Endo-ERN
European Reference Network on Rare Endocrine Conditions

European Reference Networks

Adrenal MTG1


Nicole Reisch


Svetlana Lajic


Johan Beun


Jette Kristensen


Manuela Brösamle

+ new ePAGs: Allessandro Lazzerini + Giorgio Dalmaso

On-going activities

- **Survey on the use of prenatal Dex across Europe –** publication accepted in EJE

Hanna Nowotny, Oliver Blankenstein, Uta Neumann, Faisal Ahmed, Stephanie Allen Federico Baronio, Tadej Battelino, Jérôme Bertherat, Marco Bonomi, Aude Brac de la Perrière, Véronique Tardy-Guidollet, Rita Menassa, Sara Brucker, Marco Cappa, Philippe Chanson, Claire Bouvattier, Annamaria Colao, Martine Cools, Justin Davies, Wiebke K. Fenske, Ezio Ghigo, Claus H. Gravholt, Angela Huebner, Eystein Sverre Husebye, Anders Juul, Florian Kiefer, Juliane Léger, Gesine Meyer, Leonidas A. Phylactou, Julia Rohayem, Gianni Russo, Carla Scaroni, Philippe Touraine, Nicole Unger, Hedi L. Claahsen-van der Grinten, Jarmila Vojtková, Diego Yeste, Helmut-Günther Dörr, Svetlana Lajic, Nicole Reisch.

Prenatal dexamethasone treatment for classic 21 hydroxylase deficiency in Europe. Eur J Endo. Accepted for publication, Dec 2021.

- **PREDICT study:** European, prospective, randomised, double-blind clinical trial on prenatal therapy (currently used experimental dose of 20µg/kg/d vs low dose) -> positively evaluated at BMBF (German National Ministry of Education and Research). Start 2022, delayed due to pandemic.

- Improve and increase the info on the EndoERN/MTG1 webpage – info material for patients, publications of general interest.
  - HCPs need to send information if they want something on the web-page
  - Volunteers for taking care of the web-page?

- New survey on the availability of medication for adrenal insufficiency accross Europe.

  Will be sent to HCPs of EndoERN and patient organisations within a few weeks.

- We need to plan new webinars. Suggestions for topics?
- New CPMS sessions.
- Suggestions for other activities?
- ePAG activities?

[MTG2/Ca-P]

Agnès Linglart

Lars Rejnmark

Martha Kirchhoff

ePAG

European Reference Network

[1- Guidelines]

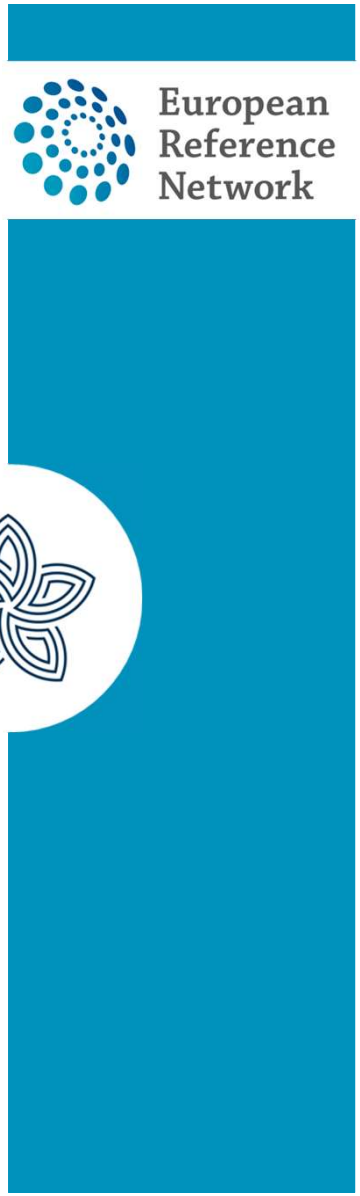
endo ERN + BOND + ESPE + ESE

PARAT program activities 2020–2021 supported by the European Society of Endocrinology (ESE)

