Skin grafting	RDEB	Phase 3	NCT05725018	Abeona Therapeutics, Inc
Injection of COL7A1-genetically modified autologous fibroblasts into wounds (FCX-007)	Intradermal	RDEB	Phase 3	NCT04213261	Castle Creek Biosciences, LLC.
Grafting of epidermal sheets containing epidermal stem cells, corrected with a retroviral vector carrying LAMB3 cDNA	Skin grafting	JEB	Phase 2/3	NCT05111600 HOLOGENE 5	Holostem Terapie Avanzate s.r.l.
Grafting of epidermal sheets containing kertinocytes corrected with a gamma-retroviral vector carrying COL7A1 cDNA	Skin grafting	RDEB	Phase 1/2	NCT01263379	Stanford University
Transplantation of COL7A1-SIN retroviral engineered autologous tissue-engineered skin	Skin grafting	RDEB	Phase 1/2	NCT04186650	INSERM, France

All studies are listed in the new online tool. The identification number takes you directly to the study on clinicaltrial.gov.

Update on selected studies

Black Pearl Award for Amryt Pharma

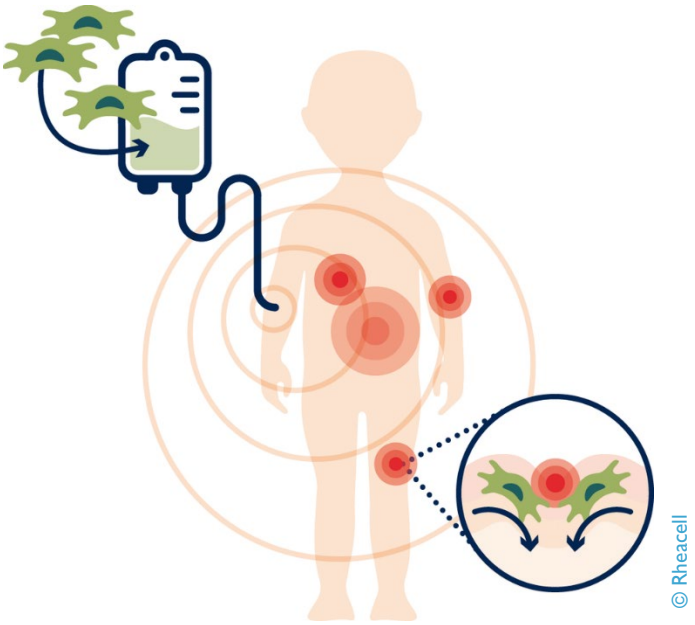
© Amelie de Wilde

This year's EURORDIS Company Award went to Amryt Pharma and was presented on 21 February 2023 for their comprehensive and exceptional Patient Engagement. The award is given to companies that are committed to helping patients with rare diseases through meaningful collaboration.

Amryt Pharma is a long-standing supporter and, more importantly, a consistent and transparent communicator with DEBRA groups worldwide. Their success confirms their path, as thanks to their patient-centred approach, the pharmaceutical company was able to get the first treatment for EB approved in the EU and the UK.

On behalf of all EB patients worldwide, we offer our warmest congratulations. Amryt Pharma should serve as a role model for other Biotech companies committed to developing treatments for EB.

Upcoming pivotal phase 3 clinical trial for EB: Rheacell's systemic stem cell therapy



© Rheacell

Due to their immunomodulatory and anti-inflammatory properties, ABCB5+ mesenchymal stem cells can offer a new innovative therapeutic approach for EB patients.

ABCB5+ MSCs have anti-inflammatory potential by interacting with surrounding immune cells and initiating reprogramming. The release of interleukin-1 receptor antagonists (IL-1RA) induces a shift from a pro-inflammatory stage (dominated by M1 macrophages) to an anti-inflammatory stage (by M2 macrophages). In addition, collagen VII and the structural proteins laminin and keratin 14 are produced, which are also deposited in the wound, aiding its healing. The therapeutic approach has already been tested for its efficacy and safety in the course of a phase 1/2 study. Due to the systemic effect via the bloodstream, the stem cells can migrate to the injured tissue sites - to inner (mucous membranes) as well as outer (skin) barrier - implant themselves in the wound and promote its healing.

