European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

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Webinar

"Treatment with empagliflozin in patients with glycogen storage disease type Ib"

15 September 2020 16:00-17:30 CEST

Background:
Recently two reports have been published about off-label experimental empagliflozin treatment in GSD Ib patients (PMID: 32294159 and PMID: 32838757). In addition, Nina's parents briefly mentioned their experiences in the 'View from inside' editorial (PMID: 32379349).

Target Audience:
Health care professionals and patients

The Aims of the Webinar are:
1. To inform about the treatment
2. To share experiences
3. To discuss next steps

Registration:
Register in advance for this webinar:
https://us02web.zoom.us/webinar/register/WN_Ee9CPmRNTlmiqJVMw9PXhg
After registering, you will receive a confirmation email containing information about joining the webinar.

Program:

16:00-16:15	Introduction	presented by Saskia Wortmann and Sarah Grünert
16:15-16:30	Patient experiences	presented by Enrique L. Contreras and Marta d'Agosto
16:30-17:00	Sharing experiences between colleagues	moderated by Terry Derks
17:00-17:30	Summary and discussion about next steps	all

If you have any information relevant for all the MetabERN members; please feel free to share it with Cinzia Maria Bellettato and/or Corine van Lingen.

MetabERN Calendar (meetings and important deadlines)

Meeting	Date	Who	Details	Contact person
Medical Executive Meeting (MEC)	10/09/2020	SNW+WP leaders + Patient Steering Committee		Coordination Office
Comment on the internal monitoring process	15/09/2020	All HCPs	See article below in this document	Coordination Office
Check the Activity report running from September 2019-July 2020 that was made by the Coordination Office based on the presentations from the SNW-specific TCs that took place in April-June	05/09/2020	SNW+WP leaders	See article below in this document	Coordination Office
Check the information for your WP and/or SNW in the Activity Report that was made for the period of May-August 2019.	05/09/2020	SNW+WP leaders	See article below in this document	Coordination Office
Input for the DCTEP in the form of concrete webinars	15/09/2020	SNW leaders	See article below in this document	Coordination Office + Francois Eyskens
Survey about Phenylketonuria (PKU) patients missed for diagnosis and/or	07/09/2020		See article below in this document	to a.m.j.van.wegberg@umcg.nl

missed for follow-up.				

Your attention is needed: MetabERN Continuous Monitoring and Quality Improvement System (CMQS)

The legal framework for European Reference Networks (ERNs) sets out the objectives, principles and criteria of the ERNs and their Members and defines the general implementation process including the assessment, approval and evaluation of performance. The legal basis for membership criteria can be found in Directive 2011/24/EU on the application of patients' rights in cross-border healthcare and the Commission Delegated Decision 2014/286/EU2.

Based on this legal background, **the ERN Continuous Monitoring and Quality Improvement System (ERN-CMQS) was developed by the ERN Continuous Monitoring Working Group and approved by the ERN BoMS4 in September 2018.** The system includes several sets of common and ERN-specific indicators that are being implemented over a period of several years.
Consequently, every ERN establishes its own rules of procedures for continuous monitoring, quality improvement and termination of membership in case of non-compliance.

For the purposes of monitoring we have set up the MetabERN CMQS. It consists of:

⇒ **The core set of 18 Indicators** (common to all ERNs) as mentioned above. The MetabERN Coordination Office (CO) adds the data to the European Commission Data Collection Platform. A MetabERN data collection database was established for data collection of some of the 18 indicators (http://data.metab.ern-net.eu/pass.php).

⇒ **A set of MetabERN-specific indicators;** these indicators collect additional data such as participation in surveys, MetabERN Board meetings and other indicators are collected by the CO.

Every year, an annual MetabERN CMQS Plan shall be established by the CO in cooperation with WP3-coordinator Birute Tumiene (Evaluation & Monitoring) and its members. The annual plan which will include a set of indicators, timelines and thresholds for compliance for Full Members and Affiliated Partners. The Plan shall be presented to and approved by a two-third majority vote by the MetabERN Board in a written procedure. Every MetabERN HCP has a mandatory obligation to collect and provide MetabERN CMQS monitoring data.

The whole procedure for non-compliance and termination of membership can be found here. We ask you to read it carefully and send us any comments or your non-agreement before 15/9/2020. **If no comments are made, we consider your silence as approval of the procedure.**

Second call for ERN Research Mobility Fellowship to come up soon!

