



# Rare Cancer Charity UK Annual Report and Financial Statements 2023





## Epithelioid Haemangioendothelioma (EHE)

# EHE Facts

A **destructive vascular sarcoma** that is found in the walls of blood vessels

Commonly appears in **liver and lungs** but can appear anywhere

Can present as **indolent** (passive) or **aggressive**

Typically more aggressive in **young people**

**Can re-present** after long period with no disease

Often presents with **multiple tumours** called 'multifocal'





May turn **aggressive at any time** without warning

Clinical signal that onset may be tied to **pregnancy** and **puberty** in young women

Living with EHE causes **enormous psychological stress**

Affects both males and females but is **more prevalent in women**

One of the **world's rarest cancers**, with approximately 20 patients per year in the UK

**No recognised treatment**, so treatment is by trial and error

**No known cure.** Aggressive disease is **normally fatal**

Find out more at: [www.ehercc.org.uk](http://www.ehercc.org.uk)





# The UK National Epithelioid Haemangioendothelioma Biobank

Eniola Ayeni<sup>1</sup>, Stephanie Elston<sup>1</sup>, Emma Perkins<sup>2</sup>, Robin L Jones<sup>1</sup>, Bader Al-Badri<sup>1</sup>, Paul Huang<sup>2</sup>, Hugh Leonard<sup>3</sup>  
<sup>1</sup> The Royal Marsden NHS Foundation Trust, <sup>2</sup> The Institute of Cancer Research, <sup>3</sup> The EHE Rare Cancer Charity

## Introduction

The National Epithelioid Haemangioendothelioma (EHE) Biobank supports research into this rare sarcoma subtype where limited tumour material is available for research. The overall aim is to facilitate research into improving diagnostic accuracy, identifying new drug targets and developing new biomarkers to be able to better understand the unpredictable course of this disease.

## EHE Biobank Patient Enrolment

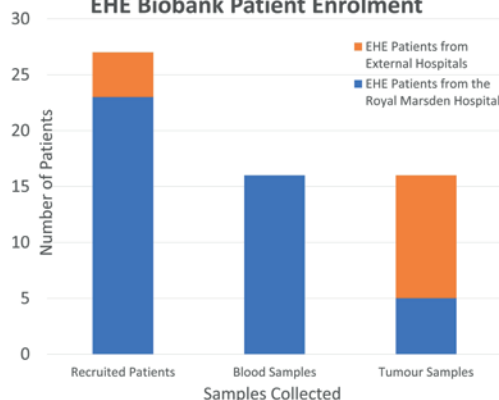


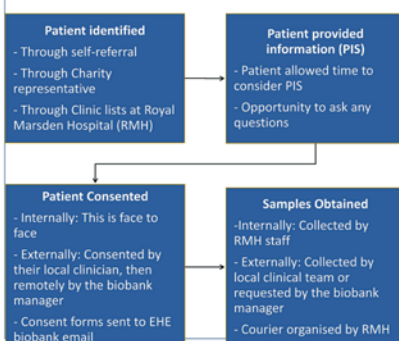
Figure 1: EHE Biobank patient enrolment figures. Recruitment of these patients and the collection of their samples started when the biobank was established in 7<sup>th</sup> April 2021

## Inclusion Criteria

The only inclusion criteria for the biobank is that the patient must have histological confirmation of their EHE diagnosis.

After a formal consent process, the collection and storage of blood and tissue samples from patients will be facilitated by the biobank manager and subsequently stored in the biobank.

## Patient Recruitment Process



## Method

This research is purely observational and involves the collection of peripheral blood, biopsy cores, surgically resected material and other relevant fluid surplus to diagnostic requirements. Blood samples have been processed, stored and frozen as plasma, buffy coat and whole blood. Core biopsies and surgically resected tissue has been stored as fresh frozen tissue and formalin fixed paraffin embedded (FFPE) tissue blocks. They are processed in this manner in order to reduce the chance of degradation.

## Samples Currently Stored in the Biobank

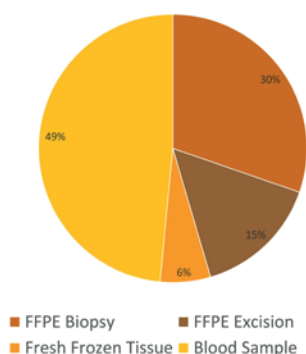


Figure 2: Representation of the EHE Biobank samples currently stored at RMH

## Results

Research conducted on these samples will relate to the prevention, diagnosis and treatment of EHE. Currently 16 whole bloods, 2 fresh frozen tumour tissue and 14 FFPE samples have been collected. Though the biobank is still accruing samples and is not yet open to receive applications for tissue/blood access from researchers, we anticipate that in time, the biobank will support collaborative research projects in the UK and internationally. These projects may involve a wide range of biomedical analytic techniques including, for example, microscopy, cellular and in vivo imaging using fluorescent or luminescent probes, nucleic acid analysis, microarrays of DNA and mRNA (whole genome sequencing), protein analysis, small molecule assessment and functional analysis.

## EHE Biobank Patients within the UK

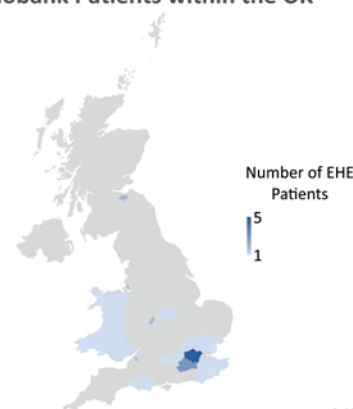


Figure 3: Regional representation of where the samples have originated from

## Conclusion

The EHE biobank has been successful in recruiting patients with this rare disease. Despite this, we need more physicians to continue referring new EHE patients to the biobank for the advancement of future research.

## For More Information

Including patient consent forms, patient Information sheet and how to recruit patients at local centres:  
<https://www.ehercc.org.uk/national-ehe-biobank-uk>  
Email: [rmh-tr.ehebiobank@nhs.net](mailto:rmh-tr.ehebiobank@nhs.net)

## Acknowledgements

The ICR and RMH work in partnership as a National Institute of Health Research (UK) Biomedical Research Centre. This biobank has been funded by the EHE Rare Cancer Charity.



# Annual Report and Financial Statements 2023

---

Message from the Trustees	4
Achievements and Future Objectives	6
Our Forward Focus for 2024	7
Foreword	8
<b>01</b> Patient Support and Advocacy	10
<b>02</b> EHE Research	18
<b>03</b> Fundraising and Finance	28
Wonderful support for EHE in 2023	30
Financial Accounts for 2023	36
Trustees' Declaration	44
Charity Information	44



# Message from the Trustees

---

**2023 has been another very good year for the EHE Rare Cancer Charity ('EHERCC' or 'Charity'), although not without its challenges.**

Our annual patient support programme has once again allowed us to both welcome new patients into the group and at the same time continue supporting and communicating with our existing patient network. As always, this support is largely provided by our patients through their extraordinary energy and compassion for one another. The Charity has also engaged during the year, and become an active participant, in two new closely linked multi-stakeholder programmes. The first is an initiative seeking to obtain a pan-European approval of the drug sirolimus for the treatment of EHE. The second initiative is seeking to set up and establish a platform to streamline and optimise ultra-rare sarcoma clinical trials and research, to reduce costs and uncertainty and so maximise the chance of success. You will find more on both these initiatives later in this report.

The EHE collaborative research we are funding continues to produce positive results. Evaluation of different categories of biomarkers is ongoing, with strong candidates already identified. Our funding continues to support three important initiatives: (i) the EHE observational study involving centres in Milan and London; (ii) the first ever multi-centred prospective observational registry of EHE, coordinated from Milan; (iii) the UK National EHE Biobank centred at the Royal Marsden Hospital. Our research, which is seeking to develop zebrafish models of EHE, based at the Bateson centre in Sheffield, is also ongoing.

Our supporters have once again excelled in the area of fundraising, with their usual determination and energy. This has been particularly important in the current cost-of-living crisis that inevitably means there is less funding available and more people competing for it. So we could not be more grateful for their unbelievable efforts to raise the funding we need to drive EHE research.

Once more, as we prepare our annual report, we are reminded that all our activities have only been possible because of the commitment and passion of our patient community and their supporters, and the dedication and expertise of the doctors and researchers who help in the fight against EHE. As always, therefore, we want to recognise every single person who provided their support, in whatever form, to the Charity and our EHE community, in 2023. Without your extraordinary efforts there would be no EHERCC and no exciting results to present. So please accept our deep and sincere gratitude. "Thank you!"

## Thank you!

**Left to right:**

Hugh Leonard (Chair of Trustees),  
Jeff Collins (Trustee),  
Kate Hooper (Trustee),  
Sally Baker (Trustee),  
Dr Oliver Pearce (Trustee).





## 01 Patient Support and Advocacy

As in all previous years, the Charity was keen to engage with any opportunities where we could talk about epithelioid haemangioendothelioma, explain the challenges faced by our patient community, and all that the Charity and indeed our global EHE Group are doing to help in the fight against this ultra-rare sarcoma. Hugh Leonard was delighted to give such talks at charity fundraising events, including in London and Derby. Awareness is also spread through The Pledge, the quarterly newsletter of the EHE Group that is produced in London (see inside back cover).

We were also delighted to participate in two EHE Group coordinated events held during the year. The first was the Scientific Saturday virtual meeting for our global patient community where Hugh Leonard and Denise Robinson jointly presented a broad overview of the global EHE research that is taking place. The second event was the larger EHE360 Global Patient Conference held in April, where patients, patient-advocates, clinicians and researchers come together to provide a wide range of highly informative talks about the disease; and closes with the ever-popular 'Ask the Experts' Q&A session.

One area where the Charity has made less progress than hoped is the establishment of a coordinated pan-European EHE patient network. This has been delayed partially because we were waiting for the INT-led pan-European prospective observational registry to start. This happened at the end of 2023 and we hope that we can now progress with this important European initiative. Some progress, however, has been made with the Charity engaging and building a strong collaborative relationship with the newest EHE foundation, EHE Italia Associazione Non Solo Laura ODV (EHE Italia), as well as with existing patient groups such as the German cohort.

The Charity is also excited to be part of two important multinational initiatives. The first of these is a European initiative seeking to secure a label extension for the drug sirolimus (marketed as Rapamune®) for the treatment of EHE, as there is now a substantial body of clinical evidence that clearly indicates the efficacy of this drug. As part of this label extension application process with the European Medicines Agency (EMA), the EHE Group undertook a sirolimus-focused survey of its global patient community. Results showed both the activity of the drug in treating EHE, and that results were substantially better than for any of the drugs generally approved for soft-tissue sarcomas, most of which show little or no activity for EHE.

At year end, the Charity also became a member of the Executive Committee of the PUSH Consortium, a new multi-centred international group seeking to establish a new platform to streamline drug approval applications and all pre-application scientific trials and procedures. We hope that this platform will help future EHE drug applications as well as those for all other ultra-rare sarcomas.

## 02 Research

A key focus for our ongoing research is the European collaboration involving Istituto Nazionale dei Tumori (INT), Milan, together with the Institute of Cancer Research and the Royal Marsden Hospital, in London. This multi-faceted programme has already identified the cytokine protein GDF-15 as a likely EHE biomarker. Six different miRNAs have also been identified as possible EHE biomarkers, with one of these six looking a particularly strong candidate.

The identification of GDF-15 has allowed the team to investigate GDF-15 levels in patient samples for different disease presentations. In addition, and using the PDX cell line developed at INT, they have been able to measure GDF-15 levels as part of the assessment of activity of different drugs. These results have continued to support the identification of this cytokine as a valid biomarker of the disease.

In the UK, our ongoing work with the Bateson Centre to develop a zebrafish model of EHE has continued to be both frustrating and encouraging. We now have a TAZ-CAMTA1 fish, yet levels of TAZ-CAMTA1 seen in these fish are typically lower than would be expected from the recoded activation levels of the TAZ-CAMTA1 transgenic construct. The team are trying to understand this. At the same time they continue to work on the development of a YAP-TFE3 fish, as this fusion protein is far shorter than TAZ-CAMTA1 which may be one reason why the TAZ-CAMTA1 expression is low. Finally, INT are providing cells from their PDX cell lines to allow the zebrafish team to test injecting these cells into fish embryos and so create a new form of xenotransplant where living EHE cells are sustained *in vivo* for use in ongoing research.

The Charity, which has funded the establishment of the first ever EHE-dedicated, prospective observational registry at INT, and involves both European and UK hospitals, was delighted to see the initial launch of the registry in September, and its first patients entered into the registry at the end of the year. A total of 21 hospitals across Europe are engaged in the registry, which is an excellent outcome of which the INT registry team should be very proud.

The National EHE Biobank, funded by the Charity and based at The Royal Marsden Hospital in London (see page 2), continues to gather critical tissue and fluid samples. We are continuing to work with the Royal Marsden to promote awareness of the biobank with hospitals across the UK.

Discussion of the development of a global EHE research strategy was also started late in 2023 and now remains as a priority for the EHE Group, both to ensure our growing research programme is optimised and to act as the foundation for larger, broader and longer-term funding applications.

## 03 Fundraising

There is no doubt that the most important part of our ongoing activities is our fundraising, as this provides the funding we need to drive all other aspects of our programme of activities. And 2023 was another promising year, despite the cost-of-living crisis, which has had an impact on the funding available to all charities.

Our supporters turned out in numbers for the London Landmarks Half Marathon, matching the 2022 record of 50 runners registered. Once again Team Dean, supporting EHE patient Paul Dean, himself a participant, turned out in huge numbers with a team of 19. Paul Preston also led a team of 19 from Ginger's Fitness from south London, running in support of Kelly Denton whose daughter has EHE. It was an amazing event.

In early summer we had 17 riders participating in The RideLondon-Essex 100-mile-long cycling sportive. As Chair of Trustees, and having spent several years encouraging others to participate for the Charity, Hugh Leonard had ridden in the 2022 event, and decided to ride once more in 2023, this time accompanied by his son, Sam. They were riding in support of Hugh's wife and Sam's mother, Sally Baker, an EHE patient and Trustee of the Charity.

Hugh Leonard attended several fundraising events, to represent and speak about the Charity. These included the second annual Hazel Peak Quiz Night, organised by Hazel's colleagues at the Rolls Royce facilities in Derby in memory of their colleague, and the Laptops and Lipstick quiz night in Peckham, south London.

Perhaps the most vibrant event was a small and intimate music evening hosted by Hannah, cousin of an EHE patient, at one of the Pizza Express music venues in London. Hannah was a successful participant on The Voice, the major UK musical TV talent show. She was accompanied by two other brilliant singers and by her husband (piano) and brother (guitar); the evening was fantastic and was hugely enjoyed by all present, who ended the event dancing around Pizza Express.

This year also saw individuals running in memory of lost friends. Mia Sallet ran for Isabelle Miller, Darren Thomas ran for Janet Griffiths and Adam Patrick and his team ran in the London Landmarks Half Marathon in memory of Allana Parker. These lost friends left us far too early, yet our memories of them burn brightly.

All of these wonderful contributions, together with those in prior years, have combined to provide the amazing fundraising the Charity has enjoyed, which has allowed us to contribute to the vital EHE research described in this and our previous annual reports.

**More information about these and other events can be found in this report.**



# Achievements and Future Objectives

Every year we review our activities and achievement against the goals that we set for ourselves. We believe that this honest appraisal is important so that all our supporters and stakeholders can see how we are progressing. Below is the 2023 assessment; while on the opposite page you will see our objectives for 2024.