The multicentre pivotal phase 3 trial aims to enrol

74 patients (children and adults) worldwide. The EB House Austria will be the first study centre to enrol patients in the study starting in summer 2023.

Rheacell has created a dedicated microsite with clear and patient-friendly information about the trial. This can be viewed via this link: https://www.rheacell.com/en/eb-trial/

Abeona announced positive results in its Pivotal Phase 3 VIITAL Study of EB-101

'Abeona's phase 3 VIITAL study assessed the safety and efficacy of EB-101 for the treatment of patients with recessive dystrophic epidermolysis bullosa (RDEB).

EB-101 is an autologous, engineered cell therapy. Treatment with EB-101 involves using gene transfer to deliver the *COL7A1* gene into a patient's own skin cells (keratinocytes and its progenitors) and transplanting those cells back to the patient. EB-101 is being investigated for its ability to enable normal type VII collagen expression and to facilitate wound healing.

The VIITAL study met its two co-primary efficacy endpoints demonstrating statistically significant, clinically meaningful improvements in wound healing and pain reduction in large chronic RDEB wounds.

Main results

- Primary endpoint measuring >50 % wound healing
- Other endpoints measuring >75 % and complete wound healing at six months all met
- Co-primary endpoint measuring pain reduction at six months met; greater magnitude of pain reduction benefit was observed in post-hoc analysis of EB-101 treated wounds with severe baseline pain
- EB-101 was well-tolerated with no serious treatment-related adverse events, consistent with past clinical experience
- Based on the efficacy and safety profile of EB-101 in VIITAL, Abeona is looking forward to sharing the VIITAL study results with the FDA and progressing toward submission of a BLA in the second quarter of 2023.

These results show new clinical evidence of EB-101's potential to treat the more difficult chronic and large wounds.

Decision on approval of Krystal Biotech's gene therapy gel B-VEC expected by mid-May

© Krystal Biotech

By mid May 2023, the US Food and Drug Administration (FDA) will decide whether to approve this new therapy for butterfly children.

The US company Krystal Biotech has developed a gene therapy (VYJUVEK, also known as B-VEC) based on a genetically modified herpes simplex 1 virus (HSV-1; the cause of fever blisters). A technology platform called STAR-D was patented, in which a vector based on HSV-1 that is no longer capable of reproducing can "infect" a whole series of skin cells. In the process, the genetic material of the virus itself is not incorporated into the genome of the target cells. Only the gene for the collagen is "unloaded". Another advantage: gene therapy is applied "topically", i.e. by applying it directly to the skin. Gene therapies previously intended for other applications are administered "systemically" via infusion. However, this also exposes the gene vectors to the immune system and can cause side effects.

The US Food and Drug Administration (FDA) could make a decision on approval as early as 19 May. This should be based on a phase 3 clinical trial (efficacy and safety) published in mid-December in the New England Journal of Medicine. In the scientific study (DOI: 10.1056/NEJMoa2206663), Shireen Guide from the University of California and co-authors had treated 31 patients aged more than six months. In each subject, a pair of Epidermidis bullosa wounds were randomly and "blindly" treated once a week with either VYJUVEK or a placebo preparation. The treatment ran for 26 weeks.

The results were good. After six months, two-thirds (67 percent) of the wounds that were treated with the drug had healed. With placebo, this was the case in only 22 % of the open skin areas. After only three months, the corresponding success rates were 71 % (B-VEC) and 20 % (placebo). The side effects were minor. According to the scientists, even larger and longer studies should investigate how long the effect of the treatment lasts. So it is quite possible that the FDA will issue a provisional approval with the obligation to conduct further scientific studies in this regard.

InMed Pharmaceuticals has completed enrolment for Phase 2 trial

InMed Pharmaceuticals Inc., a leader in the manufacturing and clinical development of rare cannabinoids, announced that it has fully enrolled its phase 2 clinical trial of INM-755 (cannabinol) cream for the treatment of Epidermolysis bullosa. This is the first time cannabinol has entered a phase 2 clinical trial to be evaluated as a therapeutic option to treat a disease.

This study is being conducted at eleven sites in seven countries, including Austria Germany, Greece, France, Italy, Israel and Serbia.