As part of its educational activities, EJP RD runs a Research Mobility Fellowship Programme dedicated to young researchers in the European Reference Networks (ERNs). PhD students and medical doctors in training from ERN member and Affiliated Partner institutions can apply for funding of short-term (1 to 3 months) training visits at another ERN center outside their country of residence. The aim of the programme is to foster the acquisition of skills and knowledge relevant to rare disease research. Both clinical and translational research projects are eligible for funding.

The first round of applications has been concluded successfully in July 2020. Out of 16 applications received, the Scientific Evaluation Committee selected six outstanding applications by fellows from Belgium, Denmark, The Netherlands, Slovenia, Spain and the UK. The exchange visits will involve research units from the following ERNs: ERN-RND, EURO-NMD, ERKNet, eUROGEN, ERNICA and ERN-Eye.

All proposals were evaluated of the Scientific Evaluation Committee (SEC) composed of three WP17 leaders, three independent external scientific experts and one representative of the EJP RD office.

For the next programme call, EJP RD encourages junior physicians and PhD students to apply to this prestigious programme and add this exciting and unique experience to their professional education path and background.

This second call will open on 1st October 2020. All relevant information will be published on the EJP RD website https://www.ejprarediseases.org/

Message from the CPMS-Helpdesk

Dear MetabERN members,

I hope you are well and have had a pleasant summer.

I am sending this monthly friendly reminder to ask you to please take a minute to log on to the CPMS, unless you have done so, already, in the recent days.

This is to both ensure that your account remains active, and that you complete any eventual outstanding tasks in the system.

I also take this opportunity to welcome the many new MetabERN members and affiliates who registered their account in the CPMS over the summer, and to thank the new and old members who have been enrolling patients and actively participating in panels, as their work and contributions reflect very well on the project.

As usual, I remain at your disposal for platform assistance, and wish you all a beautiful day.

Anita

Anita Bressan, PhD
MetabERN
CPMS Helpdesk & Training
Mob. +39 331 45 366 25

MetabERN Interim Report

Dear All,

Please be aware we are reaching the half-way point of the 3-5 year period of MetabERNs existence which is on 31 August. This means that **we will need to submit the Periodic interim Report by end of October 2020** (60 days after the end of the reporting period). We will specifically involve all SNW and WP leaders in the writing process asking for a summary of the activities done in the different WPs during the reporting period (from 1st March 2019 to 31st August 2020) and the dissemination activities. To this last aim **All members** are asked to **update the following whole list of congresses/ conferences/ meetings** at which the ERN activities and results were presented via a dedicated slot in the programme/agenda, acknowledging the Network and including the ERN logo.

We kindly ask All SNW+WP leaders to:
1. Check the Activity report running from September 2019-July 2020 that was made by the Coordination Office based on the presentations from the SNW-specific TCs that took place in April-June and that replaced the cancelled Board meeting in April.
2. Check the information for your WP and/or SNW in the Activity Report that was made for the period of May-August 2019. For this period there is quite a lot of information missing from certain SNWs.

We kindly ask you to add any missing information and check the content of the two reports.

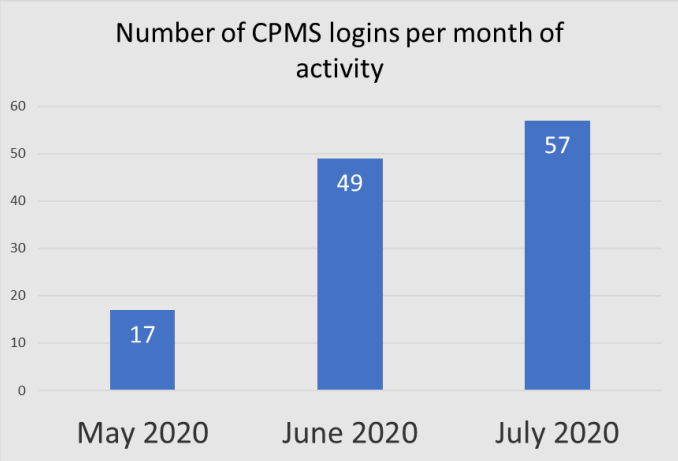
The deadline for both these actions is 15/9/2020

ERN CPMS/ECP Status Report July 2020

Dear All,

Please find here the **ERN status report for July 2020**. In this document, you will find a report for the activity of each ERN in European Collaborative Platform and Clinical Patient Management System (CPMS).

MetabERN Status Report July 2020



As you know since May 2020 MetabERN has a fully operational CPMS Helpdesk, leaded by Anita Bressan, that is providing CPMS training and helpdesk support to the centres. Thanks to the incredible efforts done by Anita in contacting the centres to assess their needs and supplying targeted personal assistance with the use of the CPMS platform the situation inside our network has rapidly improved and in July we had 57 logins, marking a 16% increase from June (49 logins), and a 235% increase compared to May (17 logins). 7 new users were registered (including 2 guests) and 7 old users were reactivated.