## What we said we would do... ...and what we achieved

### 01 Patient Support and Advocacy

Continue sirolimus repurposing	Engaged throughout 2023 process
Assist patients with engagement with charity activities	Ongoing promotion of biobank and global patient registry
Launch new website	Launched by year-end
Revitalise other social media	Not yet started
Engage with European patient community	Excellent relationships built with EHE Italia and German patient reps. Full European engagement delayed waiting on pan-European registry from INT



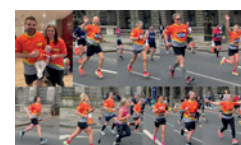
### 02 EHE Research

Support existing research	Continued through the year
Review and communicate results	Continued through the year
Engage with EHE partner foundations in research review	Progress continues regarding EHE strategy
Develop and promote coherent EHE research strategy	Ongoing, with close coordination with global EHE partners
Organise additional research review meetings	EHE360 Conference presentations coordinated. No specific research review meetings held.



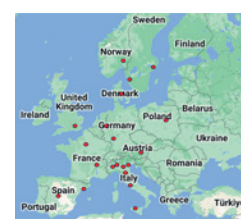
### 03 Fundraising and Finance

Support and encourage grassroots fundraising	Continued to promote and support fundraising
Coordinate key charity events (LLHM and RideLondon 100)	LLHM and RideLondon 100 completed
Continue to develop fundraising strategy with NOVA fundraising	Reports received and reviewed. Excellent guidance requires implementation
Coordinate review of research strategy and develop draft fundraising programme	Awaiting research strategy



### Charity Organisation

Consider appropriate support for research strategy	Awaiting progress on detailed strategy
Implement fundraising strategy	Delayed pending research strategy delivery
Establish structures for European engagement	Delayed
Evaluate need for additional structures and personnel for the above	Insufficient progress so deferred to 2024





# Our Forward Focus for 2024

Because rare cancers are not rare to those who have them

## 01 Patient Support and Advocacy

- Continue sirolimus repurposing
- Support PUSH platform
- Revitalise other social media
- Engage with European patient community

## 02 Research

- Support existing research
- Develop and promote coherent EHE research strategy
- Organise additional research review meetings
- Coordinate with EHE Group entities

## 2024 AND BEYOND

## 03 Fundraising

- Support and encourage grassroots fundraising
- Coordinate key charity events (LLHM and RideLondon100)
- Continue to develop fundraising strategy with NOVA fundraising
- Coordinate review of research strategy and develop draft fundraising programme

## Charity Organisation

- Consider appropriate support for research strategy
- Implement fundraising strategy
- Establish structures for European engagement
- Evaluate need for additional structures and personnel for the above



# Foreword from Dr William Tap

**William Tap, MD is the Chief of the Sarcoma Medical Oncology Service at Memorial Sloan Kettering (MSK) Cancer Center in New York, and Co-Director of the MSK Sarcoma Center and the Lisa and Scott Stuart Center for Adolescent and Young Adult Cancers. He has a large clinical practice and develops and runs clinical trials of new anti-cancer treatments. His academic research focuses on genetic and molecular nuances of rare cancers, identifying and validating therapeutic targets, treatment biomarkers, and modeling drug resistance.**

This has been an amazing year for epithelioid hemangioendothelioma, one that provides me with tremendous satisfaction regarding the accomplishments and spirit of our community, and in turn, hope and excitement for what the immediate future holds. I do not make these comments lightly, as we all have experienced the significant frustrations and devastating impact that is inflicted by an ultra-rare cancer, particularly one as complex and confounding as EHE. Years ago, as our experiences with EHE grew, it became evident that it was not a disease that should be approached, treated, or studied through individual efforts. Rather, it requires an all-in collaborative effort that challenges established academic approaches and is centered around EHE patients. In essence, dissolving artificial barriers and coalescing individual efforts to exact real-time change, redesigning approaches and infrastructures in order to enhance patient care and accelerate research and drug development. Years in development, we are now beginning to experience the strength and promise of this collaborative approach and the foundation it has created.

Central to all of this has been the partnering of patients and patient advocacy groups, such as the EHE Rare Cancer Charity UK, academic sites including sarcoma oncologists and scientists, the Ultra Rare Sarcoma Working Group, the PUSH Platform, not-for-profit organizations focused on drug repurposing and meeting unmet needs in cancer care and research, and regulatory agencies. All are represented with an equal voice, sharing experiences and expertise, and an unbridled passion to better understand EHE,

enhance and accelerate research processes and drug development, achieve global equality in treatment paradigms and available agents, and to ensure the patient remains central to the whole process.

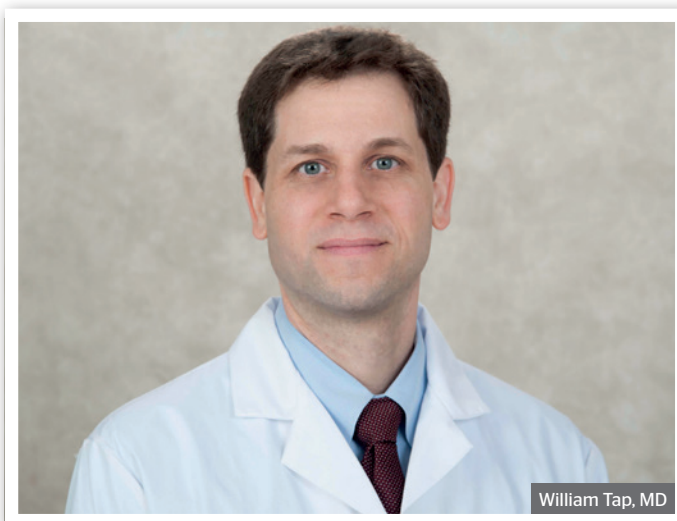
Two clinical opportunities emerged that underscored the dramatic need and urgency of this movement. The first is an ongoing effort to make rapamycin (sirolimus) universally available as a treatment for EHE patients in Europe and the second is the potential entry of TEAD inhibitors into EHE specific clinical trials. The former required the collection of 'counterfactual' clinical data in EHE, that is comprehensive data inclusive of the various subtypes of EHE that could be used by data models and machine learning to predict outcomes of certain 'what if' situations under various conditions, i.e., how our best treatments do under the various clinical situations EHE patients experience, examining standard cancer and EHE specific/pertinent outcome measures. This data would be needed to direct retrospective and prospective studies and to guide regulatory discussions. Closely linked to this was the later opportunity which was the entry of a novel and promising class of compounds, the TEAD inhibitors, into the clinic, underscoring the importance of ensuring accurate drug development strategies and clinical trial designs in EHE. This is not a straightforward endeavor due to the complexity of EHE and, as few agents have been tested in clinical trials and there are inherent challenges to ensuring biopharma interest in ultra-rare diseases, it is necessary for the EHE community to have developed and aligned on viable approaches that minimized risk and uncertainty.



So, what has been accomplished and why is it so exciting? EHE has now been incorporated as a formal working group in the PUSH Platform. PUSH is a novel and exciting new patient-centric venture designed to change and accelerate research in ultra-rare cancers through the active participation of diverse and vested stakeholders as mentioned above. PUSH facilitates the rapid collection and sharing of comprehensive data with the goal of optimizing research with an emphasis on accelerating drug development and availability. Through PUSH, of which members of the EHE Rare Cancer Charity UK and The EHE Foundation are on the Executive Committee, comprehensive data regarding the natural history of EHE is being collected and organized. This includes comprehensive data extracted from full medical records in the United States with people's consent through the Health Information Exchanges Act, comprehensive clinical and treatment data from academic sites throughout the world through the Ultra Rare Sarcoma Working Group, a multi-centered prospective EHE observational registry in Europe which we hope will go global, and direct information from patients regarding their experiences to better understand how EHE affects them, their family, and caregivers. These data are critical in that it will help us define the natural history of the various clinical and genetic subtypes of EHE, help us better understand how EHE affects the lives of people and how we can better mitigate its symptoms and life impact, provide data about the efficacy patterns of our best treatments, identify meaningful treatment outcomes for patients, allow us to design novel clinical trial approaches and run simulated clinical trials with historical data, and gather counterfactual data to inform regulator discussions. In addition, PUSH has developed a prospective treatment study of sirolimus to capture real-world data and practical usage data regarding mTOR inhibitors, established ongoing discussions with regulatory agencies in the US and Europe to inform the regulatory process for novel and repurposed drugs in EHE and other ultra rare cancers, and developed novel clinical trial endpoints and response criteria in EHE that best represents outcomes and symptom assessments

that are meaningful to patients. In addition, PUSH is helping to evaluate serum biomarkers in EHE that can help us understand a person's disease and how well our treatments are working and is engaging with the broader sarcoma community to support novel clinical trial ideas to ensure that individual efforts are connected to the EHE community and benefit from all of the data, infrastructure, science, and opportunities that have been developed and organized by this effort.

Overall, we still have so much work to do, but I am so hopeful that these efforts will continue to grow and rapidly accelerate progress for EHE patients and set the paradigm of how to approach and cure ultra rare cancers around the world. None of this would be possible without the direction, passion, commitment, and presence of EHE patient advocacy groups and our patients and their caregivers. Together we are making a difference!



We want to thank Dr Tap for taking the time to write the Foreword for our annual report. We are very grateful indeed. We also want to thank him for the time, energy, compassion and care that he gives to EHE patients and the EHE cause. It is wonderful to know that people like you are fighting this horrible disease along side us. Thank you.

# 01

# Patient Support and Advocacy

---

**The Charity's Patient Support and Advocacy (PS&A) programme is one of our core areas of activity and lies at the heart of everything we strive to achieve. In this section, we hope we have been able to provide a sample of the inspiring work that is done to help promote awareness of EHE, support patients, and advocate for greater focus, support and funding for all EHE-related activities.**



## Review by Sally Baker, Trustee and EHE patient

### Patient support

**Patient support and engagement is one of the most important parts of our PS&A programme, allowing us to keep patients updated on the latest EHE developments, help them where they are facing challenges of whatever nature, and encourage and promote support for all our activities. Some of these engagement activities are summarised below.**

#### Our EHE community continues to grow



One of the most common accolades the EHE Group receives from clinicians, researchers, regulators, donors and other stakeholders, concerns our EHE patient community that has been established globally, and who contribute so much to patient support, to research and to fundraising. Much of this comes from the community's EHE Support Group page on Facebook, established in 2013, which at the end of 2023 had more than 2,600 members, representing patients and their support groups from nearly 80 countries.

It was this same community that in 2015 established the EHE foundations and charities in the USA, Australia and the UK, to act as the focal points for fundraising and EHE-specific research. Canada and Italy have followed more recently, while other countries have established EHE patient networks. Now, as we look back, we can see how much our EHE community has achieved in building awareness and knowledge about EHE, in driving an active and very successful fundraising programme, and in advancing a growing international collaborative EHE research programme. This has only been possible due to the support of our global EHE family, and is why maintaining engagement with them is so important.

### Everyday engagement

The foundation of all our patient engagement activities is the support provided by the patient community itself, through both local and global EHE social media platforms, allowing the patient body to share experiences and provide valuable information on a range of topics. As EHE has both variable presentation and course, having access to others with similar disease presentation and facing similar challenges is hugely important and comforting for those involved. It is both humbling and inspiring to see first-hand the depth of compassion and selfless provision of support that our community members provide to each other, and the strength and comfort they gain from this interaction.

### Patient-targeted communications

We communicate directly with our patient and support community through different forms. Every quarter, the Charity produces **The Pledge**, the quarterly newsletter of the EHE Group, with a summary of the Group's global activities. We hope that this provides all our supporters with an inspiring summary of all that is taking place to help defeat EHE. Copies of all the 2023 editions are shown on the inside back cover of this report.













The EHE Group also organises periodic informal videoconferences with its members to update them on key initiatives. In 2023, the EHE Foundation held its 'Science Saturday' event at which Hugh Leonard, Chair of Trustees for the Charity, and Denise Robinson, Director of Research of The EHE Foundation in the US, updated participants on the global EHE research programme. This was a well-attended event with participants finding the presentation both informative and inspiring.



# 01 Patient Support and Advocacy - continued

The largest of the EHE Foundation's patient-engagement events is EHE360, the EHE Foundation's annual patient conference. This event brings together patients, advocates, clinicians and researchers in an online environment where updates and information are provided on a range of topics. More than 200 people from 21 different countries attended the conference. EHE researchers presenting their latest findings are hugely popular, as are presentations on a wide range of different treatment options. The highlight for many is the 'Ask-the-expert' panel session at the end, where participants can post questions that are discussed by leading experts in the field. Hugh Leonard was delighted to be one of the featured speakers where he presented the preliminary analysis of the EHE Group sirolimus survey, as described later in this report.

### Featured Speakers

 Denise Robinson THE EHE FOUNDATION <i>Patient-Led Research: Power in Numbers</i>	 Brian Rubin, MD, PhD CLEVELAND CLINIC <i>EHE 101: What You Need to Know</i>	 Breelyn Wilky, MD UNIVERSITY OF COLORADO CANCER CENTER <i>Systemic Treatment Options and Triaging EHE</i>
 Ajaybabu Pobbati, PhD CLEVELAND CLINIC <i>Why TEAD is a Convincing Target for EHE Treatment</i>	 Denise Adams, MD CHILDREN'S HOSPITAL OF PHILADELPHIA <i>Sirolimus as a Treatment Option for EHE</i>	 Hugh Leonard CHAIR OF TRUSTEES   EHE RARE CANCER CHARITY UK <i>Patients' Perspectives on Sirolimus</i>
 Michael J. Wagner, MD FRED HUTCH CANCER CENTER <i>Indolent or Aggressive? EHE Outcomes and Monitoring Strategies</i>	 Vinod Ravi, MD MD ANDERSON CANCER CENTER <i>Ask the Expert Panel</i>	 Abha Gupta, MD PRINCESS MARGARET CANCER CENTER <i>Ask the Expert Panel</i>
 Tamara Vesel, MD UPTON UNIVERSITY SCHOOL OF MEDICINE <i>Ask the Expert Panel</i>	 William Tap, MD MEMORIAL SLOAN KETTERING CANCER CENTER <i>Ask the Expert Panel</i>	

## European initiatives

The Charity is also seeking to establish a pan-European patient network, building off the foundation of the pan-European prospective observational registry being coordinated in Milan and funded by the Charity. This registry was formally launched slightly later than hoped in late 2023 (see Research section of this report) with the result that the Charity's European patient engagement was also delayed. We hope that this initiative will now be launched in 2024. In the meantime, any opportunities were taken through 2023 to engage with different European patient representatives, either as individuals or as country-specific patient groups.



Hugh Leonard was delighted, for example, to have the chance to meet with Dora Balda in London. Dora is from Greece and her daughter has EHE. Hugh and Dora had a brilliant two hours talking about all things EHE and plan to meet again in the future. For Hugh the meeting also amplified both the need for, and the benefits that could flow from, the establishment of a coordinated European patient group.

In September, Hugh also travelled to Milan to participate in the Charity -organised research discussions with the research team at the Istituto Nazionale dei Tumori in Milan, Italy. This also gave Hugh the opportunity to meet with the newest of the EHE global foundations, *EHE ITALIA Associazione Non Solo LAURA ODV*. Hugh and Andrei Ivanescu, President of EHE Italia, discussed their ongoing collaboration including their joint desire to establish the European patient network.





## Remembering absent friends

At this point we also want to remember all those members of our patient community who contributed so much but who sadly left us far too early. They are a major part of the reason why we all spend so much time and energy working to find new treatments and a cure for EHE. We owe that to all those who are no longer with us.

## EHE awareness opportunities

The Charity is always keen to engage with opportunities to talk about the disease, the research we are funding and the advances being made. Such opportunities often arise as part of a fundraising event, and two such opportunities arose early in the year.

