The EHE Foundation (USA)
The EHE Rare Cancer Charity (UK)
The EHE Rare Cancer Foundation (Australia)
EHE Italia - Non solo Laura
EHE Canada

Quarterly Newsletter for the EHE Group
April – June 2022

the pledge

Edition 29

Contents

Welcome

Welcome to our 29th edition of **The Pledge,** the quarterly newsletter of the EHE Group and the global EHE community, covering the second quarter of 2022. We hope you enjoy the articles that cover the three main areas of focus, namely patient support and advocacy, research and fundraising.

We hope you will enjoy reading about what the global community are doing. As always, we also want to say a huge thank you to everybody who contributes to the overall objective of finding new treatments for EHE, and ultimately a cure. ***"Just Live".***

Highlights

CZI funding extended

CZI funding was extended to cover a third year for the EHE Foundation, providing vital resources to allow the Foundation to continue to build capacity and participate in the Rare as One program.

INT-ICR research expansion progressing

Contracting completed for expansion of the INT-ICR collaborative research, focusing on PDX mouse model development, bio marker analysis, and radiography review to improve prognostic capabilities.

Pan-European prospective registry contracting nears completion

Contracting of the ‘PROSPHERE’ EHE prospective registry within the European STARTER programme is nearing completion, while the EHE Group works to harmonise registry questionnaires worldwide.

UK charity secures important grant award

EHE Rare Cancer Charity (UK) is awarded a grant of £25,500 of unrestricted funds by the Texel Foundation, helping to expand the charity’s operations through 2022 and into 2023.

Big fundraising events are back on in the UK

EHERCC had large teams in both the London Landmarks Half Marathon and Ride London Essex 100 events, with over 60 participants raising over £30,000 for EHE research.

'Challenge 2022' a huge success 'down-under'

The EHE Rare Cancer Australia's 'Challenge 2022' April campaign was a huge success raising over $26,800 to support ongoing EHE RCFA-sponsored research.

The EHE Foundation runs another inspiring EHE awareness campaign

The EHE Foundation launched another inspiring global EHE awareness programme, asking patients to "tell us about EHE in your words". You can see their stories in this newsletter.

Further details on these stories, and much more, can be found in this edition

the pledge

Edition 29

Just live

01 Patient Support and Advocacy

Some of the best people to provide support, advice and encouragement for EHE patients and their families, or to advocate for greater EHE awareness and support, are fellow EHE patients who know what an EHE diagnosis means and the effect it can have.

That is why the numerous EHE-dedicated Facebook pages and other social media sites, that link EHE patients to each other, are so valuable for the EHE global community. The EHE Group foundations also continue to strive to provide information and assistance to patients who are seeking help and support, while at the same time driving a dynamic EHE-focused advocacy programme. We thank all those who contribute their time, encouragement and energy, whether that is through social media, through contact with the EHE Group foundations, or through direct one-to-one communications. And here are just some examples of this wonderful support that has been given over the last quarter, and the impact it has had.

New Patient Services Initiatives!

EHE Community Connections

In May, The EHE Foundation launched a new initiative, EHE Community Connections. This program is designed to be an ongoing collaboration of the entire EHE community. Guest speakers highlight EHE specific topics and issues. Each virtual session is truly unique in content and delivery. Some sessions are recorded, but others will remain private to those who register.

Attendance is cost-free. The overall goal is to drive information dissemination while advocating for and improving the lives of EHE patients. We want patients to be able to share their thoughts and express the issues that matter most to them, while ensuring they have the tools to advocate for their personal care.

Dr. Tamara Vesel and Dr. Maeve Baechler led the first Community Connections on Saturday, May 14th, entitled ***Integrating the Cancer Identity into the Self***. The session explored questions like, "Why is it important to contemplate on identity after the cancer diagnosis"?; "How does the issue of identity relate to symptoms during cancer treatment?" and "What are the ups and down of resisting versus incorporating a cancer diagnosis into one's life?"

The second Community Connections entitled ***You didn't choose to have cancer, but you can make a difference in how the world fights it*** was held on Saturday, June 18th with featured speaker Patty Cogswell, EHE Foundation Biobank Coordinator. This was in an informal, interactive conversation on the questions, challenges, and benefits of donating tissue and fluids to the EHE Biobank. Participants learned how their contributions can directly power research and help researchers to better understand how to monitor, treat, and ultimately find a cure for EHE.

The EHE Foundation are also pleased to be able to confirm the next two sessions of the EHE Community Connections program.

What Happened at ASCO?

An EHE Update with Jane Gutkovich

Jane Gutkovich, Board Member Emeritus
The EHE Foundation

Jane Gutkovich will share what's new in EHE research as presented at the recent 2022 American Society of Clinical Oncology (ASCO) Annual Meeting. Jane will explore a few very important topics such as:

- Inflammation in EHE
- Is immunotherapy a good choice?
- Personalized mouse to figure out best treatment
- Monitoring EHE with a blood test

Jane held this session on July 23.

Integrating the Cancer Identity into the Self, Session #2.

This event took place on August 6.

The EHE Chat

The EHE Foundation organized the first "EHE Chat" on Saturday, June 11th, which was developed based on the requests from EHE patients and caregivers to stay connected in a casual and a personal format. Hosted by Julie Wahl, the Chats will be held periodically on Saturdays throughout the year. The Chats will be completely informal, without any agenda, and not recorded. It will just be time to get to know each other better. All patients and caregivers are welcome to attend!

Please keep checking The EHE Foundation website for upcoming ***EHE Community Connections*** and ***EHE Chat*** dates to keep the support, education, and conversations going! Dates will also be posted on EHE social media.

01 Patient Support and Advocacy

Laptops & Lipstick

The business group for women

Laptops and Lipstick select EHERCC as their 2022 charity member

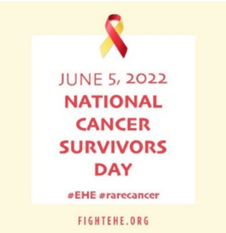
One of the objectives of our patient support and awareness programme is to engage with as many people as we can, to grow and expand awareness of EHE. We were delighted therefore when Kelly Denton in the UK was invited by Laptops and Lipstick to participate in the selection process as they sought to choose their charity to support in 2022.