This is certainly a positive trend. In order for the CPMS to continue to perform well, we need to create a critical mass of platform-fluent users who regularly log on and participate in panels. Let me provide to you some examples.

In July, 5 panels were created: 1446, 1467, 1431, 1463 and 1432.

We thank those of you who have already actively participated in panels and look forward to supporting you in increasing MetabERN's CPMS activity over the coming months.

Commission publishes evaluation of the legislation on medicines for children and rare diseases

Today, the Commission published its report on the functioning of the **EU Regulations on orphan and paediatric medicines** (2000 - 2017). The evaluation found that both Regulations fostered the development and availability of medicines for patients with rare diseases and for children which have increased in recent years. They have also become available faster and have reached a higher number of patients in the Member States. Similarly, the evaluation indicates that the Regulation on medicines for children increased the number of clinical trials in children, which are essential to develop medicines for them. Nevertheless, both Regulations have not adequately managed to support development in all areas of rare and paediatric diseases where the need for medicines is greatest. The evaluation has also shown that authorised medicines for patients with rare diseases and for children are not equally accessible by patients across the EU. As a follow-up, and based on the outcome of the evaluation, the Commission will examine the impacts of possible future policy options to update the legal framework. The first step will be a preliminary impact assessment that the Commission will publish for public feedback this autumn. Any future solution will aim to address any identified shortcomings and foster patient-centred innovation as well as ensuring the availability of, and access to, medicines for patients with rare diseases and for children. These aspects are also key objectives of the Pharmaceutical Strategy for Europe.

More information:

- Evaluation of the medicines for rare diseases and children legislation
- Pharmaceutical strategy for Europe

Proposal for a transversal cross-ERNs Study Group on Pregnancy and Family planning in Rare, low prevalence and complex diseases

Dear All,
MetabERN is collaborating to this ERN ReCONNET project for the establishment of a ERN Transversal Working Group on Pregnancy and Family Planning. A preliminary call was held on July 6th to investigate the feasibility (see related report here). The next call will take place on 15th September at 14:30.

Each **ERN Coordinator can nominate up to 3 representatives of their ERN to be included in the WG** (one Representative, one ePAG and the ERN Coordinator – optional). If interested in being part of the WG and participate in the call please let us know.

You can find here (Sheet 2 of the excel file)a draft of the **possible topics that could be addressed during the cross-ERN workshop**. We would be thankful if you could please review them and add eventual topics you think that should be included in the workshop. Please prioritise the 3 topics that in your opinion are more close to the disease area of our MetabERN in this Excel file.

ERN Study Group on Paediatric Anaesthesia for Rare and Complex Diseases

Dear all,

The ERN formation in 2017 has developed in accordance with the proposed structure by the patient organisations and EU ERN Office with 24 fields of Medicine and there is no specific ERN for Anesthesia or Pediatric Anesthesia.

However, for specific medical aspects in the care of our patients ERN cross workgroups and action groups are currently developed.

For Pediatric Anesthesia a similar approach might be set up and we send you hereby a request for participation.

Each ERN Coordinator would need to nominate up to 3 representatives of their ERN to be included in the WG (one Representative, one ePAG and the ERN Coordinator – optional). If interested in being part of the WG please let us know.

FUTURE SCOPE OF THE STUDY GROUP ON PEDIATRIC ANESTHESIA FOR RARE AND COMPLEX DISEASES:

EU ERN Connections of experts in the field.
Involvement in the development of data collections through the ERN Registries.
Potential innovative research projects.
Audits, creation/revision of guidelines and clinical decision support tools.
Preoperative assessment, premedication, anaesthetic techniques, pain management, surgical procedures, postoperative care, postoperative pain scores, destination of patients within the hospital (PICU, day case surgery, general ward), level of satisfaction of patients and parents.

Prevalence and intensity of chronic pain in different categories of patients, diseases and surgical procedures.

RD patient pathways - what do they look like in your country?

Dear All, please see below the message from the coordinator of the ERN Lung.

