Event summary:
‘Future treatments for Sickle Cell Disease’

On 2 September 2021, the Sickle Cell Society and Blood and Transplant Research Unit at University College London hosted a virtual event to about three potential new treatments in development for sickle cell disease. Read a summary of it below.

‘Thank you everyone, this was so helpful and impactful.’

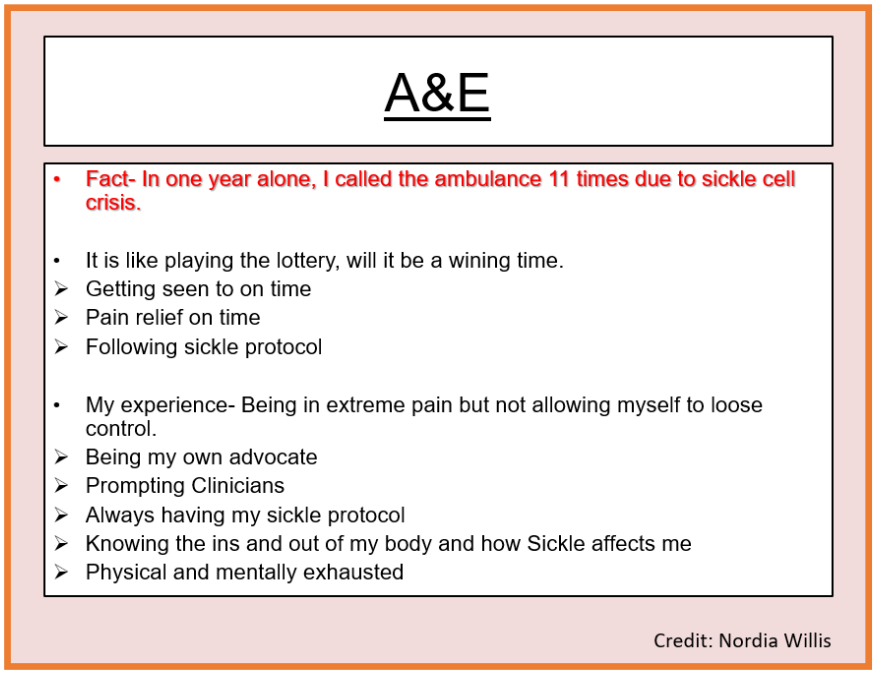
‘As I expected, the session was very informative and such a positive experience. (…), it was empowering to get information and share knowledge.’

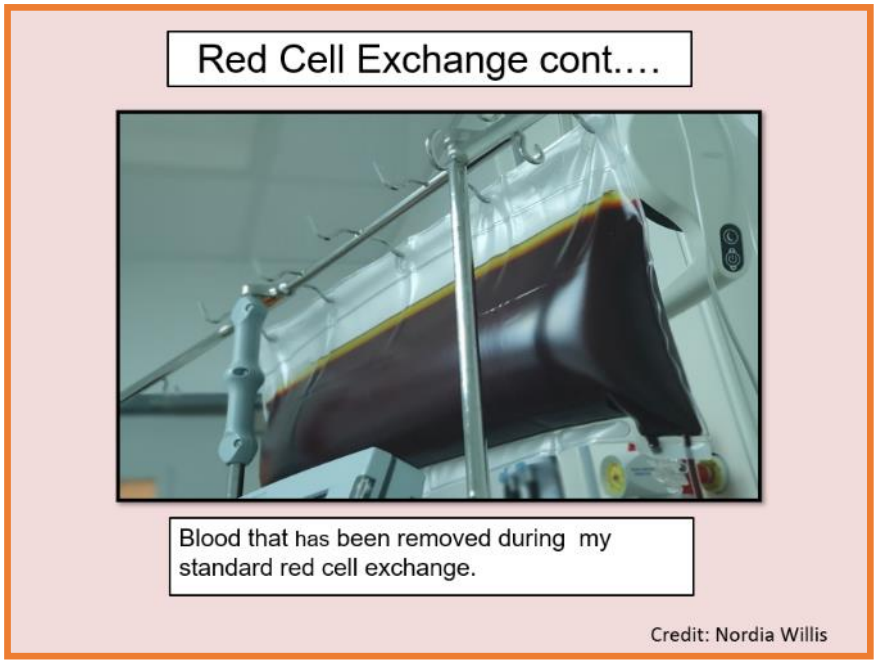
Speakers included:

1. **Nordia Willis** about her experience with sickle cell disease
2. **Javier Moncayo Arlandi** about early work on a potentially curative treatment for sickle cell disease (gene therapy)
3. **Ash Toye** about growing red blood cells that may increase supply for blood transfusions (RESTORE study)
4. **Jo Howard** about studying a sickling prevention medicine (Voxelotor/HOPE study)
5. **Edwin (Eddie) Carr** about his personal journey of getting involved in health research and his thoughts on potential future new treatments for sickle cell disease

John James, Chief Executive of the Sickle Cell Society, **welcomed speakers and 10 attendees** living or caring for someone with sickle cell disease. John highlighted the great need of new and better treatments for sickle cell disease as one of the most common inherited disorder in the UK, yet limited treatments available.