### Laptops and Lipstick quiz night

Kelly Denton is another of our global EHE community who is highly active and engaged in helping to deliver on all the objectives of the Charity. Her engagement with the EHE community, and in particular with the Charity, is driven by her daughter's EHE diagnosis.

It was thanks to Kelly's profile that a women's business network based in south London, Laptops and Lipstick, chose the EHERCC as their supported charity. As part of that support, Laptops and Lipstick organise an annual quiz night, which took place in late February.



It was an excellent night with a large turn-out. At the meal interval Hugh Leonard was able to explain what EHE is, and why it is so important that we continue to drive research into the disease. He was also able to thank them for their wonderful support.

## The Hazel Peak Quiz Night No 2

Hazel Peak was a UK patient who was diagnosed with EHE in late 2021. Sadly Hazel had a very aggressive form of the disease and passed away very early in 2022. Her colleagues at Rolls Royce Submarines in Derby desperately wanted, however, to continue with their fundraising quiz night, which they had planned for her in March, and which was ultimately a great though understandably emotional success.

Roll forward one year and Hazel's colleagues decided they wanted to hold their second quiz night in her honour. Hugh Leonard was invited to attend the event, as he had the year before, and had the chance to speak to the guests about the research in the UK and Europe that their funds were helping to drive. People were genuinely interested and Hugh had the chance also to speak to some individually and answer their questions. And of course to thank them all for their brilliant ongoing support.



It is hard to overstate how useful and important these events are in helping to build awareness of EHE and to help achieve many of our core objectives. We want to join Hugh in thanking Kelly's supporters and Hazel's colleagues for all that they have done to help us fight EHE.

## Advocacy

Our advocacy programme in 2023 has been focused on dealing with the challenges presented by an ultra-rare sarcoma like EHE. This has involved the Charity's participation, together with INT, Milan and the AntiCancer Fund, in two different but related initiatives. The first is seeking approval from the European Medicines Agency for the approval of the drug sirolimus for the treatment of EHE; the second is seeking to establish a new multi-party platform called PUSH to streamline drug approval for ultra-rare cancers.

### Approval of sirolimus and our EHE patient survey

Sirolimus is a drug (marketed by Pfizer under the trade name Rapamune®) that belongs to a group of compounds known as mTOR inhibitors. The drug is approved for use as an immunosuppressant post organ-transplant. There is also now a substantial and growing body of evidence demonstrating the efficacy of this drug in the treatment of some forms of EHE. The challenge we face is that the 'label' for sirolimus, which effectively lists all approved uses of the drug, does not include the treatment of EHE.

# 01 Patient Support and Advocacy - continued

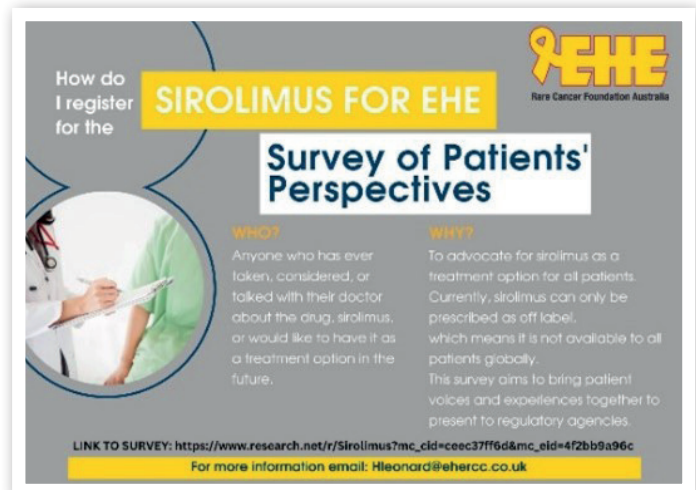
The result of sirolimus not being formally approved for the treatment of EHE means that the drug can only be prescribed 'off-label'. For many patients, that is not an impediment to accessing the drug. But, if a patient's doctor will not or cannot prescribe off-label, or the health service will not pay for the drug, then an EHE patient may be denied access to this potentially important treatment.

To counter this situation, there is now a worldwide focus on seeking approval for the treatment of EHE to be added to the sirolimus label, a process known as a 'label extension'. This process is currently most advanced in Europe at the European Medicines Agency (EMA).

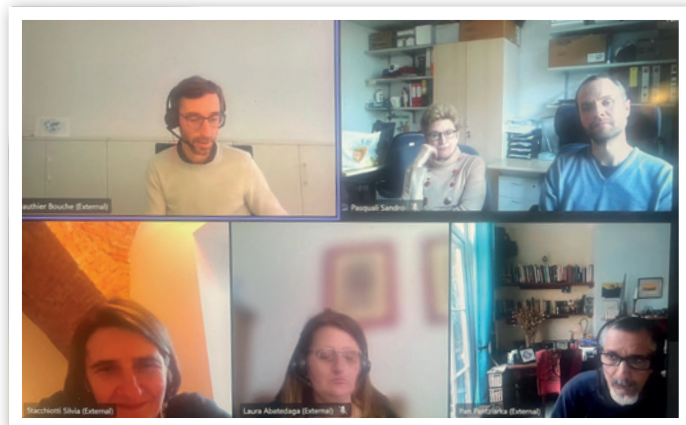
To gain the label extension, an application must be filed with the EMA, under their established procedures. This requires a significant body of research and clinical trial data to be produced, collated and integrated, delivering results to demonstrate the efficacy of the drug to support the application. The challenge for ultra-rare diseases is that it is almost impossible to generate the standard package of data that regulators are used to, a fact recognised by regulators who in most cases are prepared to work with clinicians and patient advocacy groups to try and collate different but appropriate data to allow them to approve the label extension.

Prior to submitting the formal application, the EMA process allows the applicant to present its data for review and feedback, a process known as Scientific Advice. In compiling the information for the submission, Dr Stacchiotti's team, supported by the Anti-Cancer Fund in Europe and the Charity, undertook a worldwide search of published data involving sirolimus and EHE. This extensive data base was then reviewed and integrated into the submission document.

In addition to published data, the team were also very keen to include patient-curated data provided by the EHE Group. It was to provide this data that the EHE Group undertook its survey of patient perspectives and their experiences of treatment using sirolimus. The survey was directed at our global EHE community and was strongly supported by all the individual charities and foundations that make up the EHE group.



In total, 129 patients from around the globe participated in the survey that provided extremely useful real-world data that we believe supports the call for a label-extension. Key data from the patients' perspectives survey are summarised here, with the locations of participants shown on the map.





Of these 129 patients: 32 patients who had not undergone a liver transplant were taking or had taken sirolimus, for a range of different presentations of the disease; 21 patients had undergone liver transplant; and 76 had never taken sirolimus.

The distribution of different presentations is shown in Fig. 1. The predominance of liver/lung involvement (green bars) can be clearly seen with 67/129 (52%) of cases including this presentation. The most difficult cases with pleura involvement numbered only 6/129 (5%).

The median age (years) of all participants was 47.6 (range 14-81).

The distribution of both disease presentation and age of participants corresponds to disease descriptions from literature and demonstrates that the 129 participants provide an acceptable representation of the disease.

Participants were divided into three cohorts: (i) non-liver-transplant patients who are or have taken sirolimus; (ii) non-liver-transplant patients who have never taken sirolimus; and (iii) liver transplant patients.

The non-liver-transplant patients who are or have taken sirolimus numbered 32 of the 129 (25%) participants. Figure 2A shows the reasons for sirolimus treatment initiation. The most common reason was 'progressive disease'.

At the time the survey was undertaken 20 of the 32 participants were still on treatment with sirolimus. Figure 2B shows the duration that participants have or had been on the drug. These durations ranged from 'Less than 6 months' to 'More than 5 years'; 21 participants had been on the drug for a year or longer; 5 had been on the drug for more than 5 years. Figure 2C shows the effect of the drug, with 20 participants experiencing stable disease and/or tumour shrinkage. Figure 2D shows the reason why 12 of the participants had discontinued taking sirolimus, with only 5 being directly attributed to the drug not working.

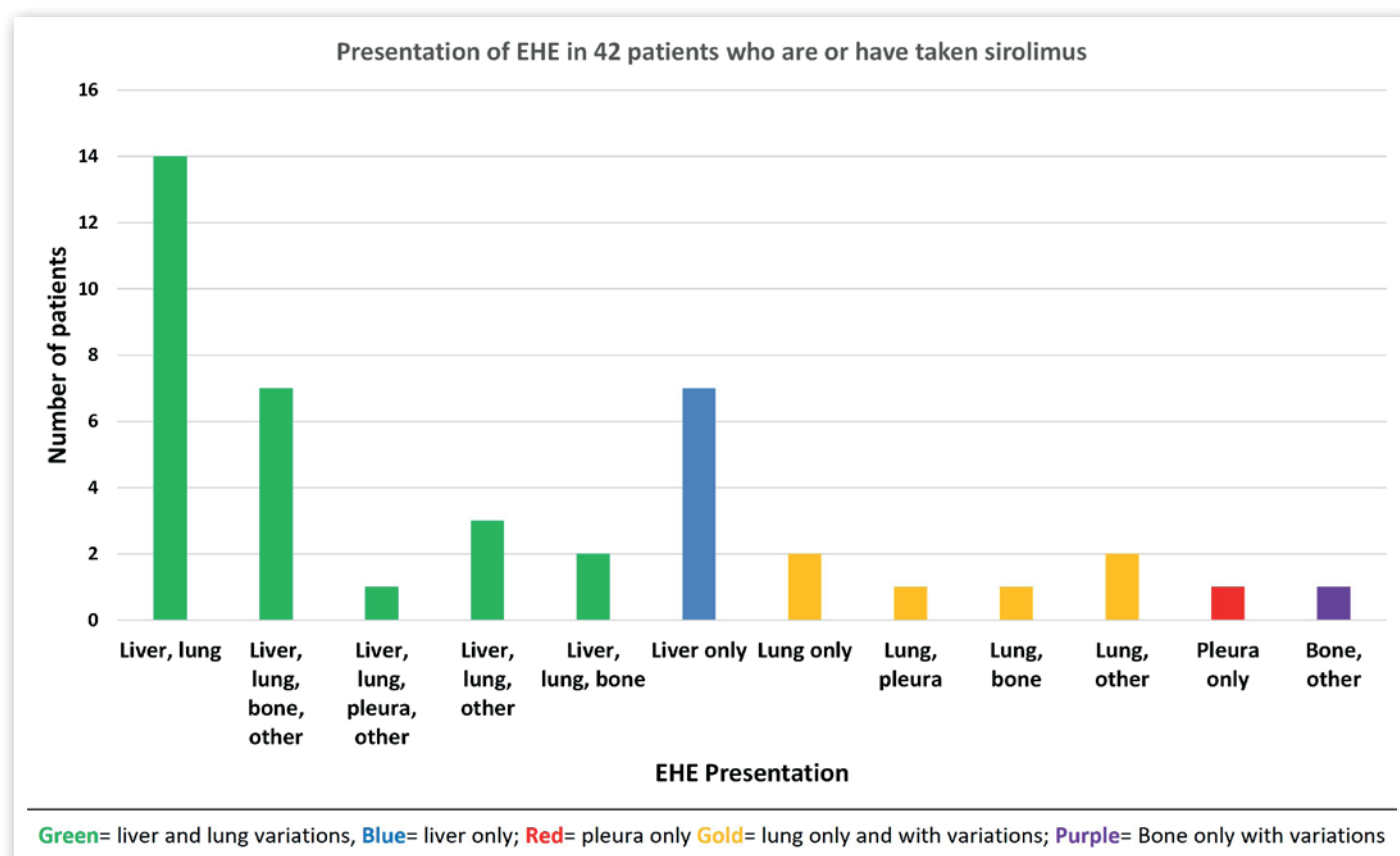
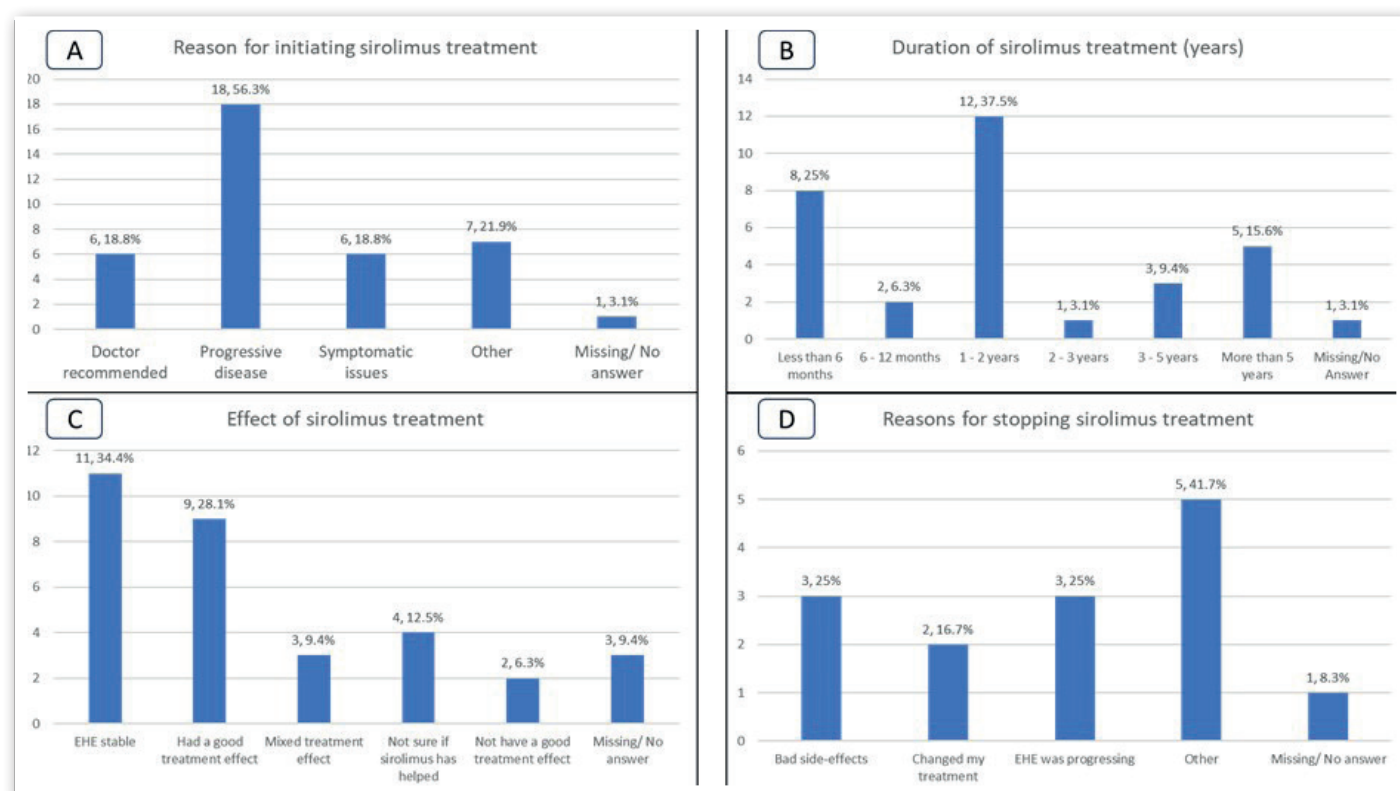


Figure 1

# 01 Patient Support and Advocacy - continued



**Figure 2** - Patient experiences of taking sirolimus. (A) Reasons for initiating sirolimus treatment. (B) Duration, in years, of sirolimus treatment. (C) Patient perspective on the effect of sirolimus treatment. (D) Reasons for cessation of sirolimus treatment.

