Newsletter Issue No. 1

Editorial

We are delighted to share with you our first CureCN newsletter.

In this first issue, we would like to introduce you to our project and partners and give some insights into our work in the first three years of the project.
CureCN is a 5,5-year research project (2018-2023) funded by the European Commission under the Horizon 2020 program with a total budget of € 6.25 million and coordinated by Genethon (France). Eleven partners from six European countries from academia, hospitals, healthcare companies and patient organisations are joining forces to develop a curative treatment for Crigler-Najjar syndrome (CN).

In the past three years of this project, we held 3 meetings in Amsterdam, Netherlands (Kick-off meeting), in Riccione, Italy (1st Progress Meeting) and a virtual one (2nd Progress Meeting) where we discussed the details of our project, our achievements and the issues ahead of us. This first newsletter will give you more information about the project and on the progress we have made so far, our next steps and upcoming events.

Thank you for your interest and support – and enjoy reading this newsletter! We also invite you to check out our website on https://curecn.eu/.

Best regards,

The CureCN Coordination team

Gérald Perret

Giuseppe Ronzitti

About CureCN

The European research project CureCN aims to develop a curative gene therapy against the ultra-rare Crigler-Najjar syndrome (CN). Crigler-Najjar is a life-threatening liver disease which affects one in a million individuals at birth. The goal of the CureCN consortium is thus to prove the safety and efficacy of an adeno-associated virus (AVV) gene therapy in a clinical trial and make it available to patients.

Partners in CureCN have been chosen for their complementary scientific excellence, technical expertise, and experience in translational research. Joining forces, they take on the mission to find a curative treatment for CN syndrome. The project's major goals are:

- Developing a curative AAV gene therapy and validating a technology

transposable to many other inherited liver-related disorders
- Proving the safety and efficacy of the vector-mediated gene transfer with AAV in a clinical trial
- Providing a treatment suitable for young individuals affected by CN syndrome as well as for older patients who potentially carry pre-existing immunity to AAV
- Verifying a way to eradicate pre-existing immunity to AAV
- Accelerating the orphan drug development towards a marketing authorisation for the treatment

One important goal of CureCN is to establish the first global Crigler-Najjar patient natural history registry, to better understand outcomes and natural history of the disease.

CureCN also strives to provide better information for patients, families, healthcare providers and the general public about CN syndrome and existing treatments.

> Learn more about the project

> Discover our consortium

First milestones

During the first 3 years of the project, the CureCN partners have taken significant initial steps towards the realization of the project's objectives.

Following recruitment and a preliminary observation period, the first participants have been enrolled and dosed in the clinical trial. Enrollment of the first participants is an important milestone not only for the patients and their families, but also for doctors and researchers working together in the CureCN consortium.

As there is no clinical trial without the supply of the investigational drug, it is important to mention that, several lots of AAV8-hUGT1A1 vector have been produced to supply material in sufficient quantity to complete enrolment and dosing in the proposed clinical trial.
At the preclinical level, the scientists of the CureCN consortium have been working hard to achieve the ambitious goal of developing novel technologies for the modulation of antibody responses directed against AAV vectors, and for the physical removal of pre-existing antibodies to AAV from the bloodstream, the respective activities are also advancing and a manuscript was recently published on the topic in Scientific Reports.

The world registry of CN patients is compiling data on the natural course of Crigler Najjar syndrome to allow for a comparison between current treatment modalities and gene therapy. Data were gathered from a pool of more than 200 Crigler Najjar patients, and the dataset is now available through the dedicated web-based platform of the registry. Such a high number of patients will hopefully ensure statistical power in the subsequent data analysis.

Patient associations

As a patient-driven initiative, the CureCN consortium comprises all active Crigler-Najjar patient associations (PA) in Europe: the French Crigler-Najjar Patient Association, the Italian Crigler-Najjar Patient Association CIAMI onlus, and the Dutch Najjar Foundation.

All three associations have a long history of cross-country interactions as well as relations with healthcare bodies. They are organising frequent meetings with CN patients and their families, workshops with experts in the disease, and discussion groups to help patients coping with their condition. The PAs also play a crucial role i) in the education of CN patients and families, ii) on the management of the disease, keeping them informed on technological advances and, iii) importantly giving patients access to phototherapy devices, filling in the gap left by the local public health systems. All Organizations have expertise in managing web content and social networks and are familiar with potential ethical issues related to communication with patients and families.

In CureCN, the PAs support the project activities by providing critical input to the clinical trial design and the efficacy endpoint definition. In addition the PAs ensure a direct link to the CN patients. They will also play a key role in communicating with health institutions such as National regulatory agencies

and the European Medicine Agency.

With their knowledge of the disease, they emphasise the patients' perspective and are deeply involved in disseminating the results of the project by informing about the progress in the project in a format that is fully compatible to the level of knowledge of non-specialised individuals. The PAs are strongly involved in the ethical oversight of the clinical trial performed in CureCN.

Finally, aside from the treating physicians, the PAs bring to the CureCN project the highest level of knowledge on CN syndrome and on the various aspects of the disease and its impact on the quality of life of affected individuals.