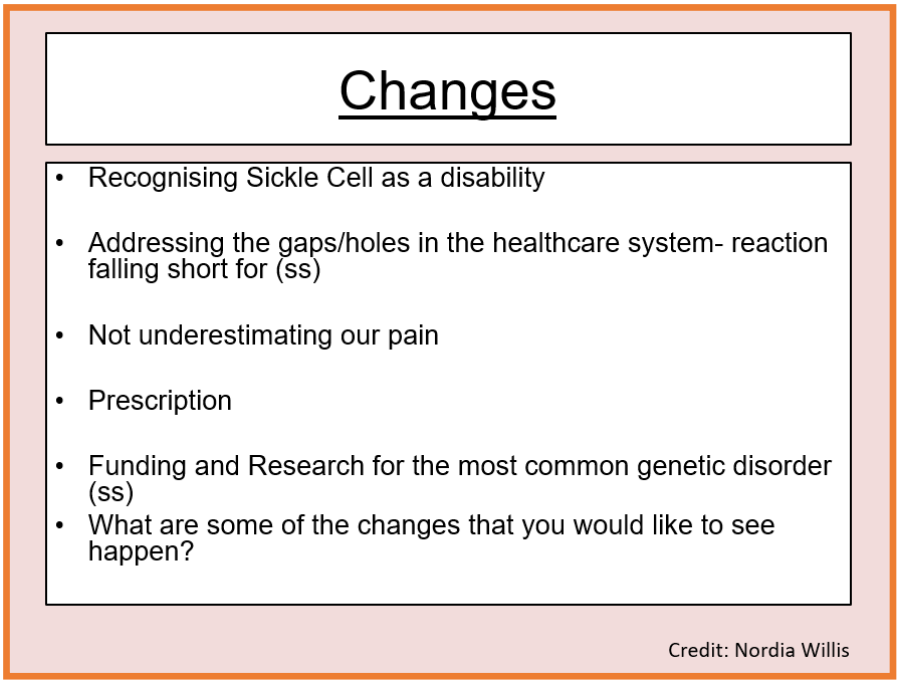
As the first speaker, **Nordia Willis spoke about her experience living with sickle cell disease**. Nordia shared the impact of sickle cell disease and treatments she is currently having, to help manage sickle cell disease. Nordia also shared how sickle cell has impacted on her education, work, personal life and well-being. She openly spoke about the challenges she faces when managing sickle cell disease and another illness, having to educate medical staff about sickle cell disease and the importance to actively be involved in health care treatment decisions. Nordia shared photos of her personal cupboard containing all her medication, which helps to manage her sickle cell at home and a folder containing all her medical records as well as her receiving blood exchange every 6-8 weeks.





She emphasised the importance of keeping her own health care record and having a summary of treatments and medicines with her to share with medical staff, especially when having a crisis. In future, Nordia hopes to see many essential changes to improve health care for people living with sickle cell disease.

'Living with Sickle cell disease is HARD. Dealing with people who do not understand or who are not caring is HARDER…' **Nordia Willis**



Nordia publicly communicates her experiences and advocates for changes she wants to see. She co-founded Broken Silence in 2004, at the time with 3 other young people who also have sickle cell disease and worked with Professor Simon Dyson, Director of the Unit for the Social Study of Thalassaemia and Sickle Cell. She actively shaped "This Sickle Cell Life", a research project looking at experiences of young people with sickle cell disease and is co-author on the article *'Study of the experiences of Young People, with sickle cell disease in non–specialist hospital'* in the Critical Public Health Journal, https://doi.org/10.1080/09581596.2019.1650893

Nordia highlighted that some of sickle cell diseases' major complications, may not be the same experience for every Sickler and ended her presentation by inviting the audience to share: *'What are some of the changes that you would like to see happen?'*

Following Nordia's talk one attendee inquired about ongoing work to recognise sickle cell disease as a disability, which has mixed views in the community and should be discussed as an available option based on individual needs.