The survey also explored the experiences and perspectives of non-liver-transplant patients who had never taken sirolimus. Of note was that of the 76 participants in this category, 32 confirmed that the drug was not available and a further 8 confirmed that it was but was not selected as it was only available off-label. In terms of actual discussions with their doctors, 45 participants confirmed that the drug had not been mentioned; a further 6 were told that it could not be used as it was not approved for EHE.

The survey concluded by asking participants to select how important it is to have sirolimus available to all EHE patients. Of the 129 participants, 87% placed availability of sirolimus to all patients as either 'hugely important' (76%) or 'very important' (11%), the two top categories of answer available. The importance was also mentioned in the following participants' comments:

***"It is extremely important. I feel lost because I think in Portugal sirolimus wouldn't be approved for EHE treatment."*** (EHE patient)

***"Although I do not know whether sirolimus would be an appropriate option in my case, I would think it is important to make it available to patients in every country - just in case!"*** (EHE patient)

***"Critically important and potentially life-saving."*** (EHE patient)

The full results of this real-world data survey have now been published in the peer-reviewed journal *Frontiers in Oncology*, and can be found at:

<https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2024.1367237/full>

The full published results will also now be included in later Scientific Advice submissions to the EMA. These results are notably better than comparable results from any other drug approved generally for soft tissue sarcomas. We believe that these results coupled with the scientific information gathered by Dr Stacchiotti's team provide a very strong case for the approval of sirolimus.



## CTOS 2023 and the PUSH Platform

In early November, Hugh Leonard, together with The EHE Foundation (US) Director of Research, Denise Robinson, attended the Connective Tissue Oncology Society (CTOS) 2023 Annual Meeting in Dublin, Ireland. Every year, physicians, scientists, and advocates from around the world come together to advance patient care and increase knowledge of connective tissue tumors (known as sarcomas) like EHE, where tumours form in the cells lining the blood vessels. CTOS is an important opportunity to engage and collaborate with sarcoma experts who are bringing novel ideas and experience together to improve the lives of sarcoma patients.

The week began with the Ultra-Rare Sarcoma Working Group (URSWG) meeting. EHE is considered an ultra-rare sarcoma, defined as affecting fewer than 1 person in every 1,000,000 people. Dr Silvia Stacchiotti led the meeting with Dr Bill Tap and colleagues, to discuss innovative approaches to conducting clinical trials in ultra-rare sarcomas.

The Charity and The EHE Foundation are working collaboratively with a team of clinicians, data experts, drug repurposing specialists and other patient advocacy groups to develop a clinical trial platform, PUSH (Pushing Ultra-rare Sarcoma towards Hope), to maximise the knowledge that can be gained from interacting with and treating every single patient affected by an ultra-rare sarcoma and to support developing new treatments to improve outcomes and quality of life. It is also hoped that by establishing such a platform, the costs of undertaking necessary trials and the risk of uncertainty of the regulatory process will both reduce significantly, resulting in greater appetite and engagement with industry.

Hugh Leonard is a member of the current PUSH Executive Committee, working to bring the PUSH concept to fruition.

Hugh and Denise also took the opportunity at CTOS to meet with the team that is spearheading the current discussions with the European Medicines Agency (EMA) regarding securing approval for an extension of the label of Pfizer's drug Rapamune® (sirolimus) for the treatment of EHE.



# 02 EHE Research

## Study of the molecular and cellular features of EHE

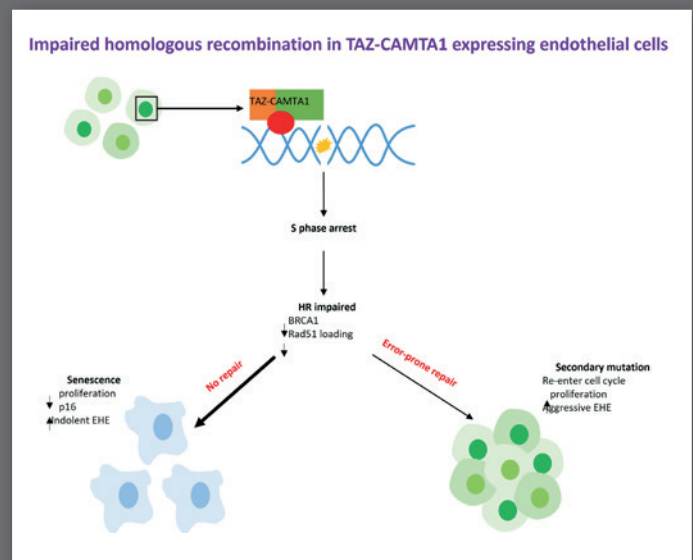
This four-year PhD project, under Dr Valerie Kouskoff at the University of Manchester, was funded by the Charity and was completed in early 2023. The research was then extended for a short period with a small grant awarded by The EHE Foundation under its annual grant cycle.

The aim of this project was to develop a model of EHE that could then be used to investigate various aspects of EHE biology. The model uses mouse embryonic stem cells, which are differentiated into endothelial cells. These are the cells that line blood vessels. The expression of TAZ-CAMTA1 (the fusion protein that drives EHE) is induced in these endothelial cells, allowing its function to be investigated in the type of cells where EHE tumours develop and grow. It was hoped that studies using this model would uncover previously unexplored mechanisms of EHE development, which may then lead to novel treatment options for EHE patients.

Investigations using this stem-cell-based model have revealed that TAZ-CAMTA1 expression causes a large amount of DNA damage in endothelial cells. DNA damage often occurs in cells, and is usually repaired without consequence by one of several DNA repair pathways. In endothelial cells expressing TAZ-CAMTA1, however, the large amount of DNA damage overwhelms these repair mechanisms, and often goes unrepaired. As a result, in many TAZ-CAMTA1-expressing cells, this causes cells to become arrested in the cell cycle, and then enter a state of senescence. This is a state in which the cells are dormant and cannot divide but also do not die. Senescent cells can accumulate in a tumour, and these results suggest that this could represent the indolent, or very slow-growing tumours many EHE patients develop.

The other consequence of overwhelming DNA damage is that a more error-prone pathway attempts to repair the damage. This leaves cells vulnerable to further genetic mutations occurring, which may then allow cells to bypass the barrier of senescence and induce uncontrollable proliferation. This could be the reason some EHE tumours suddenly become more aggressive and metastasise. At the current time, this is the only theory that has been developed that explains the difference between indolent and aggressive EHE.

In 2023, during a short extension of the research programme, the research team were investigating if using drugs to inhibit some of the proteins involved in the onset of DNA damage or senescence-bypass could induce the death of TAZ-CAMTA1-expressing endothelial cells. Some of these inhibitors are already used or are in clinical trial for treating other types of cancer. The research looked at four different inhibitors, all targeting different aspects of DNA damage and seeing if these drugs could induce cell apoptosis in EHE cells. This was a small proof of concept, and while three of the drugs did not appear to have a measurable effect on EHE cells, one of the inhibitors produced more interesting results, both when used alone but also in combination with other inhibitors. At the end of the year, the implications of these results were under review.





# Review by Dr Oliver Pearce and Dr Kate Hooper, Trustees

## Zebrafish modelling of EHE continues

In 2018, The Charity initiated research at the Bateson Centre at the University of Sheffield, to develop a zebrafish model of EHE. The Bateson Centre is one of the largest and oldest zebrafish facilities in Europe, and researchers there are experts in developing models of human diseases in zebrafish. Zebrafish are used because, if you are successful in creating the model you want, they are cheap and quick to produce. The embryos also develop outside the mother and are largely transparent, making it easy to see morphological changes as the fish develops.

### The TAZ-CAMTA1 model

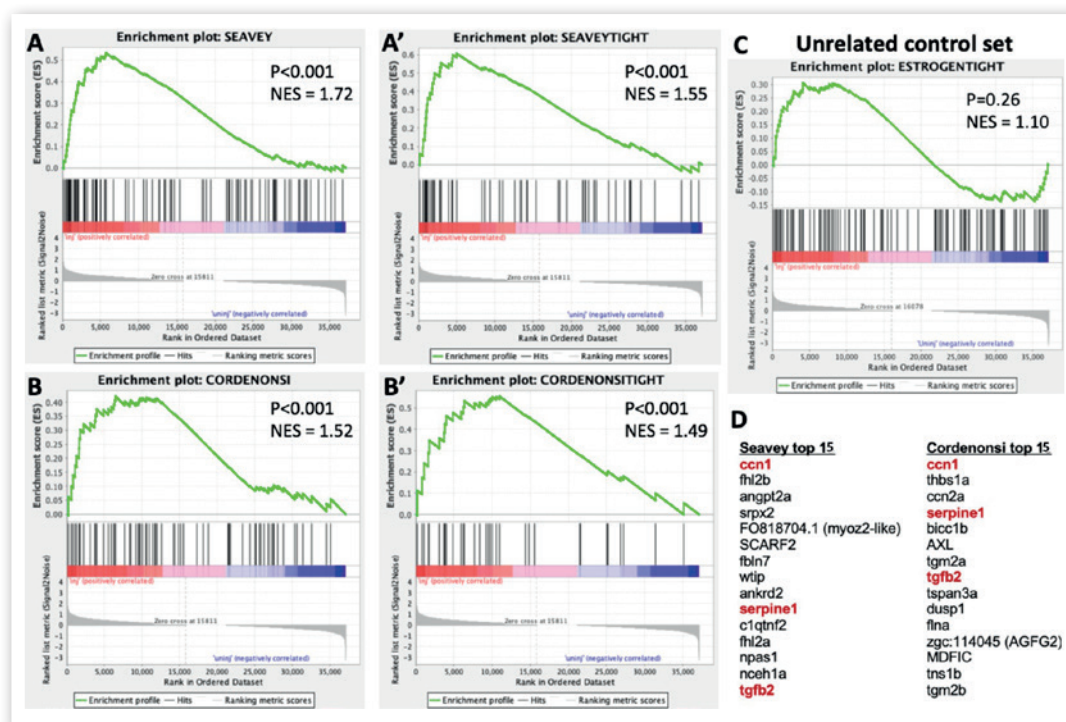
Creating a human model of a rare sarcoma is not simple in a zebrafish, and the team faced many early challenges in creating fish with EHE caused by the TAZ-CAMTA1 fusion protein. Early attempts, for example, demonstrated that the fusion protein was highly toxic to fish larvae, which did not survive. This required the team to introduce the EHE chromosomal translocation construct with a switch mechanism so that the TAZ-CAMTA1 could be 'turned on' once the fish had developed.

While several significant challenges were faced, the team in Sheffield continued to find solutions through extraordinary and painstaking attention to detail. At the start of 2023, the team, using a technology that analyses gene expression of all genes across the genome (RNAseq), initiated testing to see whether they could verify effects on other genes that are known to occur

as a result of expression of the fusion gene in EHE, called the Seavey-set for EHE and the Cordenonsi-YAP signature set.

Testing for these effects in zebrafish requires some detailed analysis as some human genes have two equivalent genes in zebrafish due to their partial genome duplication during evolution. This resulted in the team using a 'tight set' containing only genes with a single equivalent in both human and zebrafish, and a 'broader set' which included genes which have two equivalents in zebrafish. Subsequent testing (see Fig. 1) showed significant enrichment of both sets in the upregulated genes, showing that the TAZ-CAMTA1 transgene (that part of the injected construct that is inserted into the fish's DNA) was having an effect consistent with expectations if it was working.

Testing for TAZ-CAMTA1 expression was also successful, but the team noted that the level of activated TAZ-CAMTA1 when 'switched on' was significantly lower than the level of the transgene control construct seen prior to switching. This was surprising as the analysis of downstream genes had shown a very convincing effect. Further work identified a number of possible causes for this reduced expression of TAZ-CAMTA1 associated with the TAZ-CAMTA1 construct. At the end of the year, the team had made modifications to the construct in new fish and hoped to be able to identify fish where the transgene had inserted successfully (called transmitters) by the end of the first quarter of 2024.



**Fig 1 - GSEA analysis results (A,A') -** Enrichment plots of both the 'broad' and the 'tight' Zebrafish-Seavey set. We expect that such genes (shown as black lines) will cluster to the left of the graph if there is TAZ-CAMTA1 activity, which can indeed be observed. The same can be seen for the 'broad' and 'tight' Zebrafish-Cordenonsi set. (C) Shows a control set (estrogen responsive genes) as an example of a negative result, black lines are not significantly clustered to the left. (D) List of 15 most responsive genes in each set, shared genes between the sets are in red.

## 02 EHE Research Continued

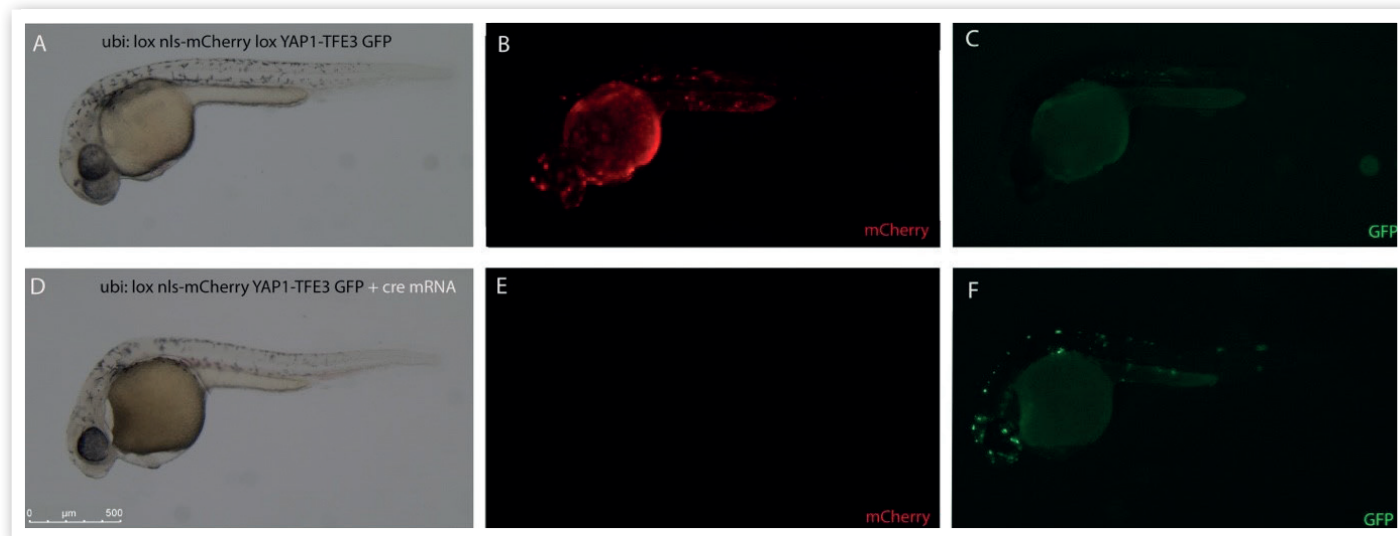
### The YAP1-TFE3 model

Due to the ongoing difficulties creating zebrafish with a high level of TAZ-CAMTA1 expression, and following discussions with the Charity, it was agreed that the research team should also start to try and create an inducible YAP1-TFE3 line as a potential alternative to creating a TAZ-CAMTA1 EHE model in zebrafish. YAP1-TFE3 is considerably shorter than TAZ-CAMTA1 and may be easier to express at a high level. In addition, it will also be a valuable additional model of this different variant of EHE.

