Linking
the Patient
and
Medical/ Science
Communities

ADVOCACY FOR
NEUROACANTHOCYTOSIS
PATIENTS

MEETING REPORT
July 2023

Thank you

To the organisers:

Dr Kevin Peikert
Prof Adrian Danek

To all our speakers:

Meet them in the report

To all attendees and everyone reading this report and helping spreading the word about our work!

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INTRODUCTION

VPS13 Forum is keeping the conversation going just as intended from the very first edition in 2021! The 14th edition on 31 July 2023 was a rather special one for us, the advocacy organisations. We shared the (virtual) stage with clinicians and researchers to show what we helped and will continue to help with "Linking the patient and the medical / science communities".

We were honoured to have **Professor Adrian Danek**, Emeritus Professor of Cognitive Neurology, Munich, who chaired the meeting attended by about 30 patients, family, carers, clinicians and researchers.

Adrian explained the connection between VPS13A syndrome (also known as Chorea-acanthocytosis) and XK syndrome (also known as McLeod Syndrome). The two conditions are extremely similar, with the difference being in the age of manifestation of the symptoms and the gender distribution:

- XK affects males (women are carriers) and it starts manifesting between age 40 to 50
- VPS13A affects both males and females and it starts manifesting between age 20 to 30.

The two conditions can often be mixed up due to their similarities and that indicated to the researchers that there might be a molecular link between them. Dr Jae-Sook Park, winner of the Glenn Irvine prize in 2020, was able to prove the link between XK (a protein found on human red blood cells) which is a 'partner' for the VPS13A gene. The loss of the VPS13A-XK complex is the basis of both diseases.

PATIENT ADVOCACY ORGANISATIONS

Retrospectively, the Advocacy for Neuroacanthocytosis Patients (NA Advocacy) took shape in the late 90's. **Ginger Irvine**, Co-Founder and Chair highlighted some milestones of the charity:

- Alex Irvine's patient journey (from first symptoms in 1995, the exams in the US & UK, the diagnosis in the UK in 1999) and meeting Professor Danek in 2001.
- participations in the international symposia (since 2002)
- charity's registration (2009)
- the funding contributions, grant calls and grants awarded and their impact
- the first Glenn Irvine Prize winner – Dr Jae-Sook Park, and
- how Neuroacanthocytosis Advocacy USA (NA Advocacy USA) was born in 2019.

Susan Wagner, Chair of the NA Advocacy USA highlighted its fruitful achievements:

- significant funding raised for relevant research
- USA patient survey, and
- partnership with Rare-X.

PATIENT VIEW

Patients and their family and / or carers were not present only in the audience. Few were also part of the presentation, kindly sharing their experiences about being involved in an advocacy organisation.

Bob Metzger, XK patient, explained how he was officially diagnosed through DNA sequencing after a journey of about two years without his condition being identified. Upon researching more about the ultra-rare condition, Bob came across the advocacy organisation. Through contacting us, he felt heard and understood, and was also able to extend contact to others affected by the same syndrome, which he found encouraging. The information resources from our website were also something Bob found useful. He particularly appreciated the opportunity to speak quite early on in his journey to Prof Ruth Walker, an experienced NA clinician. Bob also explained how he found it beneficial to be part of the Symposia since 2016 onwards, when the meeting in Ann Arbor, Michigan, USA welcomed patients along with the clinicians and researchers.

Bob explained the importance of being aware of the family medical history which may help along the diagnosis journey. He concluded that overall, it is useful to establish durable connections in the community and he values the information shared this way. He is looking forward to the 11th Symposium taking place in Homburg (Saar), Germany from 15 September 2023.

Joy Willard-Williford is family and carer to her husband, Mark, XK patient. She echoed the points already made by Bob. For Joy it was also extremely important to find a community and discover that one is not alone, especially as the ultra-rare status of conditions indicated there were so few people in the world. She also found the community

to be inspirational – how each person involved, whether patient, family member or carer, continues to support others.

Joy also highlighted the importance of advocacies keeping the focus on the future, on finding a cure as soon as possible. And that's why it's vital to keep all the communities involved in the efforts for researching new avenues and finding ways to fund these for the benefit of current and future generations.

She also mentioned how important it is to be put in contact with the right clinicians and researchers worldwide, how it can benefit to reach a correct diagnosis sooner and the subsequent steps after that. The education about the syndromes is vital and it is important that we continue to share it in lay language (through website, newsletter and media in general), but it's equally invaluable to have the support of the scientific community in disseminating this information.