Comments on Nordia's talk from the attendees and other speakers included:

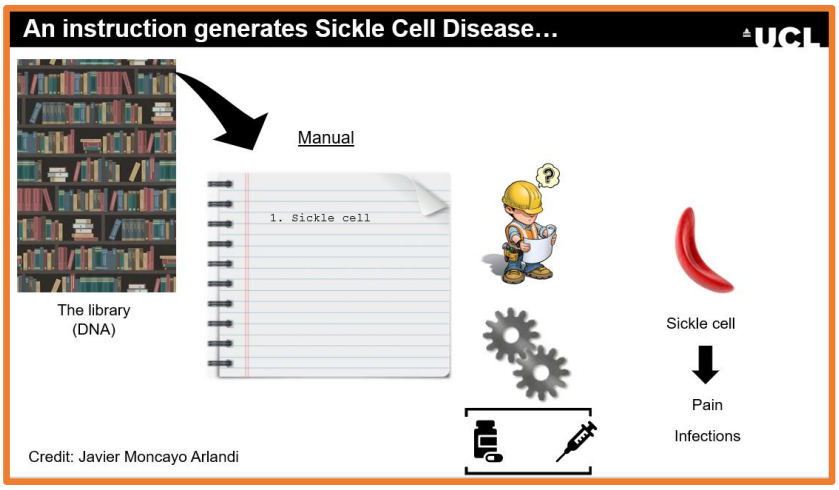
'Nordia thank you for explaining what it's like being a person with sickle disease. As scientists we don't often hear what these diseases are like live with.'

'Yes thank you Nordia...God bless you'

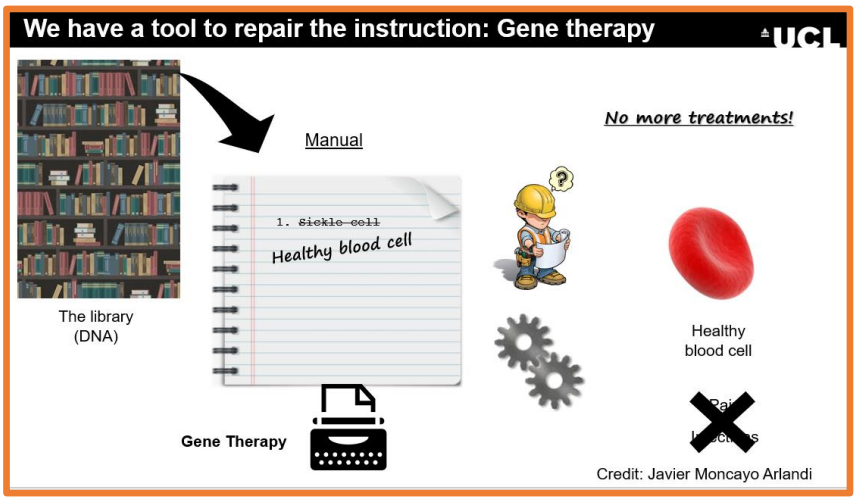
Secondly, **Javier Moncayo Arlandi,** a health care researcher at the Blood and Transplant Research Unit at University College London, spoke about his early work on **a potentially curative treatment for sickle cell disease, called gene therapy**. Javier stated that he and other people around the world are working on this potential new therapy but a lot more work is needed before it can become a safe standard treatment for sickle cell disease.

To understand gene therapy, Javier explained that we need to look at how our body is built:

'We all have a huge library (called DNA) that contains the information to build and renew parts of our body. Our DNA is like a manual with different instructions to create the characteristics that makes each of us unique.'

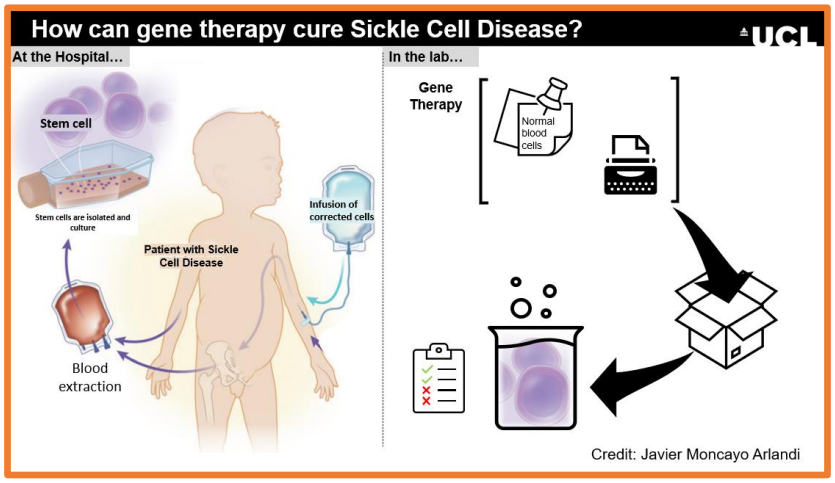


For sickle cell disease, the manual shows a slightly different instruction: Sickle cell. This leads to a different shape of the red blood cell and in large amounts the sickled cells are causing pain and other symptoms. Current medicines can help to reduce pain or numbers of infections but not completely avoid the sickle cell production in your body.