Laptops and Lipstick was formed in 2011 to provide women in business with a regular, structured and motivational forum for business and personal development. As part of their activities, the group in 2012 introduced an annual charity, as they explained on their website:

> **“Each year, Laptops & Lipstick awards a free annual membership to a local charity. The membership is worth nearly £500 and enables the charity to join our monthly meetings where they can meet and network with a range of local businesses. As a group, we also commit to organising a fundraising event (historically a quiz but we're open to new ideas!) and to supporting the charity's own fundraising ideas.”**

Following Kelly’s excellent presentation on 6th April and the submission of supporting documentation, we were thrilled when Kelly posted news that the EHERCC had been selected as Laptops and Lipstick’s charity partner for the next year. This is excellent as it allows the EHERCC to spread awareness of EHE, make even wider contacts, and potentially bring other groups into the network though Laptop and Lipstick’s contacts. Kelly was rightfully delighted. We congratulate Kelly on this great initiative and look forward to reporting on future developments in subsequent editions of The Pledge.

> **“Our research success is leading to greater understanding of the disease, but with that comes even greater research demand. Everybody is working so hard to raise the funds we need to deliver this critical research going forward. I really hope and believe that our relationship with Laptops & Lipstick can help contribute to these programmes. I think it is really inspiring to engage and partner with women’s groups as we are, after all, battling with a predominantly female cancer. Working together I believe we can make a difference.”**



June 5, 2022 - National Cancer Survivors Day

The EHE Foundation promoted National Cancer Survivors Day to celebrate all people who are living with a history of cancer and to bring attention to the ongoing challenges they still face. The day celebrates the research programs, medical breakthroughs, and treatment advances that are allowing cancer survivors to live longer, healthier, better lives than ever before. It also helps celebrate the personal milestones of cancer survivorship, no matter how small they may seem. Life after a #rarecancer diagnosis like EHE can be complicated and chaotic at times. But it can also be beautiful, meaningful, triumphant, defiant, ordinary, and extraordinary. And that is something to celebrate.

EHE Resources@fightehe.org

One of the core objectives of The EHE Foundation is to ensure that important material and information about EHE is available on its website, not just for US members, but for the global EHE community as well. During the second quarter, these important resources were once again high-lighted.

EHE Library: If you are newly diagnosed, the EHE Library is an essential resource to view and download articles. It is the largest repository of EHE information in the world for patients to access! The EHE Consensus publication is an excellent reference to share with your doctor, especially if you are seeing someone who is not familiar with EHE.

Clinical Trials Listings: Patients can check this listing to view the addition of two new Phase I clinical trials. Patients should contact the Patient Services team at info@fightehe.org with any questions or if you need assistance contacting a study center. Clinical trials information can be overwhelming, and it is suggested patients discuss trial options with their care team.

Tissue Donation with the EHE Biobank: Tissue Donation makes a difference in rare cancer! Patients do not have to wait for a scheduled surgery, they can start the process now. However, if any patient has an upcoming surgery or procedure scheduled, please contact our Biobank team. Tissue may be collected for the EHE Biobank and is invaluable for EHE research. Contact the EHE Foundation Biobank team at biobank@fightehe.org or visit https://fightehe.org/ehe-biobank/ for more information.

01 Patient Support and Advocacy

Maeve Baechler offers life-coaching sessions.

Maeve Baechler is a member of the EHE global community, living in Switzerland, and who was diagnosed with EHE herself in 2015. Maeve is a medical resident so understands the medical aspects of a cancer diagnosis. She is also training to become a life coach with a special interest in cancer coaching. Maeve explained:

> **“I am training to become a life coach with a special interest in cancer coaching, because I wished I had one when I was diagnosed and I wish I had one now. So I decided to learn the tools for myself and I hope to pass on that gift to others out there who are touched by cancer, to empower them throughout their journeys. I want to know if this could be some avenue in which I can make a difference.”**

LIFE & CANCER
Coaching

Maeve noted that while coaching sometimes involves components of working through past experiences in order to understand a client’s current narratives/beliefs, it is not therapy. Coaching is also not about advice-giving. It’s about helping clients find the answers within them, using the resources that have always been accessible to them but which they just didn’t see.

> **“My goal would be to help cancer patients and families through the transitional period around the time of diagnosis, or any time in their experience with cancer. I hope to empower and inspire them to transcend any limiting beliefs they may hold around the diagnosis and how that might be manifesting at work, in relationships, and with the self. Or how a diagnosis might provoke old limiting beliefs and patterns.”**

Wanting to give back to the EHE community by providing her coaching services, Maeve would like to charge clients (only) $15/session and donate 100% to the EHE Foundation, thereby creating a self-feeding, self-supported system. This is a very generous proposal as coaching normally goes for over $100 per session.

If you are interested, you can email Maeve at: **lifecancercoaching@gmail.com**. You can also see her website at **https://www.lifecancercoach.com** where you can learn more about Maeve and what she offers.

EHE April Awareness Campaign

This year’s campaign launched by The EHE Foundation asked the EHE patient community to “Tell us about EHE in Your Words.” Patients and caregivers shared personal insight about EHE to help raise global awareness. These excerpts capture a handful that were shared. Other stories can be found at **https://fightehe.org/category/faces-of-ehe/**.

“I want people to know that EHE can be very frustrating. I say this because EHE is so different for each of us. What works for one person, may not work for the next. It also can cause lots of anxiety for us as we wait and watch to see what it decides to do–will it grow or will it lay low for several years and then become aggressive? I believe that is why the motto of Just Live is so important for each of us. We have to press on and live our lives without allowing EHE rob us of our Joy! When you have no control over the circumstances, you simply must Live with a grateful heart for what today brings.”

- Melissa McPherson

“For me EHE is learning to live with the uncertainty, pain, and chronic fatigue. In the same day you can feel really well and then suddenly feel really bad. Although you may feel perfectly fine, the pain can hit you like a hammer. It's also lonely since there are very little cases because it's a rare cancer. I personally don't know anyone in my country with EHE, I just know one person through social media with it. I'm truly thankful to The EHE Foundation for all their work, and I want to shoutout the special support group on Facebook which makes me feel less alone.”

- Marta Iglesias

“Getting to know other cases through the EHE Foundation, I realized that, even though all cases are very different, uncertainty is something we all share. I have my hopes on the community built around EHE, where I no longer feel alone and trust that there will soon be a cure. I try to live my life one day at a time. My daughters give me the strength I need to feel that there is much more life ahead of me. I would like to say to all of you: don't be passive patients. Be active protagonists in the search for sympathetic doctors who make you feel confident and sure that they will be able to control, improve and overcome this disease. And to remind you that the EHE Foundation will support you always. You are not alone anymore.”