Bollerslev J, Rejnmark L, Zahn A, Heck A, Appelman-Dijkstra NM, Cardoso L, Hannan FM, Cetani F, Sikjær T, Formenti AM, Björnsdottir S, Schalin-Jantti C, Belaya Z, Gibb FW, Lapauw B, Amrein K, Wicke C, Grasemann C, Krebs M, Ryhänen EM, Makay O, Minisola S, Gaujoux S, Bertocchio JP, Hassan-Smith ZK, Linglart A, Winter EM, Kollmann M, Zmierczak HG, Tsourdi E, Pilz S, Siggelkow H, Gittoes NJ, Marcocci C, Kamenicky P. European Expert Consensus on Practical Management of Specific Aspects of Parathyroid Disorders in Adults and in Pregnancy: Recommendations of the ESE Educational Program of Parathyroid Disorders. Eur J Endocrinol. 2021 Dec 1;186(2):R33–63. doi: 10.1530/EJE-21-1044.

ESCEO activities

Andrea Trombetti; Nasser Al-Daghri; Maria Luisa Brandi; Jorge B. Cannata-Andía; Etienne Cavalier; Manju Chandran; Catherine Chaussain; Lucia Cipullo; Cyrus Cooper; Dieter Haffner; Pol Harvengt; Nicholas C. Harvey; Muhammad Kassim Javaid; Famida Jiwa; John A. Kanis; Andrea Laslop; Michaël R Laurent; Agnès Linglart; Andréa Marques; Gabriel T. Mindler; Salvatore Minisola; María Concepción Prieto Yerro; Mario Miguel Rosa; Lothar Seefried; Mila Vlaskovska; María Belén Zanchetta; René Rizzoli. Interdisciplinary management of FGF23-related phosphate wasting syndromes: a consensus statement on X-linked hypophosphatemia. Nature Reviews Endocrinology, in press



[2- Dissemination]

EndoERN Symposium @ ECE

EndoERN Symposium @ ESPE

[3- Registries]

European Reference Network

= involvment in = Participation to
Unique registry for bone and ca&P disorders

EuRR-Bone European Registries for Rare Bone and Mineral Conditions

EuRRECa European Registries For Rare Endocrine Conditions

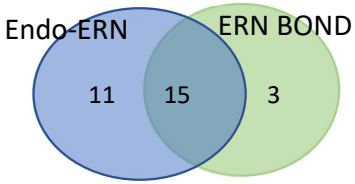
ERN BOND EUROPEAN REFERENCE NETWORK ON RARE BONE DISEASES

Endo-ERN

Country	Centers	Country	Centers
Austria	2	Israel	1
Belgium	5	Italy	9
Croatia	1	Latvia	1
Czech Republic	1	Lithuania	1
Estonia	1	Netherlands	3
Finland	1	Romania	1
France	1	Spain	3
Germany	7	Sweden	1
Hungary	1	United Kingdom	4