Interview with a mother of a CN patient

Giulia* is the mother of Sofia*, a young woman from Italy who is suffering from the ultra-rare liver disease, the Crigler-Najjar Syndrome (CNS). She is one of the patients involved in the clinical trial of the EU research project CureCN. Patients with Crigler-Najjar lack an enzyme that breaks down bilirubin, which helps the body clear worn-out red blood cells. An accumulation of bilirubin causes jaundice; too much bilirubin in the body can cause brain damage or even death. Thus, Giulia's daughter has to sleep every night under a phototherapy lamp with special blue lights which help break down the bilirubin. Albeit the disease, her daughter is trying to live a "normal" life and thus she moved alone to another town to attend a university course.

How did the doctor communicate the diagnosis of the Crigler-Najjar Syndrome?
Our daughter was born in February and we received the conclusive diagnosis in September. Even if the neonatology doctor had already suspected the Crigler-Najjar Syndrome, the disease wasn't really known and the information about its evolution in those times wasn't very good. This was a big mistake in communication, I think. Anyway, soon after we met the Italian CNS association and people with a big experience in dealing with CNS patients and we felt much better!

Your daughter sleeps every night under a special light device. Did you have difficulties with the National Health Service regarding the bureaucratic process?
We received the first device from the neonatology department. The situation has improved over the years and we have received new devices when necessary. During those first years, the disease was better examined and studied. That was a very important step.

How and when did you explain the disease to your daughter?
I have a friend who is a psychologist and she suggested I talk to my daughter sincerely from the very beginning, increasing the level of information with age according to her contextualization skills.

Do you remember any episode of discrimination? CNS patients have yellow eyes and skin, did you give explanations or did you wait for questions?
Sometimes we had discrimination episodes, but we immediately dealt with it together with my daughter and the involved people. I have always tried to explain this ultra-rare disease at school, to teachers and other parents. At a certain point, she started to explain it by herself to her schoolmates and friends.

Living with a light device is difficult. Can this preclude from a normal family life?
We have always tried not to be "crushed" by the disease. We have always travelled as best we could, to the seaside, to the mountains, abroad by car, with a portable phototherapy device we have built. We try to live as "normal" as anyhow possible.

Do you think that accepting a disease and sharing experiences is useful to live with it in a better way?
Yes, I think this is the first and most important thing to do.

Have you ever thought about a liver transplantation?
No, personally never. I have always thought that science and medical research would find an alternative therapy.

How did you hear about the CureCN project?

Thanks to the Italian CN Association CiamiOnlus, that is involved in the project. They kept us informed and some Italian patients are involved in the clinical trial like my daughter.

How do you feel having your daughter involved in the clinical trial?
I feel a little worried, of course, mainly from the psychological point of view. I worry about the reaction if the therapy is not successful. We have mixed feelings: hope, happiness, fear… patients have been waiting for this moment for a long time. We trust the clinicians and the researchers and we hope it will be successful.

What would be the main change in CN patients' life if the gene therapy is successful?
I think more freedom. Not having to turn on anymore phototherapy devices every night of your life to survive.

Do you think a psychological support for patients affected by a rare disease could be necessary?
I think it is really important, especially for children and teenagers. Often it is also necessary for adult patients, even if they usually say they don't need it.

Do you have any recommendations for people dealing with CN patients?
I can only say that communication is very important. To give as much information as possible, support the patients with a positive mood and always remember that a patient is not a number but a human being. Even if I didn't choose this situation, I have always tried to make the best of it and I think it has enriched all of our family members' lives. I have to thank the Italian CNS association because I've met great people through them. I have received help and I have given help back and this is wonderful.

*names have been changed

Dissemination highlights & upcoming events

Crigler-Najjar Day 2021
June 21, 2021

The International day of Crigler-Najjar, named "Crigler-Najjar Day" was created and launched by the French Crigler-Najjar Association (AFCN) in 2017. It is celebrated every year on June 21st. In the framework of this year's Crigler-Najjar Day, the French patient organisation involved in the CureCN project created a social media campaign that aims to raise awareness of the ultra-rare disease of Crigler-Najjar. To promote the Crigler-Najjar Day, everybody is invited to get involved: wear yellow and blue, take a picture and share it on any social media channel!

YELLOW is the color of the skin and eyes of Crigler-Najjar patients, of the sun which is good for them, and it is also the color of the sunflower, the symbol flower of the Crigler-Najjar patients. Like the sunflowers, the patients always turn towards light, whether natural (sun) or artificial (phototherapy). BLUE is the color of the light that keeps them alive. Crigler-Najjar patients have to sleep under an intense blue lamp every night.

Further information regarding the event can be found here.

Contact us

If you have any questions regarding the CureCN project or suggestions for our newsletter, feel free to get in touch! We are looking forward to receiving your feedback.

Coordination
Genethon, France
Gerald Perret
email

Management
EURICE – European Research and Project Office GmbH, Germany
Melanie Haupenthal
email

www.curecn.eu

Subscribe to our newsletter here.
To unsubscribe from this newsletter, please click here.

Privacy Policy

The CureCN project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 755225.