- Carmela Valdivieso

01 Patient Support and Advocacy

> Being diagnosed with EHE mere weeks after the birth of my third child was shocking and soul crushing. My head filled with so many negative thoughts after hearing "stage 4," "metastatic" and "incurable." I'm a 35-year-old, healthy female...or so I thought. I read a powerful message from a fellow EHE patient; "you could die with EHE and not from EHE." I began treatment, started running and switched to plant based. From that moment on, my drive and determination shifted; I can do this, I WILL do this. As a mother to three children under 5 years of age, I will do everything in my power to be present for my babies and loving husband. I am an EHE survivor with metastatic cancer in my lungs, liver, thigh and knee and I am not letting this stop me from just living.

- Michelle Hughes

> Being diagnosed with EHE showed me how important the doctor-patient relationship can be, particularly in the management of rare diseases. My former hepatologist once told me that 'As a doctor, I have to be humble enough to recognize my limits and let you know that I don't know how to manage your diagnosis. You are more informed about your diagnosis than I am, you are the expert here.' Because of this attitude and mind-set, I had complete trust in this doctor from the very first appointment I had with him. I think it is crucial for physicians to acknowledge that rare disease patients need to have an active role in their treatment process and see them as an informed and involved partner.

- Mariana Coutinho

We want to thank all those who participated in this EHE Foundation awareness campaign, for sharing your stories and hopes and fears so openly and honestly. Your spirit and determination shine through brightly; an inspiration for all. ***Just Live*** indeed.

Championing EHE at the Chan Zuckerberg Initiative Rare As One Project Annual Convening!

The EHE Foundation recently headed to San Diego for the first-ever Chan Zuckerberg Initiative Rare As One Network 2022 Annual Meeting! After working together virtually for two years, the team finally got to meet fellow Rare as One (RAO) grantees and spent four days listening, learning, and sharing resources.

Being part of this incredible network has been transformative for rare disease patient-led organizations. The Foundation looks forward to future collaborations with patients, researchers, clinicians, and the CZI RAO Network that will help power research into treatment discovery for EHE patients world-wide. Thank you Chan Zuckerberg Initiative!

02 EHE Research

As always, we are delighted to be able to report on both ongoing and new research funded by the EHE Group in this edition of The Pledge. The ongoing research in EHE, and the interest in new grants to either expand and extend existing projects or start new research, leaves us excited by the potential to deliver improvements in the care and treatment of EHE patients everywhere. We hope that our readers also will find the content in this section exciting. We particularly hope that those who have raised funds for the EHE Group understand that it is only due to your tremendous support that this research is possible.

Zebrafish looking red and positive

The EHERCC were pleased to be able to post positive news about the research being undertaken at the Bateson Centre at the University of Sheffield, in the UK, where the team are striving to develop an EHE zebrafish model. Hugh Leonard explained:

> “We started this project four years ago. After two years we could not get the EHE TAZ-CAMTA1 translocation construct to appear in the endothelial cells in the fish. We considered stopping the project but decided we should first undertake a review with independent experts in the field. As a result of that a number of ideas were proposed to address the issues, and so in mid-2021 (we lost a year due to COVID) we extended the research by a further year. Last month we received these photos of the latest transgenic fish with the construct inserted into the fish linked to a cherry red marker. As you will see the fish is red everywhere which means we have finally achieved a fish with the TAZ-CAMTA1 construct in its endothelial cells.”

That was encouraging and also exciting news, but as Kate Hooper (EHERCC Trustee) explained, there are still challenges ahead.

> “This zebrafish, with the cherry red marker everywhere, does not mean that we yet have a fish expressing the TAZ-CAMTA1 fusion protein in endothelial cells; but it is a big step closer to that ultimate objective. The research team will now seek to introduce a switch to activate the construct in the endothelial cells so that we can turn the gene mutation on when we want to. If we can do that then we will be able to see if our fish do indeed produce the EHE fusion protein, and if they do, what effects will be seen?”

One further hurdle as always is that the continued research needs to be funded, but thanks to great support, EHERCC had that covered, as Hugh Leonard described:

> “At the end of 2021, every penny we had in our bank accounts was fully allocated to fund ongoing EHE research that we had committed to. So when Dr Fredericus van Eeden contacted us in February to explore a further year of funding, we genuinely were unsure if we could produce the funds”

But then through Q1 and Q2 our supporters once again performed brilliantly, raising substantial new funding. At the same time the EHERCC was also delighted to receive a significant grant from the Texel Foundation (see the Fundraising section of this newsletter) which meant that with cashflow management, EHERCC had the funds need:

The EHERCC want to thank Eleanor Markham and Dr van Eeden for their dedication to the project. They also want to thank everybody who supported the charity in the first half of the year and raised the funds needed and which have allowed the project to be extended. Let's hope 2022/23 is the year that we finally achieve an EHE zebrafish model. That will be truly magic.

ASCO 2022

This year's American Society of Clinical Oncology (ASCO) annual conference was held in Chicago in the USA. The EHE Foundation was once again well presented, engaging with researchers and clinicians, encouraging and promoting discussion about, and research in, EHE.

For Jane Gutkovich, Board Member Emeritus of the EHE Foundation, it was the 5th ASCO conference that she has attended, and Jane was excited:

Jane also shared a few pieces of EHE-related news, demonstrating the interest and progress we are seeing in EHE:

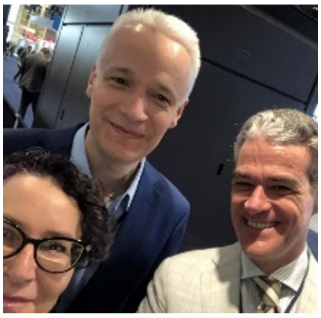
> **“This is my fifth ASCO meeting, and never before have I seen so much awareness and interest in EHE patients. This is the result of the outstanding work of the EHE foundations around the globe and YOUR involvement. Stay tuned for more news from ASCO”**

1. Dr Silvia Stacchiotti presented a poster on EHE demonstrating that there is a possible blood biomarker that can demonstrate efficacy of treatment before it shows up on scan results. Super exciting!
2. There has been a study conducted on 24 EHE tumor samples demonstrating a potential response to immunotherapy in some patients. I will follow up to see if there are specific EHE locations.
3. There are discussions taking place about a trial of ‘nab Sirolimus’ (a different formulation) in EHE patients. Nab Sirolimus has already shown better efficacy in other cancers that had responded to regular Sirolimus.

As always, a major benefit of these conferences is the opportunity to network, and Jane was delighted to be able to post just a few photos with some of the researchers and clinicians who are doing so much for EHE. Here are those photos, showing Jane with...