INM-755 is a cannabinol (CBN) cream intended as a topical therapy to treat EB and potentially other dermatological conditions. Preclinical data show that INM-755 (cannabinol) cream can help relieve typical EB symptoms such as inflammation and pain and may also help restore skin integrity in a subset of EB simplex patients.

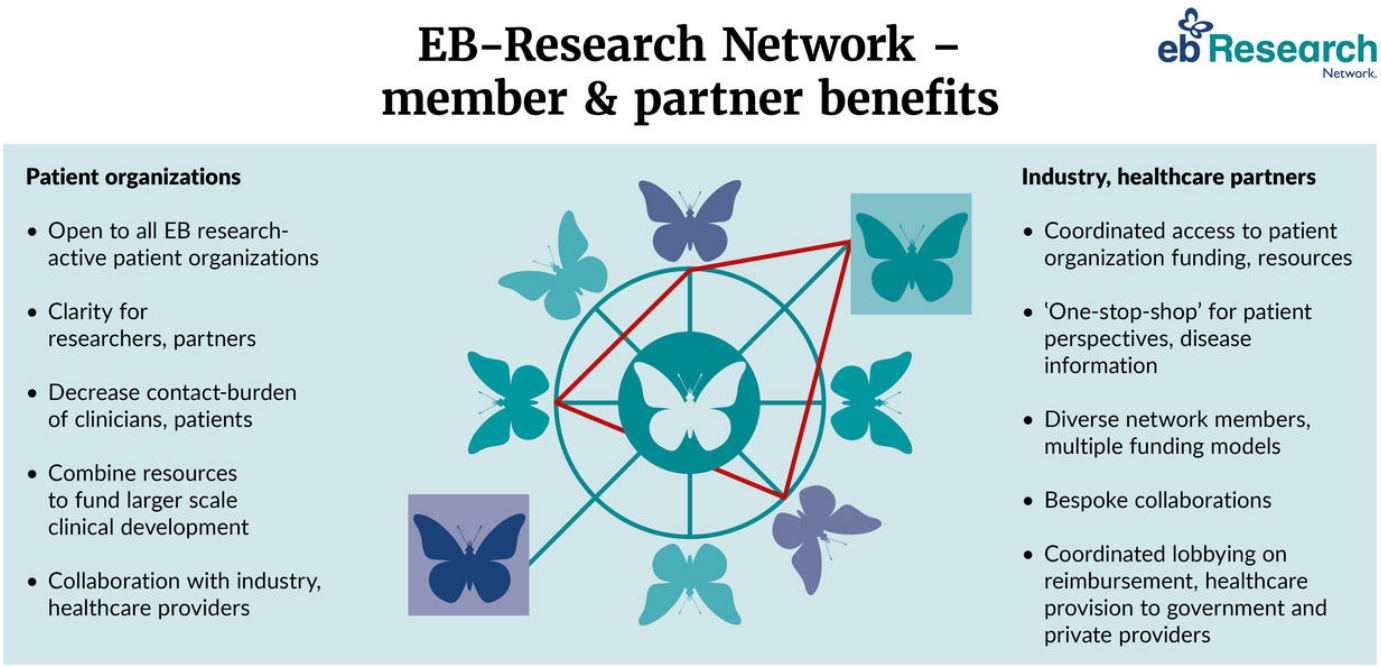
A total of 19 patients, 12 and older, with any of the four inherited EB subtypes — EB simplex, dystrophic EB, junctional EB, and Kindler EB — have been enrolled (April 2023).

Use the new online clinical trials database for searching EB clinical trials: https://www.eb-researchnetwork.org/clinical-translation/clinical-trials-database/

6. Support us

JOINING FORCES TO FIND A CURE AND THERAPIES FOR EB.

There are several ways to support EB Resnet's activities



- Join the network as a funding member: assist EB Resnet in managing and funding the grant schemes.
- Join the network as an ordinary member: share your national research projects and provide small research funding for EB Resnet funding channels and profit from peer-reviewing process provided by EB Resnet.
- Join the network as a partner: share your research knowledge on EB, your EB projects and/or profit on EB patients' access.
- Join the network as a strategic partner: to help driving research outcomes into clinical application for patient benefit.
- Help building up the Industry Partnering Panel - IPP.
- Donate to increase funds for EB research.

If you are interested in supporting EB Resnet or have any special questions about the report or about EB Resnet please contact office@eb-researchnetwork.org !