Despite the work on the TAZ-CAMTA1 model, there was still concern that expressing human genes in zebrafish may lead to difficulties in obtaining high expression levels. Therefore, the team decided to make a zebrafish equivalent of the YAP1-TFE3 gene rather than use the human genes as a starting point. This involved aligning the protein sequence of zebrafish YAP1 and TFE3 with their human equivalents and determining where, in the zebrafish sequence, the two genes should be joined. An attempt to amplify these pieces from cDNA failed. Further methods of creating a zebrafish equivalent of YAP1-TFE3 also experienced difficulties and it was therefore decided to synthesize the entire gene. This was done, and the resultant gene has now been cloned into a switchable construct, as was done for TAZ-CAMTA1. The full transformation construct has been injected into embryos and the team have confirmed that the construct can be switched on by co-injection with cre mRNA as shown in Fig. 2.

The team have now obtained the first transgenic embryos from this line and have started to raise larvae. Approximately 20 experimental fish and 20 control fish were raised. However, the team will be generating more in 2024.

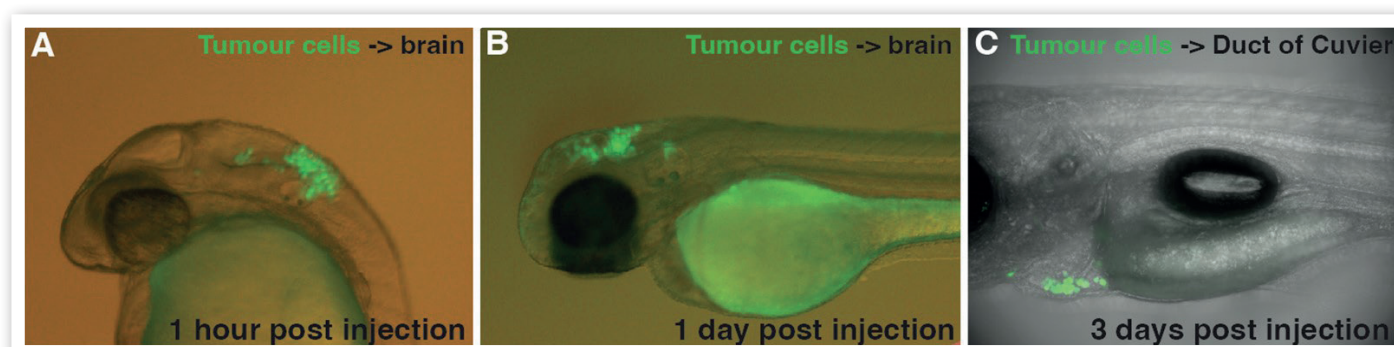
The team will also be doing further experiments to establish if YAP1-TFE3 is a more 'potent' oncogene in fish than TAZ-CAMTA1. This has already started with the team co-injecting TAZ-CAMTA1 constructs or YAP1-TFE3 constructs, together with cre mRNA to activate the switches, and testing for levels of TAZ and YAP activity. This experiment suggested that YAP1-TFE3 is indeed more potent. In these experiments, embryos are mosaic, so only some cells in the embryo will have the oncogene expressing construct. It is therefore important to perform such comparisons on the real transgenic embryos that are now available for both TAZ-CAMTA1 and YAP1-TFE3. Once the team have embryos with the new modified TAZ-CAMTA1 construct, these can also be evaluated quickly for improvement of expression.



**Fig 2 - Switch test for YAP-TFE3 construct** - The embryo injected with the construct is shown (A), and verified by mosaic mCherry expression observed as expected (B), but no GFPNeon is visible showing the construct has not been induced (C). When cre mRNA is coinjected (D) mCherry expression is strongly reduced (E) and GFPNeon can be observed (F), showing that the switch is working.

### Using xenotransplants; an alternative form of a zebrafish EHE model

Over the course of this project, it has become clear that getting zebrafish to develop EHE tumours remains difficult. If tumours continue to be low in frequency or are slow to develop, it may be difficult to exploit the zebrafish model. Therefore, following consultation with other researchers working with EHE models, the Sheffield team have contacted Dr Pasquali at the Istituto Nazionale dei Tumori (INT) in Milan in order to obtain EHE tumour cells from the EHE cell line developed by the INT research team. These cells can be transplanted into zebrafish larvae (xenotransplants) to study behaviour of these cell lines in a vertebrate *in vivo* environment. At year end the two institutes were initiating the procedures for this transfer.



(Example of a transplant of breast cancer cells is shown below (FvE, unpubl))

### Forward focus

The team in Sheffield will be continuing their work on all fronts with the following key objectives:

1. In light of the development of mouse EHE models and human cell lines, a key priority is to initiate the establishment of xenotransplantation models (injecting human cells into fish embryos) as this will provide a different form of model. If successful it also exploits the transparency and size/cost advantage of the fish system most efficiently. Once the team have established good labelling procedures, transplantation sites, cell numbers, etc. and shown that the system can work, the Charity will discuss uses of this type of model with the Sheffield team and other EHE researchers.
2. The research team will continue to directly compare the activity of TAZ-CAMTA1, YAP1-TFE3; and modified versions of TAZ-CAMTA1, to check for comparative levels of YAP/TAZ activity. This will allow them to see whether these alternative approaches have solved the expression issues that have proved to be a significant difficulty in the original TAZ-CAMTA1 model fish. If the expression issue has been resolved, the Charity will need to discuss with the research team and other EHE researchers how such models can best be incorporated into the overall ongoing EHE research initiative.
3. The team will continue to monitor and bank their current zebrafish lines.



## 02 EHE Research Continued

### The UK Biobank, The Royal Marsden Hospital, London

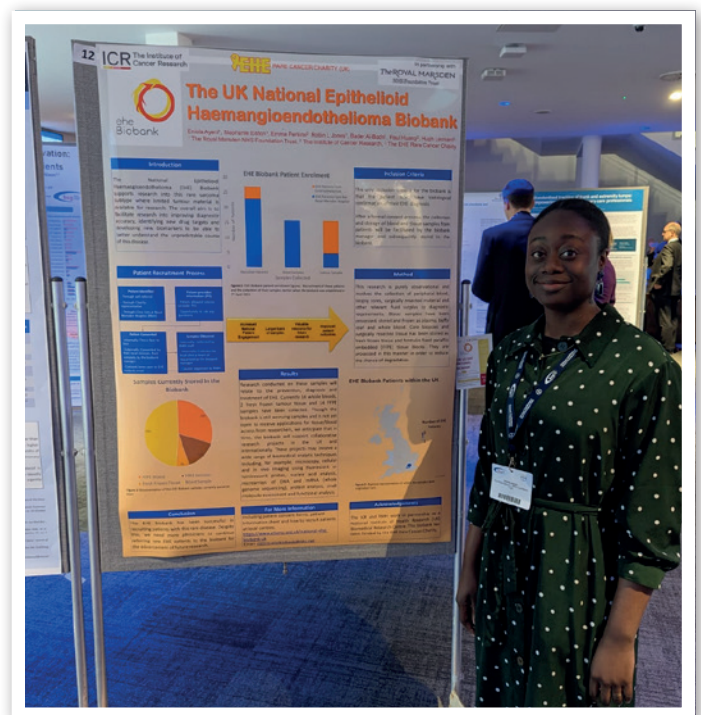
Access to biological samples is a critical component of EHE research initiatives. Tissue, fluid and blood samples provide researchers with critical access to actual EHE biological specimens that allow researchers to: investigate and understand the natural history and development of EHE; investigate new hypotheses; and develop and test both new and existing drugs to see if they will help combat the disease. The Charity was delighted therefore to fund the establishment of the UK National EHE Biobank at the Royal Marsden Hospital.

The role of the Biobank is to collate as many tissue, blood and fluid samples from EHE patients as possible. This is because there are only a tiny number of chances to capture EHE tumour and fluid samples each year, due to the extreme rarity of the disease. So all samples possible are captured and stored in the EHE Biobank to facilitate research into the disease.

The EHE Biobank has started well. Thirty nine patients have given consent for their tissue and fluids to be stored within the biobank. As this sarcoma arises in any area of the body, a range of tissue types have been captured and stored in the biobank, primarily consisting of biopsies of the lung, bone, liver and neck. A total of 27 blood samples, 24 archival Formalin-Fixed Paraffin-Embedded (FFPE) samples and 3 live tissue samples were collected in 2023.

The biobank team were also delighted to have the opportunity to present the biobank at the annual British Sarcoma Group (BSG) Conference on 22-23 March 2023. This was an excellent opportunity to promote the biobank because there were many sarcoma clinicians and professionals at the conference. Everyone that attended was able to learn about the EHE Biobank thanks to the excellent poster presented by the biobank team. The poster can be seen on page 2 of this report.

The Charity encourages all EHE patients to consider donating EHE tissue, fluid and blood samples to the EHE Biobank. The biobank team are hugely supportive and helpful and every sample is so important as they are so rare. Patients can contact the charity, visit our website or contact the Tissue Manager at the Royal Marsden Hospital if they have any questions or want to discuss any issues about the biobank.



**Eniola Ayeni**, Tissue Manager at the Sarcoma Unit, Royal Marsden Hospital at the BSG conference

## Significant EHE research focus continues at INT

The significant focus on EHE research, led by Dr Silvia Stacchiotti and Dr Nadi Zaffaroni at Istituto Nazionale dei Tumori (INT) in Milan continued through 2023. This programme focused on two main elements. The first involved INT's collaboration with the Royal Marsden Hospital and Institute of Cancer Research in London, a six-part multi-faceted research programme, including the establishment of a prospective EHE study and the identification of EHE biomarkers. The second is the setting up and ongoing administration of the world's first multi-centred prospective observational registry for EHE.

### Multi-faceted research collaboration

The overall research program entitled '*Evaluation of Cytokines and Hormones as Biomarkers for EHE*' is a multi-centre collaborative project that is comprised of six key objectives. These objectives or projects can be summarised as follows:

**Project 1:** the identification and validation of novel circulating and tissue biomarkers (prognosticators and predictors of response to medical agents) to inform patient management as well as potential therapeutic targets;

**Project 2:** the development of patient-derived xenograft (PDX) models;

**Project 3:** the assessment of the activity of drugs relevant for the disease;

**Project 4:** the generation of PDX-derived cell lines to investigate the cellular and molecular determinants of drug activity and to be submitted to a CRISPR whole genome screen to identify new therapeutic targets;

**Project 5:** the identification and evaluation of miRNAs;

**Project 6:** the description of the radiologic characteristics of EHE and their correlation with the clinical outcome.

This overall research programme is also supported and made feasible through the establishment of an observational study involving existing EHE patients at the Royal Marsden Hospital and INT in Milan. At year end the study had almost reached its initial target cohort of 50 patients, providing a material database and ongoing longitudinal blood samples from patients which have, for example, been instrumental in the biomarker arm of this research.



FONDAZIONE IRCCS  
ISTITUTO NAZIONALE  
DEI TUMORI



The Institute of  
Cancer Research

The ROYAL MARSDEN  
NHS Foundation Trust

Updates of these different projects are provided below.

### Project 1:

The assessment of circulating cytokines, hormones (and miRNAs), and ER $\alpha$ , Er $\beta$  and G-Protein-coupled Estrogen Receptor (GPER) expression etc and the identification of a novel biomarker for EHE;

Using a protein array able to simultaneously detect the expression of a hundred different cytokines in plasma samples of 15 EHE patients and 6 healthy individuals, a small panel of inflammatory cytokines was found to be differentially expressed. Among them we focused on Growth and Differentiation Factor-15 (GDF-15), a member of the TGF- $\beta$  super-family, which has multiple roles in a wide variety of cellular processes. Using a specific ELISA assay, we looked at the concentration of circulating GDF-15 in a retrospective series of 23 EHE patients and observed a statistically significant association of GDF-15 levels with EHE aggressiveness. This result was confirmed in a second cohort of 21 EHE patients prospectively collected within the currently ongoing observational study.

The assessment of circulating hormones and tissue expression of ER $\alpha$ , Er $\beta$  and GPER is ongoing.

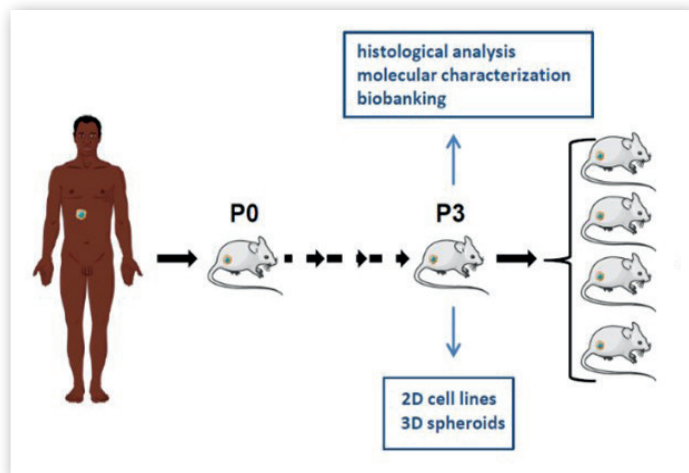
The assessment of miRNAs is undertaken in Project 5.

## 02 EHE Research Continued

### Project 2:

Development of additional PDX models;

Thus far only one fully established EHE PDX model has been developed, whose ability to reproduce the characteristics of the originating clinical tumor has been confirmed in terms of histo-morphology, presence of the *WWTR(TAZ)::CAMTA1*, overall transcriptomic profile (as detected by RNA-seq) and presence of *CDKN2A* homozygous deletion. A cell line was established following disaggregation of the EHE PDX.



### Project 3:

Assessment of activity of drugs;

The PDX model was used to comparatively assess the activity of doxorubicin and sirolimus (at different doses). Doxorubicin showed almost negligible activity whereas sirolimus caused a dose-dependent tumor volume inhibition in treated mice and induced the down-regulation of mTOR signaling. The PDX is currently being used to assess the activity of inhibitors of the Hippo pathway, such as the TEAD family of transcription factors.

This PDX and the corresponding cell line were exploited to provide further evidence supporting the value of GDF-15 in EHE. GDF-15 was detected in the medium of the EHE cell line as well as in the blood of EHE PDX but not in healthy mice or in mice carrying another sarcoma type, confirming that the cytokine was released by the EHE. Interestingly, we found that sirolimus decreased the abundance of GDF-15 in our *in vitro* and *in vivo* EHE models.

### Project 4:

Use of CRISPR in cell lines to help identify genes that confer drug resistance or sensitivity;

The EHE cell lines will soon be provided to Dr Paul Huang (ICR, London) in 2024 to start the CRISPR-based experiments.

### Project 5:

Identification and evaluation of miRNAs

The expression profiling of plasmatic miRNAs has been initially carried out using the OpenArray Technology (which evaluate the expression of 754 different miRNAs) in the retrospective series of 23 EHE patients. Six miRNAs were found to be differentially expressed between patients with indolent and aggressive EHE. In order to evaluate the overall miRNome (global profile of expressed miRNAs), we repeated the analysis on both retrospective and prospective series of patients by miRNA-seq. The results are currently being analyzed by a dedicated bioinformatician.

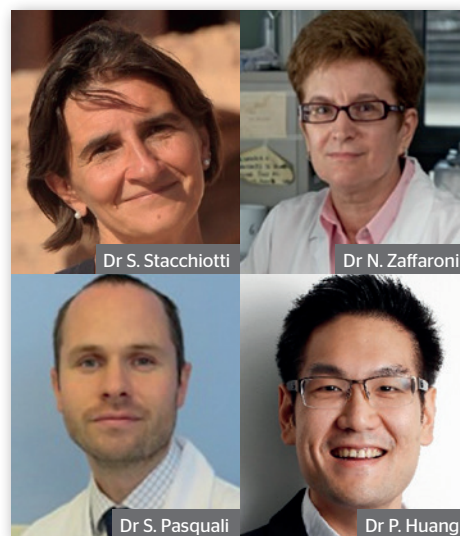
### Project 6:

Establishment and assessment of a radiological database.