Dr Breelyn Wilky

Dr Silvia Stacchiotti


Prof Robin Jones and
Dr Alessandro Gronchi


Dr Brittany Siontis

02 EHE Research

EHE biobanking is so important

The collecting of biological samples is critical for future research into any disease. With common cancers, tissue and fluid samples are abundant and collecting these samples is less important. For a disease as rare as EHE, however, banking biological samples is absolutely critical. With so few patients, and many of these not undergoing surgery, tissue samples in particular are ultra-rare.

Jenni Case Kovach, President of The EHE Foundation, explained:

> “I cannot over-state how important tissue donation is for moving forward research on EHE. We have broken down so many barriers and we have researchers that are interested in EHE but without donations into our biobank they don’t have the resources needed to move forward on research. So, if you have a surgery coming up, including a biopsy, a surgical resection or removal of a tumour, or a liver transplant, or have had such surgery in the past, please let our biobank team know, using the contact details below. Your tissue can help researchers learn more about EHE, and ultimately deliver a cure for EHE. It really is that important.”

It is not only The EHE Foundation that is championing biobanking of EHE samples. In the UK, The EHE Rare Cancer Charity has funded the setting up and operation of the UK National EHE Biobank, based at the Royal Marsden Hospital. In Australia, EHE biobanking is coordinated by the EHE Rare Cancer Foundation Australia (EHE RCFA), working with the WEHI Stafford Fox Rare Cancer Research Program where the samples are actually banked.

One of the important things about these dedicated EHE biobanks is that the use of the samples is closely controlled but also strongly promoted, as Hugh Leonard explained:

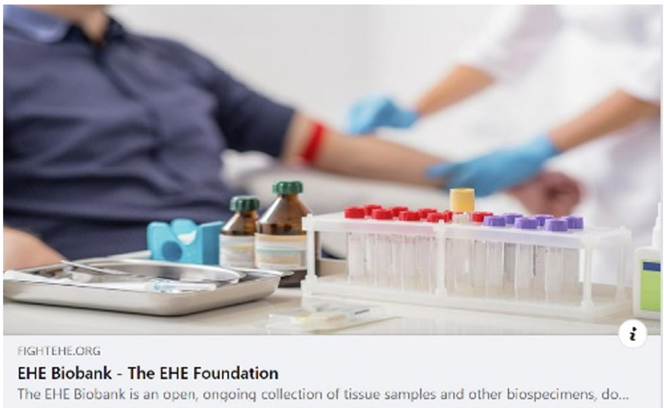
> “In many cases, EHE samples are either lost or are captured within hospital biobanks or general research biobanks. That is better perhaps than losing them altogether, but in these general biobanks we don’t have control of the samples, or any say on how they are used. If they are used, it is likely to be for more general studies and may not be useful for EHE. If we can secure these samples in EHE-dedicated biobanks, then we can ensure that the samples are used to drive EHE-specific research. We can also use the availability of the samples to attract new researchers.”

Jonathan Granek, Director of the EHE RCFA, continued:

> “We have good examples of EHE teams being able to use EHE samples to the benefit of our worldwide community. The team at INT in Milan have created a PDX model using EHE tissue from a donor. They are also researching EHE biomarkers using blood donated by EHE patients with some exciting results being presented at ASCO.”

The EHE Group cannot stress enough the value of our patient community supporting these EHE-dedicated biobanks, and thereby ensuring their samples go to drive EHE-focused research. If you have any questions, then here are some important contacts:

In the USA:
Contact Patty Cogswell, EHE Biobank Coordinator, on 1-919-619-1811, or at **Biobank@fightEHE.org;** or Visit the EHE Foundation biobanking page at: **https://fightehe.org/ehe-biobank/**



FIGHTEHE.ORG

EHE Biobank - The EHE Foundation

The EHE Biobank is an open, ongoing collection of tissue samples and other biospecimens, do...

In the UK:
Contact the EHE Tissue Coordinator at the National UK EHE Biobank at the Royal Marsden Hospital, at **EHEbiobank@rmh.nhs.uk;** or Hugh Leonard at the EHE Rare Cancer Charity (UK) at **hleonard@ehercc.co.uk**

ehe
Biobank

In Australia:
Please contact the EHE Rare Cancer Foundation Australia (EHE-RCFA) at: **info@ehefoundation.com.au** if you have any queries regarding participating in the WEHI Stafford Fox Rare Cancer Research Program, or to notify the foundation of a recent/upcoming surgical procedure.

EHE
Rare Cancer Foundation Australia

02 EHE Research

INT/ICR EHE research expanded

In the Q4 2021 edition of The Pledge, we reported on the exiting news that the EHE Group had confirmed funding for an expansion of the collaborative EHE research being conducted by 'The Instituto Nazionale Tumori' (INT) in Milan, Italy and 'The Institute of Cancer Research' (ICR) in London, UK. This expansion is a three-year project with three key objectives:

Objective 1: The generation and characterization of patient-derived preclinical models of EHE to assess the activity of anticancer agents and identify/validate novel therapeutic targets. This will involve the generation of four or more additional PDX models of EHE from patients with different variants of the disease. The models will then be used to assess the activity of drugs relevant for the disease as monotherapies and in drug combinations;

Objective 2: The validation of circulating microRNA that have been shown to be differentially expressed in EHE patients compared to healthy donors; and

Objective 3: Radiological features and response assessment involving the collation and review of a comprehensive collection of the radiological assessments performed at the foreseen timepoints by all patients enrolled. Evaluation of the imagery will be used to try and gain greater definition of radiological progression and the assessment of treatment response in EHE which remain major challenges.

Denise Robinson, Director of Research at The EHE Foundation, explained why this project is important and exciting:

> "INT and ICR together are conducting this multi-faceted research programme, building on and broadening their existing EHE research collaboration that has been in progress over the last 18 months. The project is developing critical PDX models (PDX are mice with human EHE tissue implanted to keep the tissue alive and allow it to grow); it is beginning to identify possible biomarkers; it will start to research genuine new therapeutic targets and drugs; and will also be initiating a major study of radiological imagery to try and improve our understanding of what these images are telling us about the progress of the disease in a patient. It has the potential to deliver game changing results in a number of key areas, something we find very exciting, and are very happy to be able to help fund."

Funding for this project is provided jointly by EHERCC and The EHE Foundation. The EHE Group are now delighted to be able to report that all contracting requirements have been completed and that the project will go live in Q3.

We look forward to reporting on this exciting project in future editions of The Pledge, and wish the research teams at INT and ICR every success in their ongoing work.