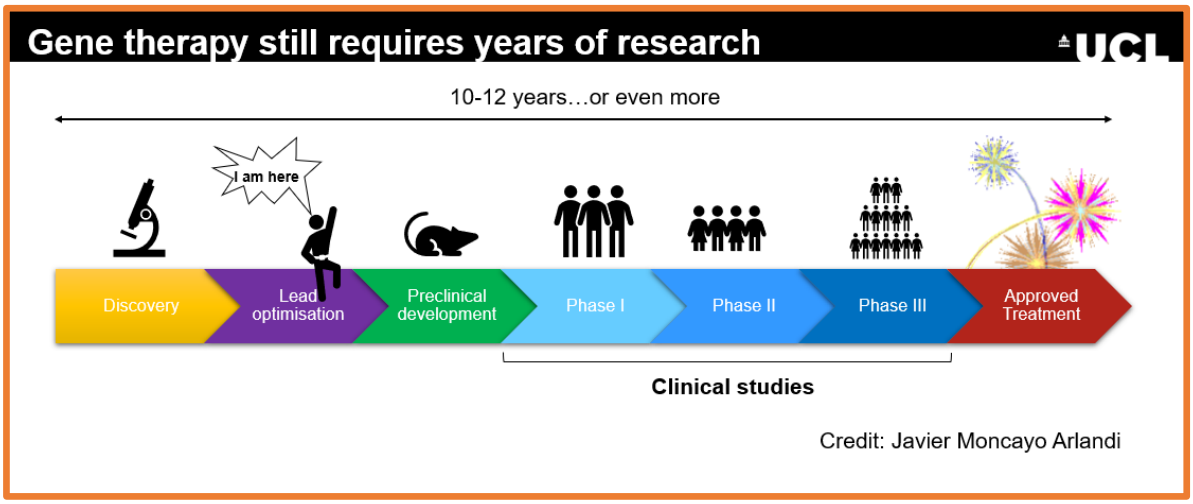
Javier shared that gene therapy could potentially change a small instruction in our body's manual (DNA), indicating "Healthy blood cell" instead of "Sickle cell". This new instruction

could remain in the body and produce healthy blood cells instead of sickled blood cells. The body now produces healthy red blood cells, which removes of the cause of pain and infections caused by sickled blood cells, meaning that other treatments for sickle cell disease are no longer needed.



How gene therapy works: Javier explained that for gene therapy currently each patient's own blood is used to grow young blood cells (stem cells) that only produce healthy red blood cells. In theory the process is simple, in practice each of these steps still need major improvements to make sure the treatment works safely.

Javier's work looks at one of the steps: Using the newest technologies to write new instructions. He said that there are promising advances, but he believes it will need 10-12 years until all different steps are ready and gene therapy can be offered as a standard treatment for sickle cell disease.



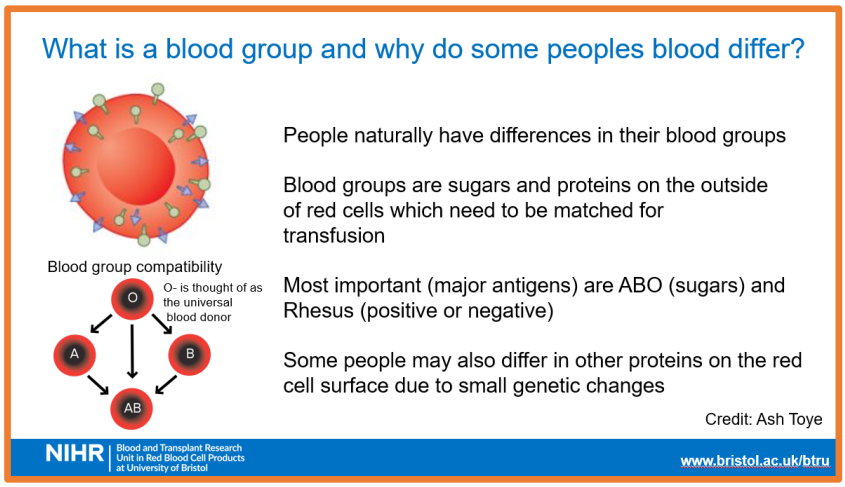
Javier finished by asking attendees 'How do you feel about this new gene therapy treatment? Would you worry if this treatment changes your DNA to cure sickle cell disease?' Main concerns raised were about side effects of treatments and access to new treatments and studies in general.