The clinically-annotated radiologic scan collection on the study platform has been started. Response assessment is also collected by REDcap CRFs. The data analysis is planned after the end of the study.

The overall project is certainly producing some good results. The research team remain excited as they believe that within a few years, the data collected within this study will provide: (1) a better picture of the disease to inform decisions on how to treat patients with EHE and to define prognoses based on disease presentation; and (2) preclinical and clinical data to identify new treatment options and design better prospective clinical studies.

Dr Silvia Stacchiotti and Dr Nadia Zaffaroni are joint Principle Investigators (PIs) of the research taking place at INT; while Dr Paul Huang is PI for the ICR, London. Dr Sandro Pasquali is also a key member of the INT research team.



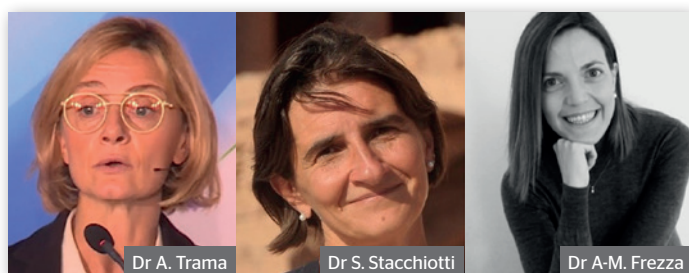


## The EHE pan-European prospective observational registry

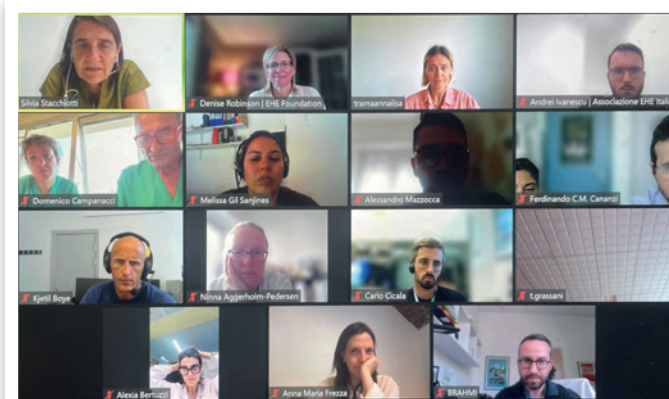
A cancer registry is an information system designed for the collection, storage, and management of data on persons with cancer. Registries for rare diseases such as EHE are very unusual as, to provide meaningful sets of data, patients from multiple centres need to be included. The need for pan-European registries for rare cancers was recognised by the European Reference Network in Rare Adult Solid Cancers (EURACAN). The STARTER project was therefore established on the basis that gathering data on rare cancers will support research, help to develop and/or improve clinical practice guidelines, support multidisciplinary discussion and consultations for patients with rare cancers, and ultimately improve quality of care across Europe. Setting up the STARTER project was also hugely important, as the project would define the registry model, set up the appropriate IT infrastructure, define and implement the legal and ethical framework, develop the registry governance, and initiate the first registries.

The Charity was therefore delighted when it was informed that EHE had been selected to be the first rare cancer within this important new data-gathering initiative, and immediately committed to funding the setting up of the first such prospective observational registry for the disease. The registry is being led and managed by Dr Annalisa Trama and the team at INT in Milan, Italy. The registry will be maintained within the European STARTER project and patients will be enrolled and data contributed by clinical providers at the participating hospitals/centres.

The EHE Registry project is being led by Dr Annalisa Trama and Dr Silvia Stacchiotti. Dr Anna-Maria Frezza is also a key member of the research team.



INT held the first briefing session of European hospitals that may be interested in joining the study in early 2023. A virtual zoom meeting was held during which Dr Stacchiotti, Dr Anna-Maria Frezza and Dr Annalisa Trama led a presentation of the study and invited expressions of interest. Subsequent interest levels were high and when the informal launch of the world's first ever multi-centre prospective registry for EHE took place at INT in September, a total of 21 hospitals had signed up.



There was understandably a lot of excitement as the INT team had been working hard over an extended period to develop the registry. This had not been easy due to the heterogenous nature of EHE, which presented a major challenge to all involved in creating the appropriate data capture infrastructure.

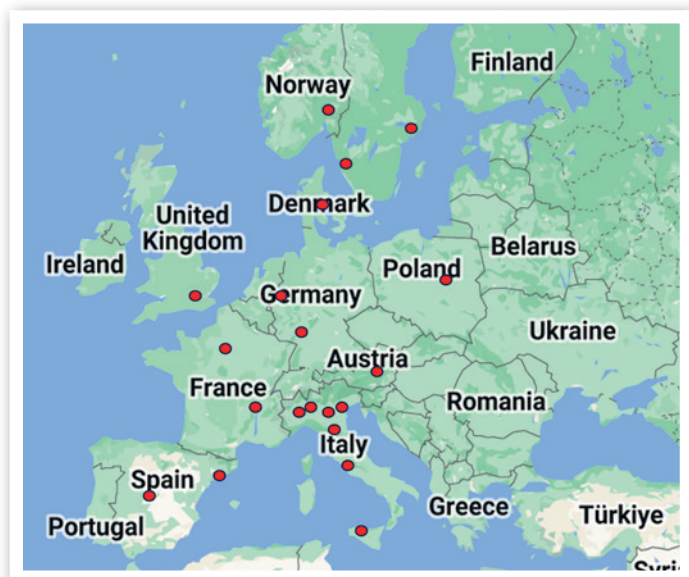


## 02 EHE Research Continued

Hugh Leonard was also thrilled to see the large number of institutes that had joined the project:

*“Joining the project is not compulsory. Each institute that is eligible has to make its own decision as to whether to join the registry or not, so we were delighted to see that 21 hospitals had already joined the project. The registry team hope to add more hospitals in the future, including international centres who have expressed interest, but the immediate focus will be on getting the project up and running with the 21 initial participating institutions.”*

*Capturing this data is so important as the design focuses on EHE, and over time the study will provide high-quality valuable data important for generating hypotheses and further interrogation of disease treatments. This was why we did not hesitate to provide funding to INT for the registry when we were approached.”*



The Charity congratulated the INT team for their dedication and hard work in getting the EHE prospective registry up and running, and are confident that this study will play an important part in the future development of the understanding and treatment of EHE.

### Progress review

As part of its overall research management programme, the Charity coordinates periodic in-person reviews of progress. Such a review of the INT research was undertaken in September in Milan. The Charity invited Denise Robinson, Director of Research at The EHE Foundation in the US and Andrei Ivanescu, President of EHE Italia, to join the review process to maximise the sharing of information and the learning for the different EHE entities.



The meeting involved the whole INT research team as well as Dr Paul Huang from the Institute of Cancer Research, joint PI of the project. The team provided an excellent review of their work and a lively and robust discussion of the ongoing research was enjoyed by all.

### Building an EHE research strategy

The meetings in Milan, involving the Charity, The EHE Foundation and EHE Italia, together with leading EHE clinicians and researchers, were a perfect opportunity to discuss the important issue of developing a broad and coherent EHE research strategy. Hugh Leonard explained:

*“The EHE global community has done an extraordinary job of promoting research into EHE and getting an exciting portfolio of EHE research up and running. This of course has only been possible because of major donations and the amazing grassroots fundraising effort of so many in our global patient community and their supporters.”*

*With continued successful fundraising, it is imperative that we develop a pro-active research agenda that prioritises areas where there are gaps in our knowledge, to bring forth critical data and advances in the development of treatments for EHE. This will also allow us to develop and promote a coherent multi-year research programme and associated budgets which we hope will in turn allow us to engage with larger sources of funding.”*

The goal is to produce a research strategy that will guide the EHE Group's research planning and help deliver the EHE Group's collective research goals, namely to find effective treatments for EHE. To date, we have funded amazing projects that have advanced knowledge in EHE; now is an appropriate time to assess the gaps in knowledge that need to be addressed in order to accelerate research that ultimately will improve the lives of people diagnosed and living with EHE.

These strategic discussions in Milan were the first in which the EHE Group had been able to engage with clinicians and researchers who are actively working with EHE, to seek their input and direction on an overall EHE research strategy. We could not be more grateful to Drs Stacchiotti, Frezza, Zaffaroni, Pasquali (all INT) and Huang (ICR) for giving us a whole afternoon to discuss and review our EHE research objectives. The debate was once again lively and excellent suggestions and observations were provided. We are now moving forward with further engagement with clinicians planned in 2024.

But it is not just the opinions of clinicians and researchers that the EHE Group want to hear. It is so important that we engage with our global patient community and also seek their input to this research process. The patients' view is very powerful when collectively voiced, and there is no group more vested in achieving positive outcomes than the global EHE community. We will ensure that they are involved as we move forward with this initiative.



Drs Stacchiotti, Zaffaroni, Pasquali, Huang and Frezza discussing an overall EHE research programme with Hugh Leonard, Denise Robinson and Andrei Ivanescu in Milan.

## EHE Global Patient Registry is growing

The Charity was delighted at the end of the year to see the excellent early progress with regard to the EHE Global Patient Registry that was established and is administered by The EHE Foundation in the USA. More than 200 people representing 19 countries had joined the EHE Global Patient Registry. This is a wonderful start, but we want and need many more to join the registry. It is hard to overstate the importance and benefit of every single patient contribution.



Denise Robinson, Director of Research at The EHE Foundation and PI for the registry, explained:

***“The value and benefit of a registry is directly related to the number of patients that are included. So please, if you haven't already joined, we encourage YOU to please consider joining today! Go to <https://eheregistry.iamrare.org/> to find out more and register to join. Your input will help doctors, researchers, and other patients know, for example, how many people have EHE that is like your disease. By collating and analysing this data your input may lead to break-through understanding of EHE. Please don't just leave it to others. Join the registry today.”***

The Charity is actively promoting the registry and hopes that doctors and hospitals involved with sarcoma will also encourage participation. The Charity is also ready to assist anybody who has any questions or concerns about the registry, and can be contacted through the Charity website.



# 03 Fundraising and Finance

---

**2023 has been another good year for the Charity. Our supporters have once again organised their own fundraising events while also engaging enthusiastically in the two big events the Charity coordinates: the London Landmarks Half Marathon and the Ride London Essex 100 cycling sportive. This has been particularly important as most charities continue to experience reduced levels of donations due to the ongoing cost-of-living crisis. The simple fact is that there is less available money for donation to great causes, and so we could not be more grateful to our supporters who have continued to work hard to raise the funding we need to drive our EHE research.**

An example of the excellent support we continue to enjoy was the fact that we equalled our record for the number of runners taking part in the London Landmarks Half Marathon. Putting out a team of 50 runners, was very exciting. We want to thank EHE patient, Paul Dean, and Ginger's Fitness owner Paul Preston for the marvellous work they did, each organising teams of close to 20 runners.

Although fundraising may be slightly more challenging now, we want to reassure everybody that there is no financial risk to our activities, and especially to our ongoing research. The Charity is run entirely by volunteers and so our Charity running costs are very small indeed. As for our ongoing research programmes, our Charity governance prohibits us from committing to research expenditure unless we already have the full amount we are committing to in our account and unallocated. So today we continue to hold in our Charity bank account sufficient funds to cover all future research that we have contracted for. This means that the new funds raised each year are available to support additional research, which is excellent and enables us to keep moving forward.



## Review by Jeff Collins

### The fundraisers

As in all previous years, the foundation of our fundraising is our wonderful patient community and their supporters and individual networks. We have already mentioned the excellent numbers of runners who took part in the London Landmarks Half Marathon. We also had a team of 17 riders who took on the Ride London Essex 100 mile cycling sportive in May, including Hugh, our Chair of Trustees, and his son Sam. Not only did these wonderful people either run or ride, but many organised fundraising events themselves to supplement their fundraising, including cake sales, mini raffles and quiz nights.

Fundraising is not just about the events coordinated by the Charity, however. The amazing sums we raise are the result of many small events and kind donations, regular monthly giving, employee matching, when available, etc. Every penny counts and there is no sum or donation that is too small to matter. In 2023 we saw Kelly Denton and Laptops and Lipstick organising their brilliant quiz night. The team at Rolls Royce Submarines in Derby organised their second annual quiz night in memory of their colleague, Hazel Peak. Hannah held an amazing concert at Pizza Express in support of her cousin who has EHE. Steph Scott and Adam Patrick organised an Easter Basket raffle. Mia Sallet ran 100 km over a month to raise funds in memory of her dear friend Isabelle, and David Thomas took on a 10k run to raise funds in memory of Janet Griffiths. We even had a Tyson Fury boxing glove to raffle. These are just examples of some of the brilliant events and activities that people organised to raise funds for EHE research, and for which we could not be more grateful.

### Key objectives

In the 2023 calendar year our supporters raised a total of £53,400 for the Charity's key objectives. The sources of these funds are summarised on the pie chart.

During 2023, the Charity provided a total of £146,500 for EHE research. This sum comprised £109,900 in sole-funded projects at Manchester University (closing out our PhD on molecular and cellular features of EHE); Sheffield University (Zebrafish model); and INT/Royal Marsden Hospital/Institute of Cancer Research (UK national EHE biobanking and pan-European prospective registry of EHE patients); and £36,600 in projects jointly funded with The EHE Foundation (USA) at INT/Royal Marsden Hospital/Institute of Cancer Research (biomarkers, observational study of EHE patients).

### Source of funds



### Administration/business running costs

In 2023, we once again received the generous support of a single donor who funded 100% of our Charity running costs. As in all previous years, we segregated these funds, donated for administration purposes, from those received from all other sources, which can therefore be allocated to fund our key objectives, in particular, EHE research. It is the intention of the Trustees that the same will be true in 2024.

The Charity received funding of £20,500 for its administration and business running costs account. During 2023, £25,100 of expenses had been incurred, which included an accrual of £1,200 for the independent examiner's fee. The remaining £23,900 funded fundraising events and support along with costs to update and improve the Charity's website and includes other administrative costs such as publishing and design costs and website maintenance.

***"We are once again so grateful to our patient community, their supporters, and the corporate groups and foundations who supported us through the year. We are also grateful to all those who helped us and volunteered so that we could keep our Charity running costs as low as possible. I also want to thank all the companies and service providers who have supported us with their services, often provided at no cost or reduced cost."***

***We predicted in 2022 that 2023 and years beyond may continue to be financially challenging, and that outlook has not changed. Our Charity governance requires us to ensure that we already hold the funds for any funding commitments we enter into for exactly this type of situation, with the result that the Charity can maintain its robust financial position. We will also continue to manage all funds with the utmost care to ensure that we get the maximum benefit from every pound that our supporters have so generously donated."***

**Jeff Collins**

# Wonderful support for EHE in 2023

The following pages highlight some of the amazing events that raised funds for the Charity in 2023.

## Laptops & Lipstick in action

'Laptops & Lipstick' is a business networking group for women that meets in Beckenham, Kent. In late 2021 the group choose EHERCC as its charity to support in 2022, thanks to the introduction provided by Kelly Denton, who lives in the area and whose teenage daughter has EHE. Kelly was delighted to then hear that the Charity's membership of the group was being extended for a further year, and in February 2023 they held their second annual Quiz Night to raise funds for EHE research.