Hippo Pathway Targeted Drug Development

Denise Robinson, Director of Research for The EHE Foundation attended the Hippo Pathway Targeted Drug Development Summit in Boston, MA (USA) in May. The meeting brought world-renowned academic researchers together with pharmaceutical companies to discuss novel protein targets within the Hippo Pathway.

The conference planners postured the event to global researchers and industry with the goal to learn, debate and collaborate – maximizing the potential of the Hippo pathway and its huge therapeutic potential.

Denise was thrilled to represent EHE patients among the esteemed gathering of scientists. Denise reported that Dr. Brian Rubin presented during the first day of the conference on "*EHE as a Paradigm for Hippo Pathway Dysregulation*." Denise said:

> “Dr. Rubin brought EHE patients to the front-and-center of this conversation, highlighting the urgency to work together to find treatments. It was a great presentation, sparking a tremendous amount of interest and conversation for the remainder of the meeting.”

Some of the pharmaceutical companies attending who are investigating therapeutic targets include Ikena Oncology and Novartis, both of which have launched Phase I clinical trials to test their compounds in EHE patients. Other companies present were Sanofi, Genentech, Vivace Therapeutics, SpringWorks Therapeutics, and Cedilla Therapeutics. With all of these companies in the room “we are going to see meaningful development and something really good is going to happen for EHE”, Denise said.

Denise had the opportunity to meet Dr. Rubin and his team in person at the conference. From left to right: Brian Rubin, MD, PhD, Ajay Pobbati, PhD, Denise Robinson, and Kepeng Che, PhD

02 EHE Research

EHE Registry Initiatives Around the World

A Word About Registries...Every Registry is Not the Same

As many of the EHE patient community know all too well, there are many, many questions about EHE, its natural history, how it develops and progresses, its response to different drugs regimens and treatment modalities, that doctors still don't have an answer to. One critical way that we can start to address this lack of knowledge and understanding about EHE is to begin to collect detailed information about patients' EHE and how it has behaved, within what is usually referred to as a 'registry'.

The word 'registry' refers to an organized method to collect information (data) about a person's health and care they receive regarding a specific disease. Most commonly, the data is used to better understand the natural history of a disease and evaluate treatment outcomes, and there are other important uses of the data such as supporting the approval of a new treatment for a disease.

Registries can collect information from different sources – patient registries are important because they ask patients with a disease to voluntarily contribute their health information and their disease journey directly. Other registries are initiated by medical doctors or epidemiologists, and this type of registry includes information that is taken from a patient's medical record and inserted by clinical staff. Both of these types of registries are essential for our learning more about EHE.

We are therefore delighted to be able to report on two different EHE registries that are progressing; one being a clinically-led pan-European registry that will based at Fondazione IRCCS Istituto Nazionale Tumori, in Milan in Italy; while the second is a global patient-led registry that will be administered by The EHE Foundation from the US. Further information on each of these registries can be found below.

Pan-European EHE prospective registry moving forward

Study objectives

With the aim of addressing the many outstanding questions about EHE, Dr Silvia Stacchiotti and her team at Fondazione IRCCS Istituto Nazionale Tumori (INT), based in Milan, Italy proposed to establish a collective effort across the EU and UK, with the establishment of a Prospective EHE Registry which will be called the PROSPHERE study. This will be a clinically-led registry.

The PROSPHERE study aims to provide a description of the population affected by EHE, giving an insight into the natural history of the disease and its variants, leading to the possible identification of clinical and biochemical prognostic and predictive factors and answering some of the outstanding questions on its management.

Study design

The original plan was to create a stand-alone registry, coordinated and run by the team at INT in Milan. However, personnel in INT quickly realised that the EHE registry would be more sensibly set up within a broader European project named STARTER, developed in the framework of EURACAN, the European Reference Network (ERN) dedicated to rare adult solid cancers, that is also being coordinated by INT. Dr Annalisa Trama (Department of Research, Evaluative Epidemiology Unit,), INT, the STARTER project PI, explained:

> **“STARTER is a Health Programme funded project, aiming to set-up a clinical registry for EURACAN. The project was launched in April 2020 and will be running for 36 months. It will exploit at a European level, data coming from individual expert health care providers, from national and European registries and it will be interoperable with already existing rare disease registries.”**

The EURACAN registry will progressively cover all the 10 families of rare adult solid cancers included in EURACAN (sarcomas; rare neoplasms of the female genital organs and placenta; rare genitourinary cancers; rare neuroendocrine tumours; rare digestive cancers; rare endocrine cancers; rare head and neck cancers; rare thoracic cancers; rare skin/eye melanoma and rare brain tumours). However, sarcomas and head and neck cancers have been selected as the two initial target groups to get the project started.

Among the sarcoma domain (coordinated by Prof. Paolo Casali, Medical Oncology, INT) ultra-rare sarcomas, such as EHE, have been selected as the topic to start with, as the community believe that, given the exceeding rarity of these sarcoma types, international prospective registries could provide an invaluable contribution, both by allowing a better understanding of the natural history of the different diseases, and in order to provide external control data, potentially useful in the process of drug development and approval.

Dr Anna Maria Frezza explained further: Incorporating the PROSPHERE study within STARTER will deliver the following benefits:

> **“Incorporating and operating the PROSPHERE study within and as part of the STARTER project represents an extraordinary opportunity to develop an EHE prospective registry that will be broader, larger and more cost effective than if PROSPHERE was run as a standalone study.”**

1. The establishment of a full registry in EHE, which with appropriate funding can be maintained on an ongoing basis with no pre-defined duration over time.
2. The use of the existing free web-based application for database management (RedCap). INT, using RedCap, will set up a case report form (CRF) dedicated to EHE that includes data quality checks based on the experience gathered in the development of the head and neck EURACAN registry.
3. A simplification in terms of administrative, legal and ethical issues implicit in the project which the STARTER project team has already addressed, through huge regulatory analysis over the last two years, and is compliant with very complex ethical and administrative issues such as current GDPR requirements.
4. The supervision of a dedicated coordination team of data manager, CRF developers and statisticians.
5. The potential enrolment of a large number of patients through the contribution of multiple sarcoma reference centers, within and outside EURACAN.

02 EHE Research

Currently, the EURACAN sarcoma domain includes more than 50 sarcoma reference centres across Europe. Originally, three centres in the UK were also part of the domain (Royal Marsden Hospital, London; University College of London Hospital, London; and Oxford University Hospital, Oxford), but these centres formally left EURACAN as a consequence of Brexit. However, given their expertise in the disease and valuable contributions, they are still working closely with the ERN as expert guests. The PROSPHERE registry will initially start with approximately 10 centres across the European Union and the UK, and by joining STARTER, the PROSPHERE registry will then be able to progressively include many more sarcoma reference centres.