Questions about gene therapy included:

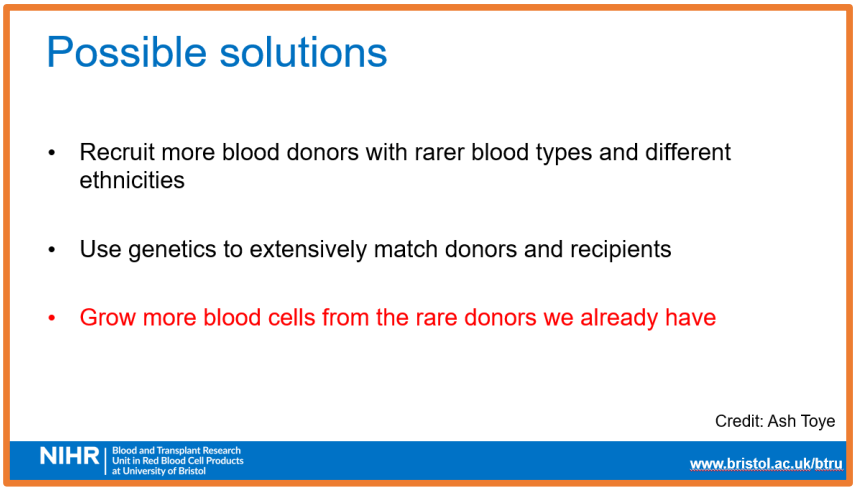
- Would the gene therapy need chemotherapy similarly to bone marrow transplant to ensure the body is receptive to the stem cells?
    - Answer: Currently, chemotherapy is often used to prepare for gene therapy treatment. There are new approaches trying to avoid chemotherapy, however.
- To understand the gene therapy, are we using the sickle cell blood into stem cell or corrected in the laboratory. So, our sickle cell blood is what is used as gene therapy right?
    - Answer: Yes, that is currently the case.
- Can the gene therapy work for people who carry the sickle cell trait?
    - Answer: Gene therapy would mainly be used for severe sickle cell disease. The sickle cell trait itself usually doesn't cause any issues and is protective from Malaria, which has huge benefits.
- Is the gene therapy on NHS choice of treatment?
    - Answer: No, it is not available as a treatment yet, but we hope it becomes an NHS treatment in future.
- Are there ways to reduce the cost for gene therapy?
    - Answer: New advances in the production of gene therapy can reduce the cost of the treatment. We still need many years of investigation before we get a secure treatment that can be afford by NHS. However, as Sickle cell disease is a quite common disorder, this makes gene therapy for it very attractive for pharmaceutical industry. I expect that this can speed up the development of gene therapy treatments and reduce the cost for the patient.

Next, we heard from Professor **Ash Toye**, Director of the Blood and Transplant Research Unit at University of Bristol, about his team's work **growing red blood cells that may increase supply for blood transfusions (RESTORE study).** The RESTORE (REcover and survival of STem cell Originated REd cells) first-in-human study will compare a mini blood transfusion, up to a teaspoon, of red blood cells grown in a laboratory from blood donors stem cells naturally present in a normal blood donation, to the same amount of standard red blood cells donated from the same donor, in healthy volunteers. This freshly grown blood may one day lead to an alternative source of fresh blood for transfusions for people with rare blood groups or for people living with sickle cell disease and thalassemia in future.

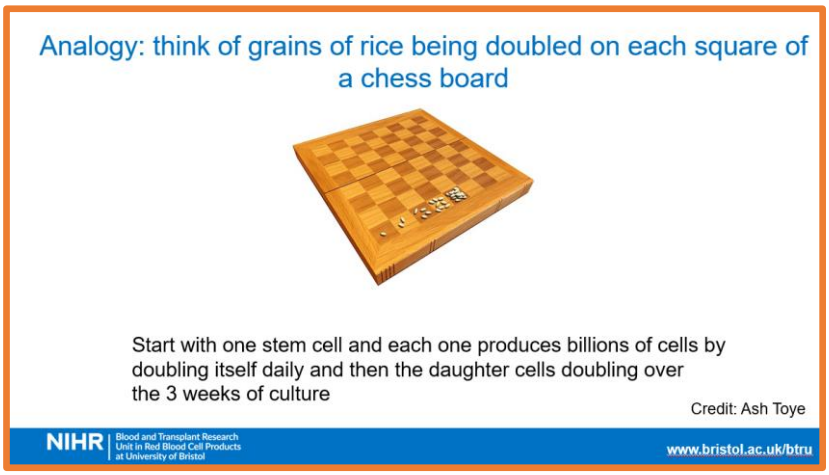
Ash explained that people have natural differences in their blood. These differences are grouped as sugars and proteins on the outside of red blood cells and matched between donor and recipient for blood transfusions. The best-known examples being ABO and Rhesus (which are the A, B or O and +/- you may see on your blood bag or donor card).