Table 1. Number of active reporting centres per country

Reporting centres e-REC
April 2020– December 2021



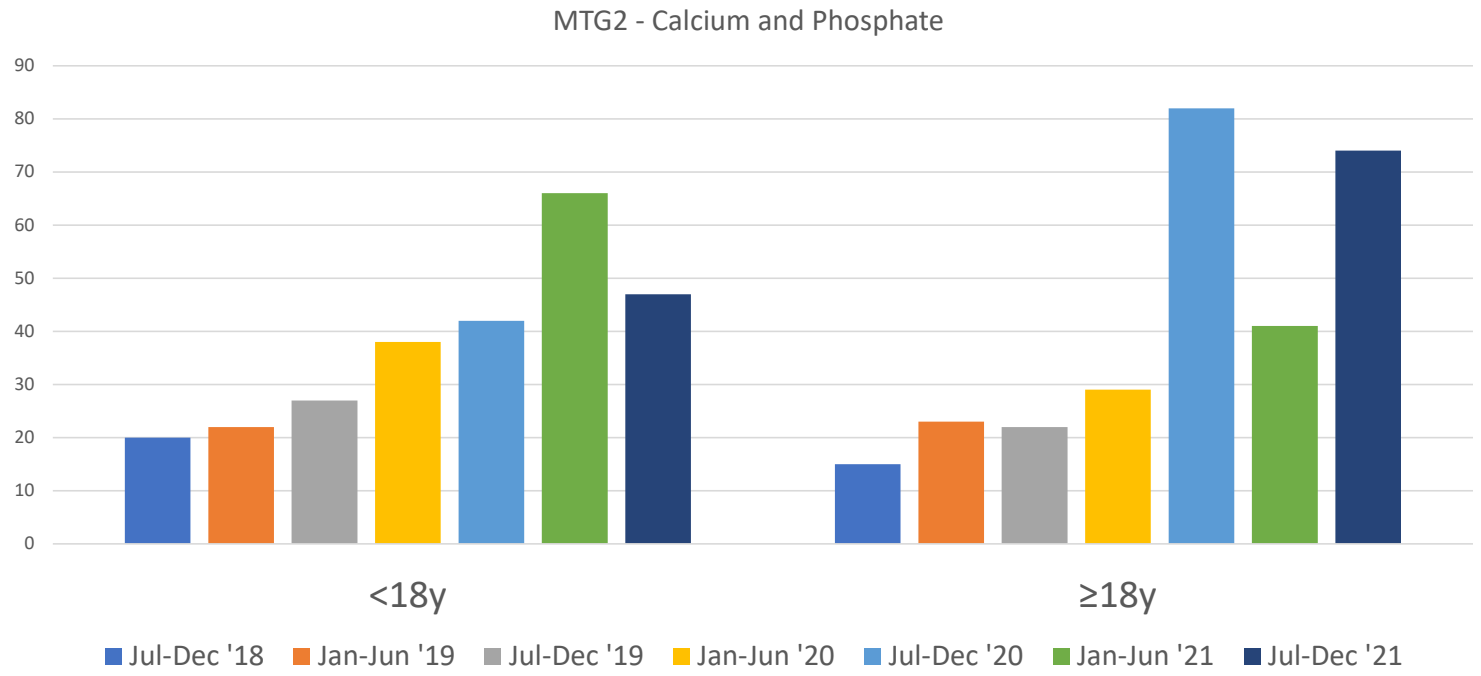
14 Non-ERN members and ERN affiliated partners

Fig.1 - Reporting centers and affiliation to Endo-ERN and ERN-BOND.