The Quiz Night packed out the pub. Kelly and the Laptops & Lipstick group had also collected some wonderful raffle prizes which added to the fundraising. Kelly explained:

*"Last night my local community all came together for a quiz night in support of EHE research. Amazingly, we raised over £2000. Hugh Leonard made a guest appearance and gave a fantastic speech explaining why these kind of fundraisers are so important. It was truly overwhelming to see how many people care."*

Hugh was also hugely grateful:

*"It was lovely to meet Kelly's family, their supporters, and some of the Laptops & Lipstick members, who have been brilliant. I was able to personally thank them for their ongoing support and explain more about EHE. With EHE being a predominantly female cancer, I think it is wonderful when we have a female-focused group that wants to help and support our work. It was also a very noisy and vibrant evening with the pub packed. I also had a wonderful opportunity over the meal period to tell them about the Charity, EHE and the work we do."*

We want to congratulate Kelly and Laptops & Lipstick for organising such a positive event, and join Kelly and Hugh in thanking them for their ongoing support. We are also delighted to be able to share some photos of the evening.



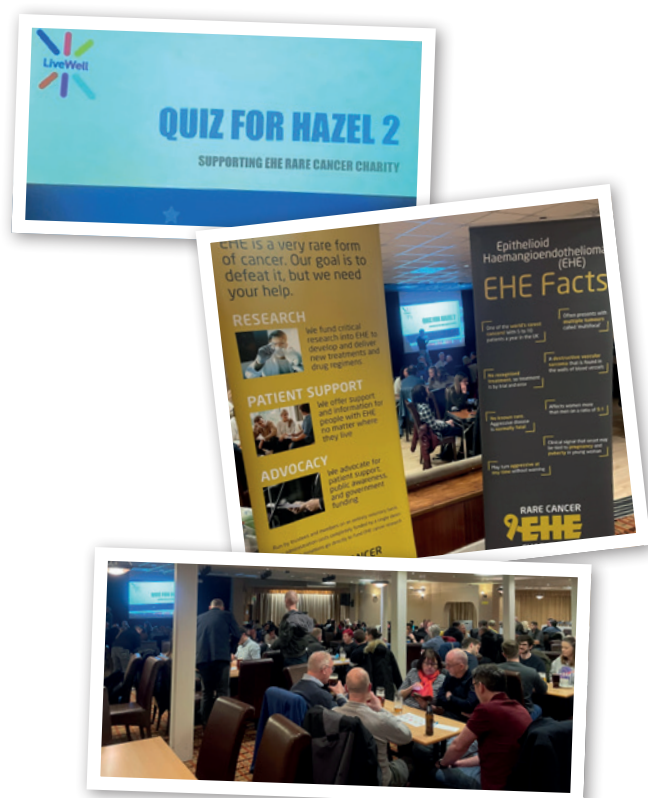


## Hazel remembered

At the start of 2022 the EHE UK patient community lost the lovely Hazel Peak. Her colleagues at Rolls Royce Submarines in Derby in the UK were understandably shattered. But they continued with their planned quiz night which Hugh Leonard from the Charity had the honour to attend. As the anniversary of Hazel leaving us approached, those same lovely colleagues decided that they wanted to continue to support the Charity, in memory of Hazel. Hugh explained:

*“Hazel’s wonderful colleagues decided that they wanted to repeat the process and so organised the ‘Quiz for Hazel 2’ in her memory. I was able to be there again and this time talked about our ongoing research, which their donations from 2022 had helped fund. Hazel’s family attended also, which was lovely. It was certainly an emotional evening.”*

The event raised more than £3,000 for EHE research, thanks to the great organisation and the unbelievable generosity of all who took part. This sum was also matched by a kind donor, taking the total raised to more than £6,000. We could not be more grateful to Hazel’s colleagues and Rolls Royce Submarines for all they have done.



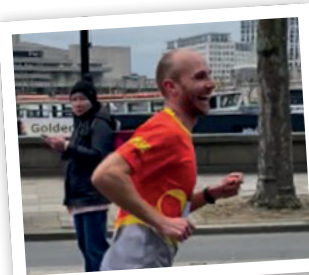
## 2023 London Landmarks Half Marathon



The 2023 London Landmarks Half Marathon (LLHM) took place in April, and the Charity had a team of 50 people running for us, both to spread awareness of EHE and to raise critically needed research funding. Sally Baker, an EHE patient and Trustee of the Charity commented:

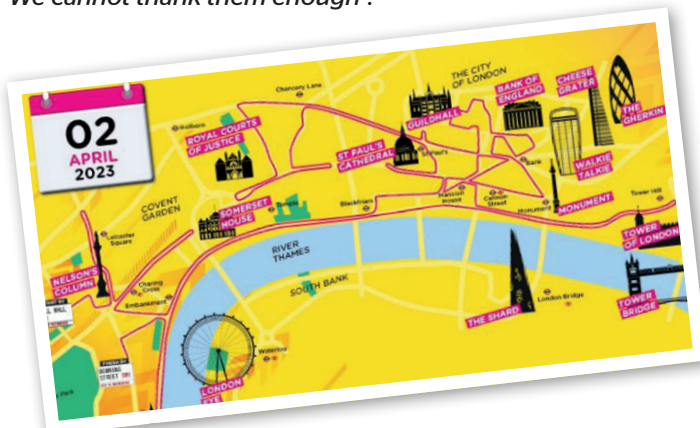
*“We had two teams of 19 within our 50 runners. Paul Dean, a fellow EHE patient, had a team of 19 runners, and Ginger’s Fitness, an outdoor fitness group from south London run by Paul Preston, also had 19 runners, supporting Kelly and her daughter, also an EHE patient. The other 12 who made up our 50 were all running in support of UK patients.”*

It was a fantastic day, not too hot, and the rain stayed away. Paul Dean was the star of the show, running the course in an extraordinary 1 hour and 21 minutes. Amazingly, Paul was disappointed as he had set his heart on finishing under 1 hour 20 minutes.



Each year the Charity sets up a cheer station on the course and this becomes a focal point for people who want to come and watch. Hugh Leonard loves the spirit of the event:

*“I find it inspiring to see so many people running for so many fantastic causes. And having 50 of those runners representing our EHE global community is really special. We cannot thank them enough.”*



## 03 Fundraising and Finance Continued

### LLHM pre-race fundraising

Some of those taking part in the 2023 LLHM were organising events in the build up to the race, using the half marathon as a catalyst for fundraising.

Paul Dean's brilliant supporters are one group that have organised a pre-race fundraising event, as Paul explained:

*"Just a few days before the run, at the end of March, Lucy Calrow organised a pre-run EHE quiz and bingo night which Simon and Lesley Calrow hosted at the Fordhouses Cricket Club to raise funds for EHE research. Around 100 people took part and raised £520 for EHE research. It reminded me once again that I have some truly awesome support, but to be honest, I never ever forget that!"*

Paul provided us with these great photos of the night. We want to join Paul in thanking everybody who took part and of course all those who ran.



### An Easter Basket

Adam Patrick ran the LLHM with Jessica Rawdon and Adam and Jayne Sausby-Gallimore in memory of their dear friend Allana Parker, who many of our EHE family knew well. They decided to boost fundraising by raffling an Easter chocolate basket. We thought that was a great idea. We also loved Adam bringing his gorgeous new arrival to the race - the smallest ever person to wear a Charity running shirt!





## Ginger's Fitness including cakes

Ginger's Fitness is an outdoor fitness group based in south London, who also had a team of runners participating in the LLHM in support of Kelly Denton, whose teenage daughter has EHE. As part of their campaign the group organised a cake sale in their local park on a Sunday. Paul Preston who runs Ginger's Fitness explained:

*"We held the cake sale in the park immediately after our Ginger's Fitness class to boost our fundraising for the LLHM. Nineteen of the Ginger's Fitness community are running for the EHE Rare Cancer Charity. Cakes were available from 9.30 am. We had soft drinks, coffee, prosecco and bucks fizz all available for a donation of the person's choice. We asked people to tell their friends and family and to bring lots of cash to donate. It was great fun and we raised over £700 from this one event which was wonderful."*

Paul wanted to say a huge thank you to Anja Workman, from Anja's Gingerbread, for baking so many brilliant cakes and gingerbread men for the sale. We loved the EHE gingerbread men runners.

We want to thank everybody in Paul Dean's team, in Ginger's Fitness's team, Adam and all the other runners and supporters for their brilliant efforts.

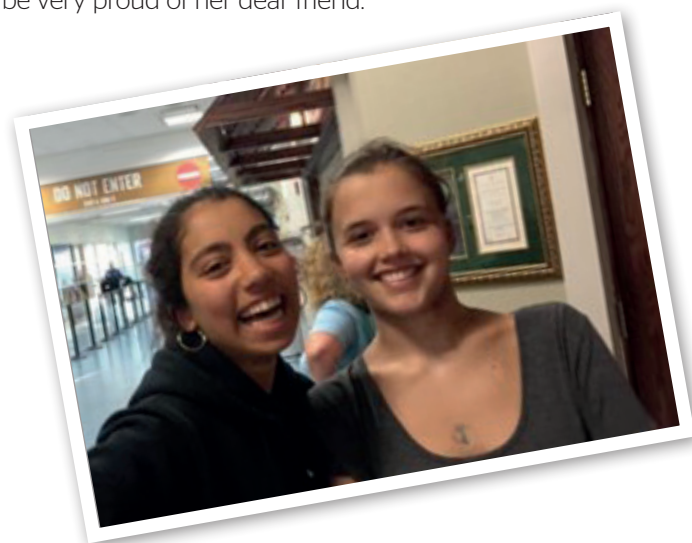


## Mia ran 100 km for her 'Zaza'

When Mia Sallet lost her dear friend Isabelle to EHE in February 2018 she, like Isabelle's family, was utterly devastated. Below are her words:

*"Hello everyone. I will be running 100km in a month in memory of my best friend Isabelle, gone too soon. My Zaza, my Isabelle, I still think of you every day, more than once a day. I miss you just as much as the day you left us, and will always have a hole in my heart, a deep sadness that will stay with me forever. I am doing this for you, for all the wonderful years we spent together, and all the memories I hold on to so so tight, it was too short. I hope you'll be proud, because quite frankly, running is not my favourite sport in the world, except maybe in 6ème with the cross country ;)! I have been wanting to do something in your memory, and to celebrate you for a long time. Thank you to Andy, for asking me to run the Asics 10k with him, which will be part of my 100km challenge within a month. You've been gone 5 years, and it feels like yesterday. I am doing this for you, for your family, for all those who love and miss you and for EHE. Miss you forever mon Isabelle, this is for you. Mia".*

Mia ran her 100km in memory of Isabelle who will be very proud of her dear friend.





## 03 Fundraising and Finance Continued

### 100 miles cycled for EHE research

Each year the Charity secures a small number of places in the Ride London Essex 100 cycling sportive, where participants cycle 100 miles on closed and empty roads. The event starts in central London and goes north east out into Essex before returning to London to finish on the iconic Tower Bridge.

Why do people ride 100 miles? Simply to raise funds for one of a huge number of fantastic causes, all of which are desperate for funding. This year the Charity had 20 places in the event and had a great turn out. Hugh Leonard, Chair of Trustees of the Charity, took part again together with his son Sam, all in support of Sally Baker, Hugh's wife and Sam's mother, an EHE patient and Trustee of the Charity.

Sam Leonard said:

***"Wow, that was fantastic but very very tiring! The last 10 miles coming back into London were very hard indeed with a series of flyovers to get over. But it was definitely worth it as we have been able to raise a lot of funding for EHE research."***

Paul Dean was again the star for the EHE team, as he was in the LLHM. On his bike, Paul completed the course in 4hrs 48 mins, averaging more than 20 miles an hour over the whole ride. Unbelievable.

We want to congratulate all the riders for their brilliant performance and for helping to raise such badly needed funding for EHE research.



### Throwing punches at EHE!

Many of our EHE global community use a boxing glove or clenched fist emoji when they post about their fight with EHE. Personalising the disease gives it a targetable characteristic. So we all smiled when Kelly Denton posted news of her latest fundraising idea:

***"Hey Guys, believe it or not I have a signed Tyson Fury boxing glove which I am going to raffle for EHE, so please buy a ticket if you can."***

There was certainly a lot of interest because there will always be excitement when such an iconic item becomes available from a current reigning world heavy weight boxing champion. Kelly was certainly not disappointed with the final result:

***"Amazingly Tyson's glove helped me raise more than £500 for EHE research! Let's hope that money helps towards hitting EHE harder than a Tyson Fury punch!"***



## A stunning evening

Kelly Denton's family have been brilliant supporters of the EHE cause ever since her daughter was diagnosed with EHE. So we were not surprised when one of her relatives, Hannah, held a small and intimate concert in central London one Sunday night to raise funds for the Charity and for EHE research. Hannah had previously participated in and done very well on The Voice, a prime time music talent show, so those present were not surprised to be blown away by her phenomenal voice. Hannah was brilliantly supported by two other young singers, as well as her husband and brother, both talented musicians.

It was also great as there were four EHE patients present on the night, Sally Baker, Kim Alexander-Bird, Michaela Murphy, and Kelly's daughter. All agreed that it was lovely to be able to meet one another and their respective partners.

Hugh Leonard also had the chance to say a few words about EHE and the Charity at the start of the concert. At the end of the night Hannah had raised more than £1,000, an amazing achievement.

We want to thank Kelly and Hannah for organising this great event. Our community motto is **Just Live**, something that those present on the night very definitely lived up to.



## Darren Thomas runs in memory of Janet

We always find it moving to see people taking on a fundraising event in memory of somebody who has lost their life to EHE. In September, Colin Griffiths posted news of Darren Thomas's Swansea Bay 10k run in memory of Colin's wife, Janet, who passed away at the end of 2022.

*"As many of you know, Jan lost her brave fight with EHE Cancer in December 2022. In January 2023, 6 of our fittest lads (Dai, Darren, Scott, Stephen, Colin and Simon) started training for the Swansea Bay 10k to raise funds and awareness for this rare cancer. Unfortunately over the training period, injuries led to 5 having to drop out leaving just 1 - well done Darren! Darren will be taking part in the Swansea Bay 10k on Sunday 17th September to raise funds and awareness for The EHE Rare Cancer Charity UK. We as a family are greatly appreciative and if you would also like to support Darren and provide much needed funds for this charity please use their Just Giving page."*

Darren raised nearly £1,000 for EHE research. We want to congratulate Darren for this fantastic effort. We are sure that Janet was watching and willing him on.



EHE Rare Cancer Charity UK

# Financial Accounts for 2023

Independent Examiner's Report to the Trustees of EHE Rare Cancer Charity (UK).....	37
Statement of Financial Activities for the period ended 31 December 2023 .....	38
Balance Sheet as at 31 December 2023 .....	39
Notes to the Accounts for the period ended 31 December 2023 .....	40



# EHE Rare Cancer Charity (UK)

## Independent examiner's report

### Independent examiner's report to the trustees of EHE Rare Cancer Charity (UK)

I report to the charity trustees on my examination of the accounts of EHE Rare Cancer Charity (UK) (the Charity) for the year ended 31 December 2023.

### Responsibilities and basis of report

As the trustees of the Charity you are responsible for the preparation of the accounts in accordance with the requirements of the Charities Act 2011 ('the Act').

I report in respect of my examination of the Charity's accounts carried out under section 145 of the Act and in carrying out my examination I have followed all applicable Directions given by the Charity Commission under section 145(5)(b) of the Act.

### Independent examiner's statement

I have completed my examination. I confirm that no material matters have come to my attention in connection with the examination giving me cause to believe that in any material respect:

- 1 accounting records were not kept in respect of the Charity required by section 130 of the Act; or
- 2 the accounts do not accord with those records; or
- 3 the accounts have not been prepared in accordance with the methods and principles of the Statement of Recommended Practice for accounting and reporting by charities (applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102)).

I have no concerns and have come across no other matters in connection with the examination to which attention should be drawn in this report in order to enable a proper understanding of the accounts to be reached.