For some people it is difficult for the blood services to source a well-matched blood type for transfusion, which is the case for some people with sickle cell disease. Blood transfusion is an effective treatment for sickle cell disease, which usually means regular blood transfusions from available blood donors. With the increased frequency of blood transfusions, the body's defense (immune) system can react against small differences between the patient and the donated blood producing antibodies. Sometimes this makes if difficult, sometimes even impossible, to find matched blood for transfusion for some people.



For years, Ash, his team and researchers around the world work on one of the possible solutions to tackle this problem: Grow more blood cells from rare donors. For this, *'we take a tiny number of immature young blood cells (stem cells) from a normal blood donation and then grow large numbers of them in the laboratory.' "This uses the special properties that stem cells have to make more of themselves".*



We can now grow small amounts of this blood and will test these cells in a first-in-human study with healthy participants, to assess the safety and survival time of a small-dose, no more than a teaspoon, of lab-grown red blood cells compared with normal donated red blood cells in the healthy body.

If this study proves successful, we have lots more to do. We need to work on growing even larger amounts of blood which is a massive challenge and do further studies to make sure it is a safe and efficient treatment for people rare blood groups or for people with sickle cell disease and thalassemia, who cannot currently receive blood transfusions.

Following his talk, Ash was curious to learn about the views of attendees: 'Would you accept a transfusion of laboratory grown red cells?'

Answer	No of attendees
Yes	3
No	0
Maybe	6

Additional comments included:

- *'I would need more information. So, a maybe.'*
- *'I would. I can't have any transfusion at the moment'*

Views on Ash's second question for attendees 'If you were to have a red blood cell transfusion, would it matter to you what the starting source was, as long as it was deemed safe? were:

- ***'Safety is always key - so if the research supports it'***
- ***'Yes definitely matter, required more information and time for personal research'***
- ***'As long as it was deemed safe. Why not. As long as it does the job intended.'***

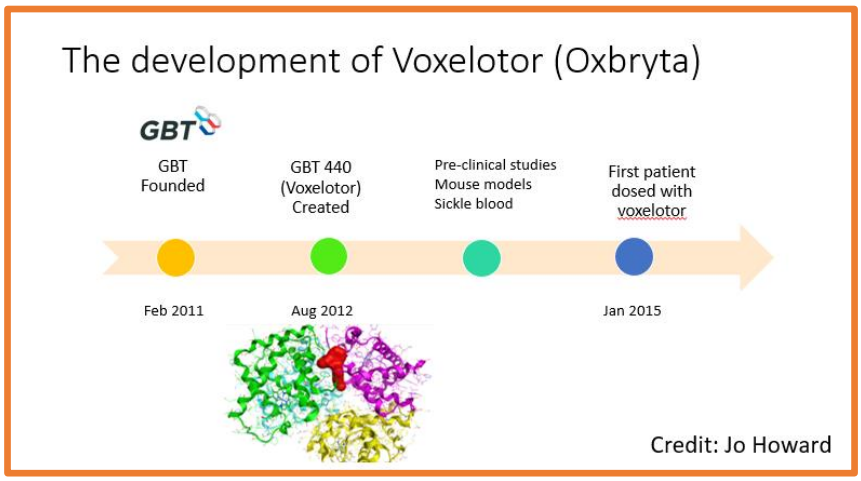
As the next speaker, we had the pleasure to welcome **Jo Howard**, consultant hematologist and lead clinician at Guy's and St Thomas' hospital (London), who was a principal investigator **on the HOPE study testing Voxelotor (OXBRYTA®) as a new sickling prevention medicine in the UK**. Very excitingly, this treatment is currently seeking approval to hopefully become a new standard treatment for severe sickle cell disease in the UK.

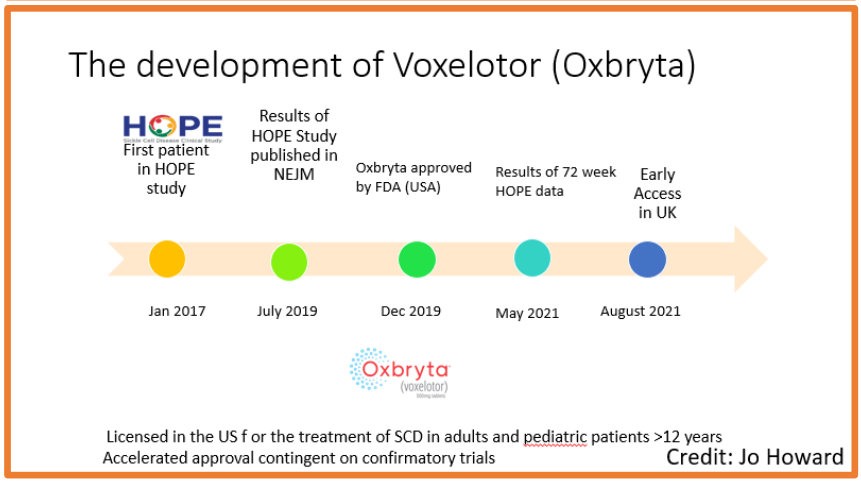
Jo explained **'When talking about this new drug, we first need to think about what is happening to the red blood cells in sickle cell disease.'** Red blood cells carry oxygen around in your body. In sickle cell disease, red blood cells change shape forming a sickle shape when the oxygen levels drop while moving round the body. This sickle shape is caused by a part of the red blood cell, the haemoglobin molecules, sticking together and forming long, stiff chains that lead to blockages in blood vessels.