This prospective registry will include all consecutive patients with a histological diagnosis of EHE and treated at participating sarcoma reference centres. For every patient included, a confirmation of the histological diagnosis performed by the expert sarcoma pathologist of each contributing institution (centralization at a national level) will be performed, and molecular testing for WWTR1-CAMTA1 and/or YAP-TFE3 will be required.

Clinical data (demographic, symptoms, disease clinical and pathological features, treatment, outcome) will be prospectively collected through an electronic CRF which will be put in place and shared with all contributing institutions. Data quality check will be performed by a dedicated study coordinator.

The initial plan is to include a minimum of approximately 100 patients (range: 80-120), 36 months, followed by a follow up time of at least 3 years.

EHE Global Patient Registry

The EHE Foundation is progressing with the set-up of a global EHE Patient Registry which will be initiated, maintained and administered from the US; however, people with EHE from all over the world will be able to join the registry and contribute their EHE-related information. The major difference between the pan-European patient registry outlined above and the global patient registry is that the latter registry will include information contributed and input directly by patients.

The Global Patient Registry will include anyone diagnosed with EHE – no matter if a person has had any treatment. Some of the key types of information the Global Patient Registry will collect include:

- Demographics
- EHE Presentation – early signs and symptoms of the disease
- EHE Diagnosis including disease location and organ involvement
- Brief Medical History
- EHE Treatments and how each patient felt they responded to the treatment or therapy
- Pain assessment and utilization of pain medications or other therapy

This project aims to be the largest-scale EHE-patient initiative ever undertaken. The data contributed to this Registry by each patient will inform EHE patients, doctors treating EHE, and researchers. Denise Robinson, Director of Research at The EHE Foundation (US) said:

> **“Today, we do not have the ability to describe EHE as a disease from the patients’ perspectives anywhere in the world. This project is critical for the planning of future EHE research and will give information back to the EHE patient community that is essential for their own health advocacy and understanding.”**

The current timeline for initiation of the Global Patient Registry is January 2023. Stay tuned for updates from the US foundation, on the EHE Patients Facebook page and in our future editions of The Pledge.

Global reach and involvement

The EHE Rare Cancer Foundation Australia is also working with the rare cancer community in Australia to initiate a similar concept. As part of this ongoing important work, the EHE foundations are working closely together to develop patient registry and observational study questionnaires so that in the future, data may be harmonized for the greater benefit to researchers and the patient community globally. As patients world-wide participate in these studies and contribute their health information to enable a better understanding of EHE, it is important that data sets provide the entire EHE community with comparable data that spans national boundaries.

Research papers

Each quarter, a number of very interesting research papers are high-lighted, with either general relevance to sarcoma and cancer research, but also some that specifically mention EHE. We cannot include all the more general papers, there are just too many, but we do like to remind our readers of the EHE specific papers, and provide a link to where these can be found. We would also remind everybody that The EHE Foundation maintains a library of such works where these papers can also be accessed. The library can be found at https://fightehe.org/ehe-library/ .

TRANSLATIONAL CANCER MECHANISMS AND THERAPY | MAY 17 2022

The TAZ-CAMTA1 Fusion Protein Promotes Tumorigenesis via Connective Tissue Growth Factor and Ras–MAPK Signaling in Epithelioid Hemangioendothelioma

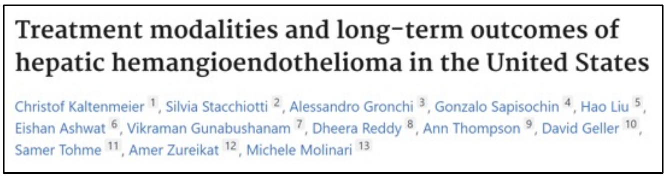
Shuang Ma; Ryan Kanai; Ajaybabu V. Pobbati; Shuo Li; Kepeng Che; Caleb N. Seavey; Andrea Hallett; Ashley Burtscher; John M. Lamar; Brian P. Rubin

https://aacrjournals.org/clincancerres/article/doi/10.1158/1078-0432.CCR-22-0421/698981/The-TAZ-CAMTA1-Fusion-Protein-Promotes?

Aurintricarboxylic acid is a canonical disruptor of the TAZ-TEAD transcriptional complex

Kepeng Che, Ajaybabu V. Pobbati, Caleb N. Seavey, Yuriy Fedorov, Anton A. Komar, Ashley Burtscher, Shuang Ma, Brian P. Rubin

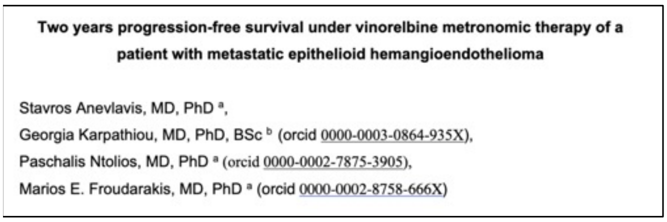
https://journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0266143&fbclid=IwAR1-0IwWvSOHuut2qJAtKP7g7zPhkWAYSrzrcjAmN_mNg26BgA1kehZdbK4



Treatment modalities and long-term outcomes of hepatic hemangioendothelioma in the United States

Christof Kaltenmeier [1], Silvia Stacchiotti [2], Alessandro Gronchi [3], Gonzalo Sapisochin [4], Hao Liu [5], Eishan Ashwat [6], Vikraman Gunabushanam [7], Dheera Reddy [8], Ann Thompson [9], David Geller [10], Samer Tohme [11], Amer Zureikat [12], Michele Molinari [13]

https://pubmed.ncbi.nlm.nih.gov/35504832/



Two years progression-free survival under vinorelbine metronomic therapy of a patient with metastatic epithelioid hemangioendothelioma

Stavros Anevlavis, MD, PhD [a],
Georgia Karpathiou, MD, PhD, BSc [b] (orcid 0000-0003-0864-935X),
Paschalis Ntolios, MD, PhD [a] (orcid 0000-0002-7875-3905),
Marios E. Froudarakis, MD, PhD [a] (orcid 0000-0002-8758-666X)

https://www.monaldi-archives.org/index.php/macd/article/view/1798/1440

Unraveling the Biology of Epithelioid Hemangioendothelioma, a TAZ–CAMTA1 Fusion Driven Sarcoma

by Caleb N. Seavey [1,2,3], Ajaybabu V. Pobbati [1,3] and Brian P. Rubin [1,4,*]

https://www.mdpi.com/2072-6694/14/12/2980/htm

03 EHE Fundraising

Today we are proud to have EHE-dedicated research being carried out in multiple labs in a number of different countries. That research, which has already resulted in excellent advances in our understanding of EHE, is also generating new research objectives, as EHE biology is slowly revealed. However, that expanding research needs to be funded. The EHE Group remains totally focused therefore on raising the critical funds needed to finance, drive and accelerate this existing EHE research programme, as well as the new and additional research that we hope will follow it. We thank all our members, their supporters and members of the public for their fundraising efforts, some of which are described below. We also want to thank other foundations and corporate groups who have provided funding, and so have joined the growing group of people and organisations that are striving to help find a cure for EHE.