Dear rare disease activist,

We (i.e. members of ERN-LUNG, the European Reference Network for Rare Diseases of the respiratory system, more info here: www.ern-lung.eu) are looking for help in a project about patient pathways of rare lung disease patients in different European countries. Our goal is to find out how patients are guided through the different levels of the resp. health care systems and what possibilities exist to detect patients with rare lung diseases earlier and achieve best possible care.
I am aware that by sending this email to different people active in the field of rare diseases, not only to doctors and patients, there will be some who will not be able to contribute too much. But, in that case, it would be kind if you forwarded this email to doctors and patients you know in as many European countries as possible. I am optimistic that - with your help - we will be able to draw an informative picture of what the patient pathways look like in the Member States of the European Union.

As a simple start, we would welcome answers to a few quick questions – please, copy the following questions and together with your YES or NO answers send them back to us. If you find the questions ambiguous or inconclusive, please see also the attached graphics, where we tried to give a more detailed look on how we think a patient's way through a health care system might work in broad terms.

After visiting their general practitioner, we assume that a patient with a presumed rare disease of the respiratory system usually/typically is referred to a specialist.
We are looking at this first step...

Your country:_____ (please state)
(if more tha one option is true, feel free to state "yes" in more than one scenario)

In your country, is this specialist typically a local practicing pulmonologist (in private office)?
In your country, is this specialist typically a respiratory consultant at a local/regional hospital?
In your country, is the patient usually referred to a practicing local pulmonologist with specific expertise in the field of the suspected disease?
In your country, is the patient typically referred to a hospital-based respiratory expert centre?
In your country, is the patient free to visit a specialist or specialized center without referral from their GP if they want to?
If none of the local specialists and/or experts can help the patient, are there provisions of referring them to a national or international specialized center?

Your answers to these questions would be greatly appreciated and would be the first step to a deeper analysis of this important topic. If you are willing to answer, please send your answers as a response to this email **until August 31st, 2020**. We would of course be happy to inform all those who responded about the results.
If you are interested in this project, we are happy to invite you to become a member of our international project team (and the paper writing committee?).

Thank you in advance for your participation.
Best regards
Thomas Wagner

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Tel.: 069 6301 87899

Surveys to be completed

SURVEY	LINK TO THE SURVEY	AIM	DETAILS
This survey is part of the activity of the MetabERN	https://www.surveymonkey.com/r/B29NWB6	Following our previous surveys this survey is aimed at understanding the effects of SARS-	This survey is part of the activity of the MetabERN

Work Package 8		CoV-2 (COVID-19) on patients with existing IMDs. The final goal is to write a paper on the prevalences of infection / disease expression / complications/management in patients with IMDs compared to the general population.	**Work Package 6**

Reminder Your input is needed: Webinars for the Education programme (DCTEP)

Dear Subnetwork Coordinators, dear all,

Françoixs Eyskens and the Coordination Office have been working hard on the **Diagnostic, Clinical & Therapeutic Education Programme (DCTEP),** which was sent to all the MetabERN members for comments in the last Monthly message.

We are now at the stage that we are asking you for very concrete input for the Webinars that are part of the programme. We invite you to have a look at the whole programme and also at the script of the webinars.

We are asking you to provide us with the following input:

1. Per Subnetworks (depending of the size of the Subnetwork-coverage) 1-3 webinars for the knowledge domain of Pathophysiology and biochemistry, with a link to the clinical aspects where possible or desirable. This should be preferably put in the form of a Powerpoint. We will then assess the outline and adjust it to our format in order to achieve harmonisation. We will not change the scientific content which remains your intellectual property.

2. We would also very much like to receive **any other information and/or content related to the topics/knowledge domains** mentioned which is maybe already available as presentations, parts of a medical course, webinars, publications, etc.

The deadline to send in the information/content was the 1st of July in order to keep pace with the time schedule. This deadline has been extended due to the fact that we did not actually receive any specific content. **The new deadline is 15/9/2020.**

MetabERN and ERNDIM EQA Schemes

By the Coordination Office

Dear All, we would like to inform you that it is our intention to display on our MetabERN website the list of the HCPs participating in the ERNDIM EQA Schemes (we got this information directly from you and your labs quite a while ago). We hope you agree with the displaying the state of your ERNDIM participation. If not please send us an e-mail. Many thanks

C4C Collaborations: FDA Consultation Response & The Rare Disease Consortium Guidebook- FOR INFORMATION

FDA Consultation Response

Firstly, jointly with the European Rare Disease community, c4c submitted a shared response to the FDA consultation about a global clinical trials network in rare diseases. On May 29th this year, the FDA opened a consultation to obtain information and comments from patients, patient advocates, the scientific community, health professionals, other regulatory and health authorities in the global community, regulated industry, and the general public regarding practical steps and successful approaches to establish a global rare disease clinical trials network. c4c convened representatives of the European Rare Disease and Paediatric clinical trial communities who developed a shared response to the questions raised by the FDA. The group includes the European Reference Networks, The European Joint Programme for Rare Diseases, EURORDIS and c4c. The submission emphasizes the importance of a multi-stakeholder approach when creating such networks and of including European initiatives in a global clinical trials network. The submission can be read here: https://beta.regulations.gov/document/FDA-2020-N-0837-0044