*(signed) "RJP LLP"*

**Simon Paterson FCCA**

RJP LLP  
Ground Floor  
Egerton House  
68 Baker Street  
Weybridge  
Surrey  
KT13 8AL

Date: 22 October 2024

# EHE Rare Cancer Charity (UK)

## Statement of Financial Activities

for the period ended 31 December 2023

	Notes	Unrestricted funds £	Restricted funds £	<b>Total 2023 £</b>	Total 2022 £
<b>Incoming resources:</b>					
Donations	2	53,387	20,450	<b>73,837</b>	106,559
<b>Total incoming resources</b>		<b>53,387</b>	<b>20,450</b>	<b>73,837</b>	106,559
<b>Resources expended:</b>					
Costs of generating donations		1,326	9,142	<b>10,468</b>	2,374
Charitable activities		146,463	-	<b>146,463</b>	155,199
Governance costs		-	1,200	<b>1,200</b>	1,200
Other administrative costs		72	14,767	<b>14,839</b>	4,9487
<b>Total resources expended</b>	3	<b>147,861</b>	<b>25,109</b>	<b>172,970</b>	163,721
<b>Net surplus for the year</b>		<b>(94,474)</b>	<b>(4,659)</b>	<b>(99,133)</b>	(57,162)
Transfer between funds		-	-	-	-
Balance brought forward		262,209	8,680	<b>270,889</b>	328,051
<b>Funds carried forward</b>	8	<b>167,735</b>	<b>4,021</b>	<b>171,756</b>	270,889

Funds carried  
forward for 2023  
£171,756

# EHE Rare Cancer Charity (UK)

## Balance Sheet

### as at 31 December 2023

	Notes	Unrestricted funds £	Restricted funds £	<b>Total 2023 £</b>	Total 2022 £
<b>Current assets</b>					
Debtors	5,9	128,246	-	<b>128,246</b>	212,171
Cash at bank and in hand		181,683	19,727	<b>201,410</b>	323,495
<b>Total current assets</b>		309,929	19,727	<b>329,656</b>	535,666
<b>Creditors: amounts falling due within one year</b>	6,9	(104,812)	(15,706)	<b>(120,518)</b>	(167,165)
<b>Net current assets (liabilities)</b>		<b>205,117</b>	<b>4,021</b>	<b>209,138</b>	368,501
<b>Creditors: amounts falling due after one year</b>	7,9	<b>(37,382)</b>	-	<b>(37,382)</b>	(97,612)
<b>Net assets (liabilities)</b>		<b>167,735</b>	<b>4,021</b>	<b>171,756</b>	270,889
<b>Funds carried forward</b>					
Unrestricted funds		167,735	-	<b>167,735</b>	262,209
Restricted funds		-	4,021	<b>4,021</b>	8,680
<b>Total funds</b>	8	<b>167,735</b>	<b>4,021</b>	<b>171,756</b>	270,889

The Charities Act 2011 requires the trustees to prepare financial statements for each financial year which give a true and fair view of the state of affairs of the charity at the year end and of the surplus or deficit for the year then ended.

In preparing these financial statements, the trustees are required to select suitable accounting policies, and then apply them on a consistent basis, making judgements and estimates that are prudent and reasonable. The trustees must also prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charity will continue in business.

The trustees are responsible for keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the charity and to enable them to ensure the financial statements comply with the Charities Act 2011. The trustees are also responsible for safeguarding the assets of the charity and hence taking reasonable steps for the prevention and detection of fraud and other irregularities.

These accounts were approved by the trustees committee on 21 October 2024 and signed on its behalf by:

*(signed) "Hugh Leonard"*

**Hugh Leonard**  
Chairperson



# EHE Rare Cancer Charity (UK)

## Notes to the Accounts

### for the period ended 31 December 2023

#### 1 Accounting Policies

**Basis of preparation:** The financial statements of the charity, which is a public benefit entity under FRS 102, have been prepared in accordance with the Charities SORP (FRS 102) 'Accounting and Reporting by Charities: Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2019)', Financial Reporting Standard 102 'The Financial Reporting Standard applicable in the UK and Republic of Ireland' and the Charities Act 2011. The financial statements have been prepared under the historical cost convention.

#### Incoming resources

**Recognition of incoming resources:** These are included in the Statement of Financial Activities when:

- The charity becomes entitled to the resources;
- The trustees are virtually certain that they will receive the resources; and
- The monetary value can be measured with sufficient reliability.

**Deferred income:** Where grants are received in advance and specified by the donor as relating to specific accounting periods, these are deferred on an accruals basis to the period to which they relate.

**Tax reclaims on donations and gifts:** Incoming resources from tax reclaims are included in the Statement of Financial Activities at the same time as the gift to which they relate.

**Incoming resources with related expenditure:** Where incoming resources have related expenditure, the incoming resources and related expenditure are reported gross in the Statement of Financial Activities.

**Volunteer help:** The value of any volunteer help is not included in the accounts.

**Investment income:** Investment income is included in the accounts when receivable.

#### Expenditure and liabilities

Resources expended are inclusive of VAT where applicable which cannot be recovered.

**Liability recognition:** Liabilities are recognised as soon as there is a legal or constructive obligation committing the charity to pay out resources.

**Costs of charitable activities:** A research grant is recognised when the Charity formally notifies the recipient of the award following scientific review. The liability is measured as the total of expected payments for the award. Grant payments that are contingent on a successful outcome of and payable after a future scientific review are disclosed as commitments. Liabilities for awards payable more than one year after the balance sheet date are recorded at the value the Charity expects to settle the grant or award.

**Governance costs:** These include the costs of preparation and examination of statutory accounts, the costs of any general meetings and the costs of any legal advice to trustees on governance or constitutional matters.

#### Administrative fund

This fund has been established by the trustees to fund all governance and administrative costs and is funded by a single donor for these restricted purposes.

## 2 Analysis of incoming resources

### Donation income:

	2023 £	2022 £
<b>Unrestricted funds:</b>		
Personal donations including fundraising events	50,949	62,593
Corporate and Foundation donations	2,438	33,216
	53,387	95,809
<b>Restricted funds:</b>		
Administration fund	20,450	10,750
	20,450	10,750

## 3 Analysis of resources expended

	Unrestricted funds £	Restricted funds £	Total 2023 £	Total 2022 £
<b>Costs of generating donations:</b>				
Just giving fees	394	562	956	1,040
Fundraising event entry and other fundraising fees	-	8,580	8,580	-
Credit card and other processing fees	932	-	932	1,334
	1,326	9,142	10,468	2,374
<b>Costs of charitable activities:</b>				
University of Manchester PhD Study	4,314	-	4,314	33,001
Royal Marsden Biobank	19,719	-	19,719	16,450
Zebrafish Study University of Sheffield	58,097	-	58,097	55,198
Fondazione IRCCS and ICR Biomarkers	36,538	-	36,538	36,608
Fondazione Prospective Study	27,795	-	27,795	13,942
	146,463	-	146,463	155,199
<b>Governance costs:</b>				
Independent examiners' fee	-	1,200	1,200	1,200
	-	1,200	1,200	1,200
<b>Other administrative costs:</b>				
Design and publishing	-	4,675	4,675	2,683
Website maintenance	-	10,020	10,020	2,088
Bank fees	72	72	144	177
	72	14,767	14,839	4,948

### Trustees' expenses

No expenses were incurred by Trustees during the period and reimbursed by the Charity (2022 - £Nil).

## 4 Taxation

The Charity is exempt from Corporation Tax on its charitable activities.

# EHE Rare Cancer Charity (UK)

## Notes to the Accounts (continued)

### for the period ended 31 December 2023

#### 5 Debtors

	Unrestricted funds £	Restricted funds £	<b>Total 2023 £</b>	Total 2022 £
Prepayment to Royal Marsden	42,442	-	<b>42,442</b>	60,685
Prepayment to Fondazione IRCSS Istituto Nazionale Dei Tumori	52,654	-	<b>52,654</b>	118,526
Prepayment to the University of Sheffield	29,382	-	<b>29,382</b>	28,715
Other debtors	3,768	-	<b>3,768</b>	4,245
	<b>128,246</b>	-	<b>128,246</b>	212,171

Included within the debtors figures above are amounts of £97,612 (2021 – £25,055) due after more than one year.

#### 6 Creditors: amounts falling due within one year

	Unrestricted funds £	Restricted funds £	<b>Total 2023 £</b>	Total 2022 £
University of Manchester	-	-	<b>-</b>	3,820
Royal Marsden	23,717	-	<b>23,717</b>	28,050
Fondazione IRCSS Istituto Nazionale Dei Tumori	51,457	-	<b>51,457</b>	95,433
University of Sheffield	29,382	-	<b>29,382</b>	28,715
Accrued independent examiners'	-	2,400	<b>2,400</b>	2,400
Other creditors	256	13,306	<b>13,562</b>	8,747
	<b>104,812</b>	<b>15,706</b>	<b>120,518</b>	167,165

#### 7 Creditors: amounts falling due after one year

	Unrestricted funds £	Restricted funds £	<b>Total 2023 £</b>	Total 2022 £
Fondazione IRCSS Istituto Nazionale Dei Tumori	12,712	-	<b>12,712</b>	54,207
Royal Marsden	24,670	-	<b>24,670</b>	43,405
	<b>37,382</b>	-	<b>37,382</b>	97,612

#### 8 Details of funds

##### Administrative Fund

This fund has been established by the Trustees to fund all governance and administrative costs and is funded by a single donor for these restricted purposes.



## 9 Commitments and contingencies

In July 2018, the Charity contracted with the **Bateson Centre at the University of Sheffield** to develop an EHE zebrafish model. In August 2019 and July 2021, a second and third phase of the project was agreed and in July 2022, the Charity contracted with the Bateson Centre to fund an additional one-year, full-time MPhil student to further assess the EHE zebrafish model that the Charity had funded in 2018 through 2021. The total cost of the project is £57,430 and commenced in July 2022. In 2022, £55,198 of payments were made and recorded as charitable activity cost (2021 – £26,483). The amounts committed to for 2023 have been included within Debtors and Creditors as appropriate.

In October 2018, the Charity contracted with the **Department of Developmental Biology and Medicine at the University of Manchester** for the carrying out of a four-year PhD study to research the impact of EHE on endothelial cells. The total cost of the contract was £173,237 to be incurred over four years from January 2019. In 2023, a final payment of £4,314 was made and recorded as charitable activity cost (2022 – payments of £29,181 and expense of £33,001). The project is now complete.

In March 2021, the Charity agreed to fund costs associated with the establishment and administration of an EHE Biobank and the provision of a Tissue Manager with the **Royal Marsden Cancer Charity and the Royal Marsden NHS Foundation Trust** with an estimated total cost of £85,150 over five years commencing in April 2021 (four years commencing April 2022 regarding the Tissue manager). In 2023, £27,567 of payments were made (2022 – £7,750) and £19,719 recorded as charitable activity cost (2022 – £16,450). The amounts committed to for future years have been included within Debtors and Creditors as appropriate.

In December 2020, the Charity contracted with **Fondazione IRCCS Istituto Nazionale Dei Tumori in Italy and the Institute of Cancer Research: Royal Cancer Hospital, UK** to fund a project to assess the presence of novel biomarkers in EHE patient blood and tissue samples to inform patient management as well as potential therapeutic targets. The total cost of the project is €115,000 to be incurred over a maximum of 30 months and separately, the Charity agreed that the EHE Foundation based in the United States would fund €40,000 of the total costs. In 2023, payments of £12,928 were made and £10,731 was recorded as charitable activity cost (2022 – payments of £24,965 and £21,634 of charitable activity cost). The project concluded in 2023..

In June 2022, the Charity agreed to expand the project contracted with the **Fondazione IRCCS Istituto Nazionale Dei Tumori in Italy and the Institute of Cancer Research: Royal Cancer Hospital, UK** to look in greater detail of the mRNA analysis and to develop additional PDX models of different variants of EHE. Total costs of the expansion over the two years of the project are estimated at £117,396 with costs funded 50% by the Charity and 50% by the EHE Foundation in the United States. In 2023, payments of £37,401 were made and £29,247 was recorded as charitable activity cost (2022 – no payments were made and £14,975 was recorded as charitable activity cost). The remaining amounts payable by the Charity have been included in Debtors and Creditors as appropriate.

In December 2022, the Charity contracted with the **Fondazione IRCCS Istituto Nazionale Dei Tumori in Italy** to fund costs associated with a study aiming 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. Total costs of the project are €91,500. In 2023, payments of £35,903 were made and £26,654 was recorded as charitable activity cost (2022 – no payments were made and £13,942 was recorded as charitable activity cost). The remaining amounts payable by the Charity have been included in Debtors and Creditors as appropriate.

# Trustees' Declaration

As Trustees of the EHE Rare Cancer Charity (UK), the undersigned have fully reviewed the content of this Report of the Trustees and confirm that they each consider it to be a true and fair reflection of the Charity's activities and operations for the year ending 31st December 2023. They each confirm that there are, to the best of their knowledge, no exceptional or special events that have occurred or that should be reported.

The Trustees also confirm that they have undertaken their respective roles and responsibilities with due regard to the public benefit requirements of the Charity, and have taken into account the Charity Commission's public benefit guidance when making any decision and producing any reports relating to the Charity's charitable objects and its associated activities.

Signed this 22nd day of October, 2024

*(signed) "Sally Baker"*  
**Sally Baker** Trustee

*(signed) "Jeff Collins"*  
**Jeff Collins** Trustee

*(signed) "Kate Hooper"*  
**Kate Hooper** Trustee

*(signed) "Hugh Leonard"*  
**Hugh Leonard** Chair of Trustees

*(signed) "Oliver Pearce"*  
**Oliver Pearce** Trustee

---

# Charity Information

**Charity Name:**

The EHE Rare Cancer Charity (UK),  
A Charitable Incorporated Organisation (CIO)

**Also known as:**

Also known by its acronym, EHERCC

**Charity number:**

1162472

**Web address:**

[www.ehercc.org.uk](http://www.ehercc.org.uk)

**Registered address:**

23 Geneva Road, Kingston Upon Thames,  
Surrey, KT1 2TW

**Charity Trustees:**

Ms Sally Baker  
Mr Jeffery Collins  
Dr Katharine Hooper  
Mr Hugh Leonard (Chair)  
Dr Oliver Pearce

Established in 2015.

Also working closely with EHE foundations in USA, Australia, Canada and Italy.

Managed and run by volunteers.

All running costs funded by single donor.

100% of all donations received therefore available to deliver core objectives.

# The Pledge

*The Pledge* is the quarterly newsletter of the EHE group of foundations. It is produced in London and provides details of the group's worldwide activities in their key areas of advocacy and patient support, research, fundraising, and any other stories of interest. If you would like to be added to the distribution list to receive a copy of *The Pledge* each quarter, please contact the Charity.







**EHE Rare Cancer Charity (UK)**

23 Geneva Road  
Kingston-Upon-Thames  
Surrey  
KT1 2TW

[www.ehercc.org.uk](http://www.ehercc.org.uk)

[contactus@ehercc.co.uk](mailto:contactus@ehercc.co.uk)

Registered charity: 1162472



A huge thank you to [eightcreate.co.uk](http://eightcreate.co.uk)  
for the graphics and design work in  
producing this report and all editions  
of The Pledge



We would like to also thank  
Bennett Brookes Chartered  
Accountants for providing  
bookkeeping services to EHERCC



Printed by Optichrome Limited

**Cover images**

Hugh Leonard visiting the Institute of  
Cancer Research in Sutton, Surrey.  
Back row, left to right: Hugh Leonard,  
Yuen Bun Tam. Front row, left to right:  
Nafia Guljar, Eniola Ayeni, Dr Paul Huang.  
and  
EHERCC runners before the London  
Landmarks Half Marathon.