So, researchers started looking at drugs that would stop these long chains forming - and if you could do this, perhaps you could stop sickling.

This is when development of Voxelotor started:

- In 2011 a biotech company Global Blood Therapeutics (GBT) was founded to look at drugs to stop haemoglobin (a part of red blood cells) forming long chains.
- By August 2012 they had developed the drug we know now as Voxelotor, which went into intensive pre-clinical testing in donated sickled blood cells and mice
- In 2014 GBT approached Guy's and St Thomas hospital about setting up a study in healthy volunteers and patients. The first patient received Voxelotor in 2015.

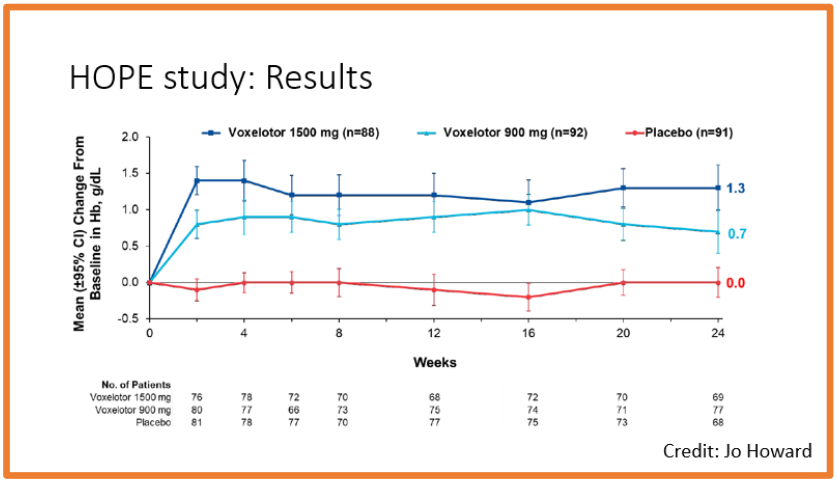




- In January 2017 the first patient with sickle cell disease got Voxelotor taking part in the international phase 3 HOPE study
- In July 2019 results of the HOPE study were published and Voxelotor (OXBRYTA®) was approved as a treatment for severe sickle cell disease in the USA
- **Since August 2021 there has been access for named patients with severe sickle cell disease in the UK** while Voxelotor (OXBRYTA®) is undergoing approval by the UK regulatory authority (NICE).

Results of the HOPE study testing Voxelotor show:

- Haemoglobin levels increased, meaning anaemia is improved within 2 weeks of starting to take Voxelotor
- This remained the same after taking Voxelotor for 24 weeks and
- Taking Voxelotor had no major side effects



Jo worked in the development of treatments for sickle cell disease since early in her career and has run numerous studies. She shared that the path to developing a new therapy for any disease is long and stressful. It starts finding a potential drug (a brand-new drug, or a drug that is already being used for something else), extensive pre-clinical testing and studies in healthy volunteers before studies become more complex and are often run internationally with patients. If studies shows that the drug is effective, the drug company must apply for a licence and needs to be approved by national regulatory authorities, who review evidence for the drug and cost effectiveness before finally giving approval for doctors to prescribe the drug to the patients it has been developed for.

As final points, Jo highlighted optimism for future changes including

- The new NHS structure of haemoglobinopathy services patients with sickle cell disease or thalassemia is improving access to both research studies and to new drugs
- Large number of research studies are either ongoing or about to open for sickle cell disease
- New treatments available for the first time in 30 years!

Jo ended thanking all patients who gave their time to take part in clinical studies, including the HOPE study, as new treatments would not be available without their contribution.