London Landmarks Half Marathon – a brilliant day

The second quarter of 2022 started with the running of the London Landmarks Half Marathon. The EHE Rare Cancer Charity had 42 brilliant supporters who were all running for the charity and raising funds for further EHE research.

The Charity were delighted to have two runners who had come over from America specifically to run and raise critical EHE funds for research. Denise Robinson and Ann Campbell, despite some pre-race nerves, ran

great times. Sally Baker, one of the charity organisers commented:

> “We are so grateful to everybody who ran for us today. These people go out and train hard all through the winter to raise money for EHE research. They are awesome. We also want to thank Denise and Ann for coming over – that was very special. We loved having Ann here who was also running in memory of her husband, Steve, who died from EHE four years ago. It was a poignant reminder of why we are fighting so hard to beat this cancer”.

The charity team raised over £17,500 for EHE research. We also think that is a wonderful achievement and extend our thanks and congratulations to all who took part.

Texel Foundation grant awarded

The EHE Rare Cancer Charity were delighted to announce in June that they had received a grant award from the Texel Foundation, the philanthropic arm of the Texel Group. The Texel Foundation, established by the Texel Group in 2015, first supported the EHERCC in that same year, shortly after the charity was started, providing the charity with its first corporate donation.

TEXEL
FOUNDATION

Hugh Leonard, Chair of Trustees, explained:

> “We were so excited when we received that very first donation from a corporate body through their charitable foundation. It really gave us hope that the charity would work. They supported us again in 2019 which was wonderful. We were therefore really delighted when at the start of 2022, we were invited to participate in their 2022 grant application round”

The application round was organised by Texel in compliance with IVAR’s Open and Trusting Grant Making programme, promoting flexible funding, and designed to make the process of grant application easier, more open, and appropriate for those taking part, and to avoid unnecessary restrictions on the use of grants made. Jeff Collins, EHERCC Trustee, explained:

> “The application process was excellent as it was indeed very focused, with an initial short written application followed up by a meeting at which we were able to answer any questions that the Texel team had, and also describe in more detail what the charity was doing.”

The charity was then thrilled when they received the news that they had been successful in securing a grant award of £25,500. The focus of the grant application had been: (i) to allow the charity to increase participation in the pan-European EHE prospective study that is currently being developed with INT in Milan; and (ii) the possible contracting of a professional grant writer. But the unrestricted nature of the grant provides the charity with greater flexibility, as Hugh Leonard explains:

> “Many grant awards are restricted, which means that you can only use the funds for a very specific and defined purpose. The Texel Foundation grant is not like this. Their grant is unrestricted, allowing us to manage its use. This is very useful, because although we will ultimately use the grant funds for the purposes listed in our application, timing of these specific payments can vary, and so in the meantime we can manage our cashflows to ensure we are always getting the maximum utilisation and return from the funds we receive.”

Hugh Leonard went on:

> “This is the largest single donation we have yet received, and it is the largest donation from a corporate/foundation group. The funds will help us expand our activities and advance research into this horrible disease. The EHERCC could not be more grateful for this wonderful award. Thank you Texel.”

CZI Rare As One Project Support Extends for a Third Year

In 2020, The EHE Foundation was selected from the Chan Zuckerberg Initiative (CZI) as part of the Rare As One Program, which provided funding to a network of rare-disease patient-led organizations. These grants were aimed at supporting and lifting up the work that patient communities do to accelerate research and drive progress in the fight against rare disease. Jenni Kovach, President of The EHE Foundation, recently shared the announcement of further funding for The EHE Foundation. She stated,

> “The EHE Foundation is honored to receive a third year of funding from the Chan Zuckerberg Initiative's Rare As One Project. This grant award is testament to our accomplishments and progress in strengthening our organizational capacity, developing the global EHE research network, convening our research community, and aligning our patient and research communities around shared priorities.
> We are grateful to @chanzuckerberginitiative for their continued support!”

Being part of the prestigious CZI Rare As One Project has strengthened the EHE Foundation's collaboration and networking power with other rare disease organizations. It has also funded critical projects like the EHE 360, two-day international virtual conferences held in 2021 and 2022 that brought together researchers, clinicians, and patients from around the world to advance the fight for treatments and a cure for EHE. The EHE Foundation are grateful for CZI for their continued selection for this program.

EHERCC Team cycle 100 miles to raise funds for research

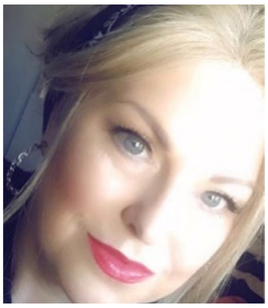
The EHERCC organises two larger scale fundraising events each year. The first of these is the London Landmarks Half Marathon, which was held in early April (see separate report in the newsletter). The second event is a 100 miles cycling sportive, that starts and finishes in London, and is called Ride London. In previous years this event had taken place in the county of Surrey, south and west of London. This year however the event had moved to the county of Essex, north and east of the capital.

EHERCC had twenty riders in the event who collectively raised nearly £20,000 for EHE Research. Paul Dean, an EHE patient himself, completed the ride in just over 5 hours, an amazing achievement. Hugh Leonard, Chair of Trustees, also took part, as he explained:

> “I have been encouraging people to take part in the LLHM and Ride London events for the charity for 7 years now and really felt it was time for me to take part. I trained for the 2020 LLHM but it was cancelled a week before it was to take place, due to COVID. So I decided it had to be the Ride London. It took me just over 7 hours which I was very pleased with. It has been great training together as a group also, and of course we have raised a substantial sum for EHE research which is wonderful.”

We also want to congratulate the team for a magnificent effort. Well done guys. Keep training for 2023!