Finally, Joy highlighted the advocacy organisations' efforts to ensure the privacy of everyone who comes in contact with us. We will not pass on to anyone any details shared with us, unless we are given permission to do so.

LAB RAT VIEW

Both Bob and Joy are Trustees of NA Advocacy USA. As is **Ricky Ditzel**, the speaker who shared his experience of becoming involved in an advocacy organisation from a scientist's perspective. His research focus is on neurodegenerative disorders and that led to him to being an advocate for brain and mental health.

He briefly presented the research project carried out at Mount Sinai School of Medicine under Professor Ruth Walker's guidance which looked at 11 tissue brain samples donated, out of which seven were from VPS13A patients. He underlined the gratitude to the donors and their families – without them the research project could not have been carried out.

There were two posters produced and presented at large neuropathology related events, which inspired other researchers working in associated diseases (e.g., Huntington's) to want to get involved. There is also a paper that has already been published and another one to be published in the August edition of the Movement Disorders Journal which talks about the findings meant to advance the genetics of the VPS13A and XK diseases.

Goals as scientist:

- advancing the science
- advancing the nomenclature to match the newest findings
- finding research funding from federal sources.

Goals as NA Advocacy USA Trustee:

- raise awareness and advocate for the diseases
- spread the word about what advocacies do
- get involved in fundraising efforts
- promote Rare-X database benefits.

CLINICIAN-RESEARCHER VIEW

The clinician – researcher view, one of the most complex aspects in the presentation was brought to our screens by Professor Danek and **Professor Ruth Walker** from Mount Sinai, New York. Professor Walker is a principal investigator for ongoing studies of VPS13A and XK brain tissue funded by NA Advocacy USA. She focused on three most important aspects:

- Diagnosis – the importance of having this confirmed, the significance of specific genetic results and the clinical setting.
- Clinical care – the importance of working with a neurologist with appropriate expertise or having one recommended. The importance of knowing and understanding the treatment options – what has or hasn't been tried and how it worked. The multi-disciplinary care is optimal.
- Research – the importance of the dissemination of novel information, the invaluable contribution achieved through brain donation, blood donation and other tissue samples for future studies.

Professor Danek spoke about the importance of clinical trial readiness and the patient data collection for a database accessible to researchers conducting clinical trials. There has been some work done in the past and the biggest issue appeared to be the incentivisation of the clinicians to share the date through such a platform.

Professor Walker also highlighted the importance of the relationships between the clinicians / researchers and the advocacy organisations:

- Research updates
- Medical accuracy of communications
- Professional comments on potential emerging therapies
- Connection to other (brain) diseases
- Input on funding requests.

LINKING IT ALL TOGETHER

Brain donation

Joy spoke about the importance of brain donation for scientific research as already mentioned by Ricky. It takes a lot of courage and vulnerability to proceed with tissue donations. In addition, the rare nature of the conditions makes this an even more challenging process.

In the USA, the most common option is to work with a brain bank and she provided example details about the arrangements made by her and Mark. It's important to work with reputable institutions (such as Mount Sinai Brain Bank in USA) and make sure that they are able to share the tissue when requested for relevant research. For the rest of the world, the principles would be similar and likely the neurologist in the care team would be in an acceptable position to make recommendations about the appropriate organisation(s).

Blood donation (XK patients only)

Joy explained that it's important for the XK patients to donate and bank their own blood in case a transfusion would be needed at some point. This is mainly because any other blood used in the transfusion (even if the right match for the usual parameters) can cause strong reactions. An XK patient can store blood for themselves, but also for other XK patients, should that be possible.

We are working to promote awareness about blood donations for XK patients. It will require some research of one's own, depending on where you are located, so please consider allocating some time to check with your local blood banks for the available options.

RARE-X database

Susan introduced RARE-X, a platform created to accelerate rare disease research, treatments and cure by removing barriers for data collection and sharing. To be noted - this is not a replacement for any current research or clinician-sponsored patient registries.

RARE-X has completed a merger with Global Genes this year, so they are now acknowledged together as one entity.

The official partnership with them is already established through the Community Page for McLeod (XK) Syndrome which is being set up and the VPS13A Community will follow soon. An important aspect of the community pages is that they are not exclusively in English, there are eight other languages available.

The input of the data is entirely patient driven and the patient, or their respective family or caregiver is in control at any point of the data being uploaded and shared.