From the audience Jo was interested to learn about:

- How can we best share information about research trials and the availability of new drugs with patients?
  Replies included:
  - *'I ask at appointments, as it is not what they readily bring up either due to managing expectations or not being abreast themselves.'*
  - *'I think it should be known to all specialist doctors about the drugs available to all consultants, so they notify sickle cell patient, explaining in details and any sickle cell groups.'*
- How can we ensure that the public understands and believes the results of research?
  Suggestions included *'Via radio, and churches and certain support groups formed around Sickle Cell Anaemia'*

As the final speaker, **Edwin (Eddie) Carr**, Patient and Public Research Panel member at the Blood and Transplant Research Unit (BTRU) at University College London (UCL), entered the virtual stage to talk **about his personal journey in getting involved in health research and his thoughts on potential future new treatments for Sickle Cell Disease**.

Eddie shared his own background as a patient and his interest in sickle cell disease. He acknowledged that navigating the health care system can be challenging at times. When he saw an opportunity to get involved in health care research to develop new and better treatments for blood disorders at the BTRU his curiosity to learn more and interest to drive change for the better made him pick up the phone. ***'I want to be both part of a solution and push along the important message of ethnic inclusivity.'*** said Eddie about his motivation to give his time and experiences to shape future treatments.

Today – more than 2½ years later – Eddie acquired a wealth of knowledge and contributed his perspectives to the development of pioneering new therapies for blood cancers, sickle cell disease and other blood disorders to make sure they are relevant, acceptable and designed in the best possible way for those they are for.

Eddie worked with the BTRU at UCL on today's event to bring people working on new treatments and people living with or caring for someone with sickle cell disease together to learn from each other. He started when the unit first applied for money to begin work on a potential future gene therapy for sickle cell disease. A message that Eddie encourages people to think about is: *'If we complain to our friends and family, little change happens. If we come together to make our voices heard, we can change much!'*

*"**Change is not always instant, but we owe it to a better future to do what we can in the present**".* **Eddie Carr**

Comments from attendees and other speakers following Eddie's talk included:

'Thank you to Eddie and Nordia to being involved in research. This is so important. We are running a new trial looking at the natural history of sickle and we have 3 amazing patients who have been involved right from the beginning.'

'Not selfish at all, you are an important component to research indeed. Thank you, Eddie'

'Thanks, Eddie, for making that phone call. We are all beneficiary of the useful information offered today.'

Opportunities to give your views and perspectives to help the development of new health care treatments (health care research) to ensure these are relevant, acceptable and designed in the best possible way for people they are for:

1. **Public Advisory Group of the RESTORE study** on growing red blood cells that may one day increase supply for blood transfusions, see Ash Toye's talk above. More at http://www.bristol.ac.uk/btru/work/public-patient/
    - Contact for more information: Andy Gibson, Patient and Public Involvement Lead, on 07941 344653 or e-mail to andy.gibson (at) uwe.ac.uk
2. **Patient and Public Advisory Group at NHS Blood and Transplant** (NHS service delivering blood, organ, stem cell and tissue donations for transplantation to NHS patients) More at: https://www.nhsbt.nhs.uk/research-and-development/patient-and-public-advisory-group/
    - Contact for more information: Lucy Kershaw, Patient and Public Involvement & Engagement Officer via email to ppag.research (at) nhsbt.nhs.uk
    - Link to registration form: https://www.cognitoforms.com/NHSBT1/PatientAndPublicAdvisoryGroupRegistrationForm
3. **Help us write a blog post** about how to best communicate updates about potential new treatments and opportunities to shape them. This is a paid 1x 1-1.5-hour virtual meeting using Zoom plus reviewing the blog post via email before publication in November 2021.
    - If interested, contact: Linda von Neree, Patient and Public Involvement, on 020 3108 7641 or email to l.vonneree (at) ucl.ac.uk

If you wish for more information about Gene Therapy, the RESTORE study or HOPE study/Voxelotor (OXBRYTA®), please find the following links below:

- **Gene Therapy:** The animation 'Gene therapy explained: How to change your body's recipe to treat disease' explains more about gene therapy (please note: the

animation is not specific to sickle cell disease as gene therapy is developed for different inherited disorders), https://www.youtube.com/watch?v=i9snq5l-IVI

- **RESTORE study:** Find out more about the study at http://www.bristol.ac.uk/btru/work/trial
- **HOPE study/Voxelotor (OXBRYTA®):** You can find more information about
    - Results of the HOPE study testing Voxelotor, as a new medicine preventing sickling of red blood cells, https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(21)00059-4/fulltext
    - Updates on UK regulatory approval for Voxelotor (NICE), https://www.nice.org.uk/guidance/proposed/gid-ta10505
    - Official U.S. patient website for OXBRYTA®(voxelotor) tablets, ttps://www.oxbryta.com/

For any questions on this event or to speak further with Eddie about the general benefits of getting involved in health research, please contact:

Linda von Neree, Patient and Public Involvement Lead at the Blood and Transplant Research Unit at University College London via email at l.vonneree (at) ucl.ac.uk