Courtesy of N. Appelman

Conditions reported e-REC, Jul18 to Dec 21

EuRR-Bone
European Registries for Rare Bone and Mineral Conditions



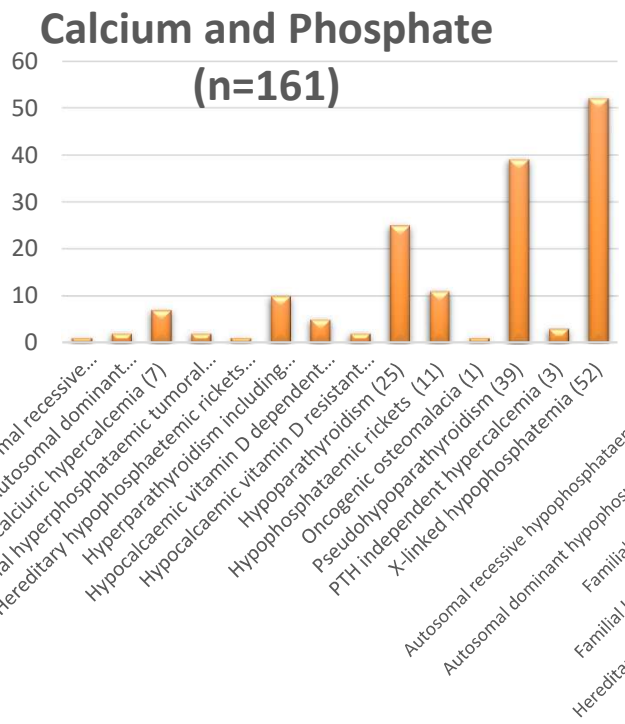
Courtesy of . Bryce and F. Ahmed

Conditions reported e-REC, Apr20 to Dec 21

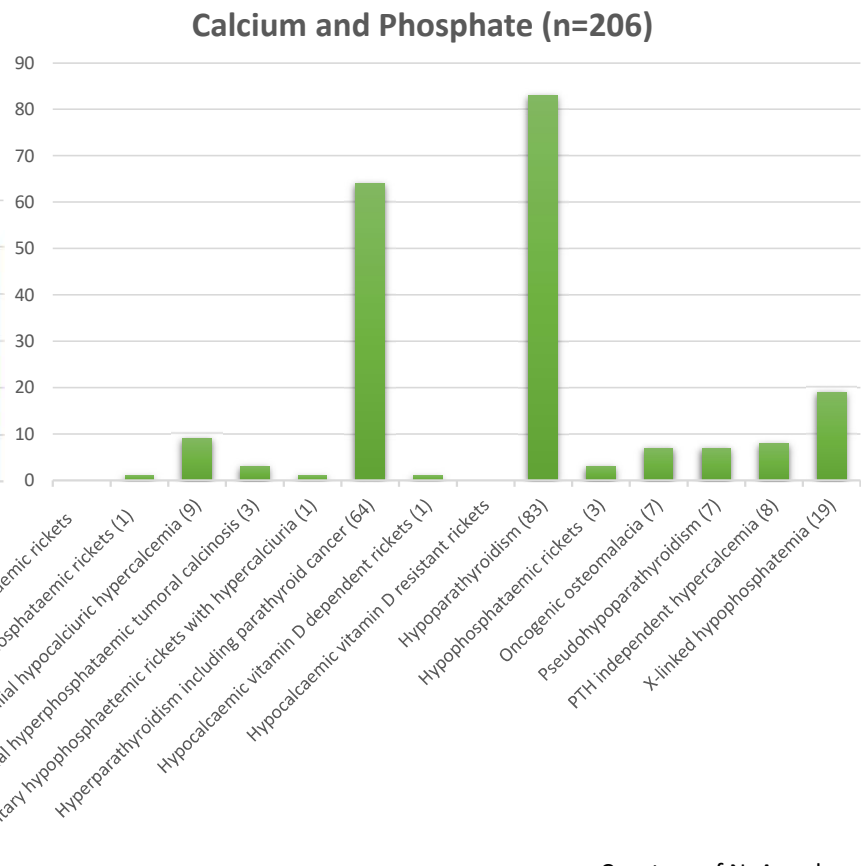
EuRR-Bone
European Registries for Rare Bone and Mineral Conditions