The RARE-X benefits for the researchers:

- Free access for researchers on the data as shared by the patient
- Data is standardized
- Data is consented
- Input and sharing of data is global
- Curated genetic data from genetic reports where available
- Ability to do analysis in the cloud across diseases
- Can query based on genetics, symptoms or disease
- Federated data access & analysis platform (use data where it resides instead of having to migrate it locally or use different interface or platform).

Susan is a test user for herself as an XK carrier and on behalf of her brothers. Also, Bob is a test user. They are all contributing to building feedback about the process so that the advocacies can encourage and support the input into RARE-X of those interested in doing so.

Communications

Joy reminded those present about the NA News, which is a source of the latest information, as well as the social media presence. We are always interested to hear from patients, their families or carers who are willing to share stories. It can be in words, in images or any other creative way which would make sharing easier – just contact us. As mentioned before, these shared experiences can help someone else around the world by being inspiring or encouraging, and enable the sense of community that other patients said they had found useful.

Patient journey

The model below is based on a model for Huntington's disease which was developed by European Reference Network – Neurological Diseases (ERN-RND), the European Huntington Association and members of the Disease Group 'Chorea and Huntington's disease'. Thank you.

	First symptoms	Diagnosis	Treatment	Monitoring
Clinic	Complex symptoms Similar to other conditions	Genetic testing Genetic counselling (essential)	No disease modifying treatment Symptoms management Functionality management	Physical activity Supporting therapies Psychological wellbeing Nutrition
Challenges	First symptoms = onset Fear / Denial	Symptoms complexity Possible misdiagnosis	Multidisciplinary and holistic approach Long-term perspective	Continuous need to adjust
Goals	Educate clinicians Educate families on how to best cope and how to seek support	Accurate diagnosis Follow-up process Availability of information Support network	Connect the multidisciplinary teams	Build trusting relationships between: * Patients * Families * Clinicians

Professor Margit Burmeister, geneticist by career, was in attendance and she raised an aspect that wasn't covered in the presentation: the impediments in collaboration between organisations 'owning' the genetic materials / samples and the research institutions requesting access to those. The 'red tape' encountered in these instances causes unnecessary delays in the actual research process. It is likely that this usually comes because of legal reasons and arrangements made for the respective materials / samples.

Joy suggested from personal experience that in certain instances it may be possible to add one's own clauses in the legal documentation and clearly specify that an institution / entity isn't allowed to be proprietary with it when required for specific research purposes related to the syndromes. This will be something that the advocacies will investigate on how we can help and offer guidance for it.

Third party cooperation

	Patients / Advocacy	Research / Consultants	Pharmas	* Public health institutions / Funders
Value / Qualities	Have unique views of all aspects of the disease Informs research & pharma, i.e., how to prioritise needs Have samples for bio-research	Bring knowledge and experience of other research and patients Use patients on panels to plan research steps	Provide funding and previous successes Recognises power of coordination	Form the landscape of research and provide general guidance Provide funding
Challenges	Languages, access to healthcare / resources, paths to reach patients £ $ Euros! and guidance	Need patient stories and evidence of patient / advocacy input for grants Need feedback, "Burden of Illness Survey" for support	Policies / rules may not meet wide-enough cohort with one advocacy	Difficult to navigate the right paths for information and guidance
Future / Gold Standard	"Ask the patient" "Patient is the Expert" Ask as early as possible	Understand the 'real world' data, especially regarding medications Use lived experiences and numbers	New and evolving Proceed step-by-step to gain mutual benefit	Establish the appropriate contacts and develop trustworthy relationships Patient involvement is heard and considered

* This column and its content has been added after the meeting at Prof Danek's suggestion. NIH in US research guiding institution – form the landscape of research

Professor Danek concluded the meeting highlighting the importance of continuing the research work that's already been carried out. The researchers we heard today gave us reassurance through their enthusiasm and determination. We know that the research future is in capable hands, but the work in recruiting new forces, both in research and for the advocacy organsiations needs to continue!

11TH INTERNATIONAL SYMPOSIUM ON NEUROACANTHOCYTOSIS SYNDROMES

15 – 17 September 2023
Homburg (Saar), Germany

Registration - free until 31 August 2023: https://tickets.kwt-uni-saarland.de/IMNS2023/

NEXT VPS13 FORUM

Monday, 20 November 2023
The exact timings will be confirmed through the zoom invitation from the organisers.

Thank you!

ADVOCACY FOR NEUROACANTHOCYTOSIS PATIENTS

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