In addition, the FDA in collaboration with the University of Maryland Center of Excellence in Regulatory Science and Innovation will host a two-day **virtual public** workshop entitled **"Pediatric Dose Selection"** on **October 22** (10 AM- 3 PM ET) and **October 23** (10 AM – 12.30 PM ET) to discuss the present state of dose selection and how it pertains to pediatric drug development. The workshop aims to review the current methods used to determine the pediatric dose and address ways to overcome dose selection challenges seen in pediatric drug development.
Information about this event, including details about registration and an agenda, is available at: https://www.pharmacy.umaryland.edu/centers/cersievents/pedsdoseselection/.
To register, please visit: https://www.eventbrite.com/e/pediatric-dose-selection-tickets-107974167642.
This workshop is intended for clinicians, drug developers, and regulators. If you have any additional questions about this workshop, please contact cersi@umd.edu.

The Rare Disease Consortium Guidebook

The International Rare Diseases Research Consortium (IRDiRC) has drafted a Guidebook to navigate and optimally use tools for drug development for rare diseases existing in the USA, Japan and Europe, c4c featuring as one of the 'building blocks' for development - its role is described here.

A taskforce for the Guidebook mapped 110 building blocks available to orphan drug developers to create concise factsheets for each supportive tool. The taskforce selected the most relevant building blocks and defined their optimal use during rare disease drug development, placing them into a milestone-based drug development framework. In this way, the Guidebook will reduce delays in developing drug development by enhancing the use of available tools that will also reduce risks and costs, and improve patient and regulatory acceptability.

Survey about Phenylketonuria (PKU) patients missed for diagnosis and/or missed for follow-up.

Dear colleague,

We would kindly ask you to participate in this short survey which will take you approximately 5 minutes.
This survey is about Phenylketonuria (PKU) patients missed for diagnosis and/or missed for follow-up. Even though newborn screening programs (NBS) for PKU have been successfully implemented in many countries for over 50 years, there are still late diagnosed and untreated PKU patients. Reasons for this can be the lack of NBS or NBS failures, but also due to immigration of patients from countries without NBS or treatment. With this survey we would like to explore how frequent this occurs.

By contributing to this survey, you can be a co-author when the results of these survey are published.

The data we collect will be processed anonymously. This survey does not process any personal data from your patients.

Link to the survey:
https://rug.eu.qualtrics.com/jfe/form/SV_ehBHPcildC57gY5

Feel free to share the link with your network and colleagues.
Any questions regarding this survey can be sent to **a.m.j.van.wegberg@umcg.nl**
The deadline for the survey is 7/09/2020

Webinar "Treatment with empagliflozin in patients with glycogen storage disease type Ib"

Webinar

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16:30-17:00	Sharing experiences between colleagues	moderated by Terry Derks
17:00-17:30	Summary and discussion about next steps	all

Acknowledgements policy

In order for publications to be counted towards as output for us as a network, the authors need to specifically acknowledge MetabERN. This means not just putting the MetabERN name behind their author information (as we have noticed has happened a couple of times) but to really mention our network in a specific way. We have drafted three formulations for the acknowledgements that can be used by you in your publications. The formulation will also be used by other ERNs.

Acknowledgement MetabERN	**Situation**
1. " The/One of the/Several author(s) of this publication is/are (a) member(s) of the European Reference Network for Rare Hereditary Metabolic Disorders (MetabERN) - Project ID No 739543."	A general option that members can use regardless of there being 2 or more HCPS involved. This gives attention to the existence of MetabERN without it acknowledging any direct input from it.
2. "This work was generated within the European Reference Network for Rare Hereditary Metabolic Disorders (MetabERN)	An option that an HCP can choose to add if the work has come into being by the efforts carried out by at least 2 or more MetabERN members from 2 different Member States 1 working within the structure of the network (WP/SNW).

[1] This aligns the formulation with the current definition used in continuous monitoring objective 5.2 for ERNs.

3. "This study/project/publication/Guidelines/survey* has been supported by MetabERN. MetabERN is co-funded by the European Union within the framework of the Third Health Programme "ERN-2016 - Framework Partnership Agreement 2017-2021." *Choose appropriate wording	If funding is allocated to a publication/ project.