03 EHE Fundraising



In memory of a very special woman

Wendy Cassidy wanted to celebrate the 50th birthday of her wonderful sister, Allana, who was diagnosed with progressive EHE in August 2018, and left us in 2020.

> “Hello everybody! This is a fundraising event that is very special for me, but one I dearly wish wasn't necessary. As most of you know, my brilliant, wonderful, funny and simply gorgeous sister, our Larney, left us far too early last year after her battle with an ultra-rare cancer called EHE. Allana would have been 50 on the 13th June, so I am organising an event the day after in remembrance of her, and to celebrate her 50th, because I know that is what she would want us to do.”

Wendy's event, held in the Embassy Theatre Foyer in Skegness, gave those who knew Allana a chance to drop in and remember her, share lovely stories about Allana. They also sold cakes, biscuits, tea and coffee to raise funds for EHE research, and set up a fundraising page so that people who could not make it were still able to contribute.

The event was a huge success, and many stories about Allana were indeed shared. Allana would have also been delighted and proud as Wendy raised over £500 for EHE research on the day. Thank you Wendy for organising this lovely tribute to a very special woman indeed.

EHERCC fundraising passes £1 million

The EHERCC in the UK was delighted this quarter to announce that the total funds it had raised since its inception in 2015 had exceeded £1 million. Jeff Collins, Trustee of the charity, commented:

> “We are in reality a tiny charity with a tiny support base, due to the rarity of EHE, so it's pretty amazing that we have reached £1 million. To everybody who donated, ran, rode, swam, sold cakes, put on shows, quiz nights, race nights, rowed the Atlantic, sky dived, raffled, auctioned, and in any other way contributed to that total, including providing just encouragement and support, we just want to say a huge THANK YOU.”

Hugh Leonard agreed:

> “Our supporters are just awesome. This achievement is staggering. So take a bow everybody. But we also need to remember that EHE is a relentless adversary. While the EHE Group has made a huge difference to EHE research that is now taking place, we need to recognise that there is still a huge amount still to do. So while we thank all our supporters for all they have done in the last 7 years, we at the same time encourage them to plan for the next fundraiser. That second million needs to be raised!”

Australian challenge a huge success

The EHE Rare Cancer Foundation Australia held its inaugural national awareness and fundraising campaign during the month of April. The campaign, under its banner headline “**BE AWARE OF RARE & TOGETHER LET’S CURE EHE**”, encouraged people to take on an activity in the month and use it to raise awareness of EHE and raise funds for EHE research.

Jonathan Granek, Director of the EHE RCFA, posted news later in the quarter, thanking everybody who had taken part for their wonderful contributions:

“**A huge THANK YOU** to each and every one of you who helped spread the word, participated in the campaign, bought a T-shirt, or donated! Together we raised over $26,800 to support more ground-breaking research into EHE!”.

It is wonderful to see this level of organisation and engagement from the Australian cohort of our global EHE family. Congratulations on the amazing sum raised which will be used to support more critical EHE research.

A small stall raises £900 for research

Kelly Denton has been actively campaigning for EHE causes since her daughter’s EHE diagnosis. Grabbing any opportunity with both hands and huge motivation, Kelly has enrolled supporters to EHERCC fundraising events; she pitched successfully for EHERCC to be the selected 2022 charity for the Laptops and Lipstick business group for women; and has engaged as an active volunteer assisting with the administration of the EHERCC itself.

No opportunity is lost, and so it was no surprise to hear that Kelly and her daughter would be hosting a raffle stall at the Penge Festival Grand Fete on 11th of June. They also took the opportunity to tell everybody about EHE, and why supporting EHE research was so important. Kelly’s daughter even set up a QR code so that people without cash could still donate.

The day was very successful, with many people stopping to hear all about EHE, and either buy raffle tickets or just make donations. Kelly and her daughter raised over £900 on the day which is huge. We congratulate them on such a great result.

04 And in other news…

Every quarter, people will post stories or short messages that are not necessarily related to EHE. We always include a small selection of these as we think it supports the spirit of so many of our EHE community, namely that they will not let EHE control or dictate how they lead their lives. They will "Just Live"! Here are the contributions for this quarter.

The photo-therapy section

Carl Dickson is a regular contributor to the EHE Facebook pages, posting inspirational messages and also frequent photographs. In April he posted photos of a spring morning. For many of our readers, it was a huge surprise to see the 'spring morning' involved a lot of snow! WOW

Shortly afterwards Carl posted some completely different types of photos of himself and the family in altogether warmer climes. Carl said

> "There are so many different things in this world that are important to maintaining a healthy mind and soul. Whatever those things might be for you it is essential for you to keep them in your life as you live with cancer or any other life struggle."

Q2 also saw Carl return to one of his most common topics, his kids. Carl explained:

> "I just wanted to share an update, my little guy played hard this weekend at their AAA tournament in Vegas. I am so proud of him, he was named MVP. He has put in a lot of work this year and I am glad it paid off. He loves hockey and I love him. Great job again, and another one of those moments why we fight to defeat EHE!"

Keep the stories and photos flowing, Carl. You are indeed *"Just Live"* personified!

Getting together:

One of the facts that many people comment on with regard to EHE social media is how close their friendships become with people they have never met. Often living miles apart, and frequently in different countries, the opportunity to physically meet is very limited. So we love it when people post photos of such meetings. This quarter it was Sarah Bright Yaneza and Julie Rivers Wahl who posted this lovely photo. Sarah summed it up perfectly. "EHE is so devastating. Yet, the opportunity for lifelong friendships and connections while we work toward a cure is our bright spot! ***"Just Live"***

We love happy news!

We know that our EHE global community love happy stories, and they probably don't come happier than the news of Delaney Wahl's engagement. Laney has been a poster girl for the EHE Group from the moment she received her diagnosis, so the EHE community were overjoyed to hear her great news. Congratulations to both Delaney and Ethan. We wish you love and happiness in your future together.

We love a laugh too.

Living with EHE is incredibly stressful and challenging. One of the most important aspects of dealing with this is trying to maintain a sense of humour and fun. It's not always easy, so we love it when we see posts that are taking a humorous look at EHE and cancer. This quarter included an unusual take on CAT scans!

We loved it, and wonder if PET scans work in a similar fashion, but with a greater variation of the animals involved?

The EHE Foundation (USA)
www.fightehe.org

The EHE Rare Cancer Charity (UK)
www.ehercc.org.uk

The EHE Rare Cancer Foundation (Australia)
www.ehefoundation.com.au

EHE Italia – Non solo Laura
website not yet available

EHE Canada
website not yet available