Fig. 5,6 – Specific diagnosis reported from April 2020 to December 2021

<18 years



>18 years



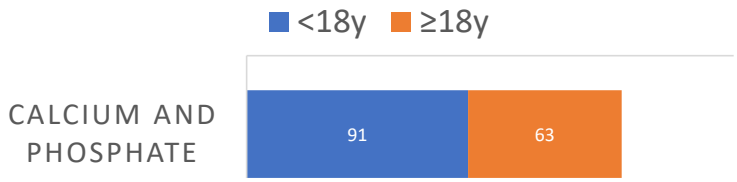
Courtesy of N. Appelman

Core Registry registered conditions

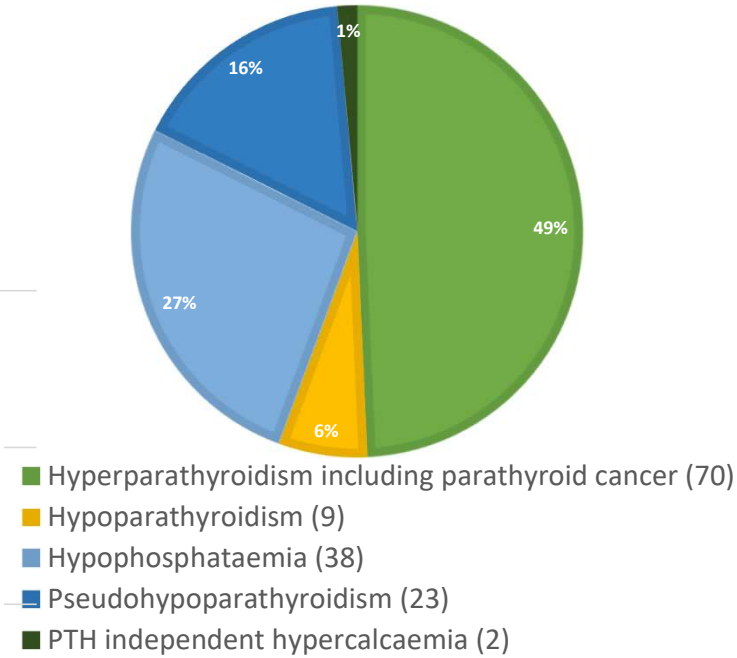
EuRR-Bone
European Registries for Rare Bone and Mineral Conditions

13 centres from 10 countries
154 patients

CONDITION GROUPS AND AGE



CALCIUM AND POSPHATE - PRIMARY CONDITION (N=154)



Expert Working Group 1 – Ca & PO

- **Team**

Agnès Linglart (EWG deputy)	Paris, FR
Lars Rejnmark (E co-WG deputy)	**Aarhus, DK**
Anne-Sophie Lambert	Paris, FR
Arnaud Peramo	Paris, FR
Guillemette Devernois	**Paris, FR**
Justin Davies	Southampton, UK
Susanne Thiele	Luebeck, DE
Wolfgang Holger	Linz, AU
Gabriele Hausler	Vienna, AU
Alexandra Ertl	Vienna, AU
Kassim Javaid	**UK**
Corinna Grasemann	Essen, DE
Carola Zillikens	**Rotterdam, NL**
Natasha Appelman-Dijkstra	**Leiden, NL**
Hans Zmierczak	BE
Karine Briot	**Paris, FR**
Ralf Oheim	**Hamburg, DE**

Regular Financial meetings @ local institution
AL + IN + Thibaut Vanrietvelde
Chargé d'affaires européennes – APHP
~ 15k€ available to facilitate the project

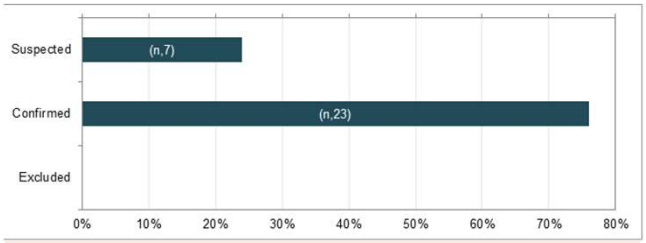
The project '777215 / EuRRECa' has received funding from the European Union's Health Programme (2014-2020) and is part of the project '946831 / EuRR-Bone' which has received funding from the European Union's Health Programme (2020-2023).

1st step: use data from e-REC and Core Registry/ Surveys

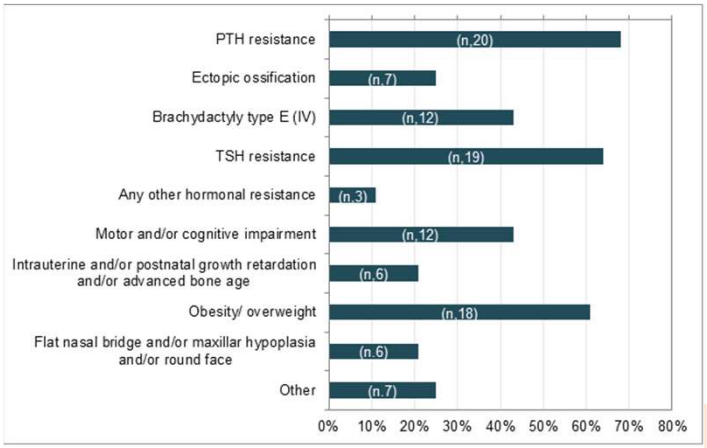
Surveys conducted by the EuRRECa office at 2 time-points August 2020 and March 2021

Data on reported data on iPPSD cases from July 2018 to August 2020

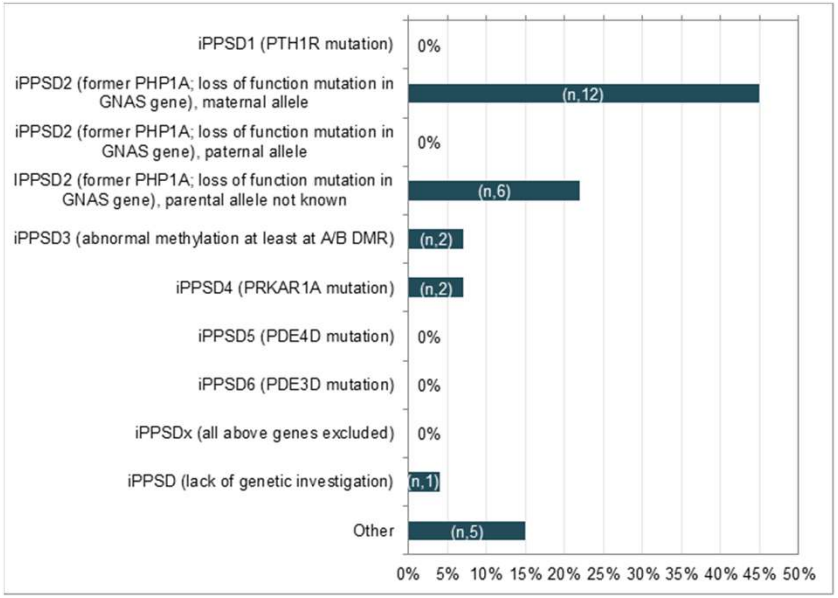
- Feedback on 30/39 reported cases (77%)
- Respondents: 80%
- 13/15 centres (87%)



30 cases of iPPSD in EuRRECa/ *76% of genetic confirmation*



Important data on the major and minor diagnostic criteria



Overview of reported pathologies

EuRRECa Surveys Inactivating PTH/PTHrP signaling disorder (*iPPSD)/PTH resistance*

iPPSD Survey team - Agnes Linglart, Alexandra Ertl
EuRRECa Project Team - Salma Ali, Jillian Bryce, Faisal Ahmed

Findings

- 77% of iPPSD cases for whom e-REC IDs responded positive to the survey
- 76% of cases had a confirmed diagnosis of iPPSD
- Clinical, biochemical and/or genetic analysis were the most commonly performed tests to obtain or exclude a diagnosis
- PTH and TSH resistance: most common diagnostic findings (>50%)
- The vast majority of genetically confirmed cases: loss of function mutation in the GNAS gene

Audio ePoster at e-ECE 2021, online from 22-26 May 2021

Ana Luisa Priego Zurita, Jillian Bryce, Salma Rashid Ali, Diana-Alexandra Ertl, Corinna Grasemann, Gabriele Haeusler, Lars Rejnmark, Faisal Ahmed, Natasha Appelman-Dijkstra & Agnès Linglart

Submission number: 1441

Title: European Registries for Rare Endocrine Conditions (EuRRECa): the Use of an e-Reporting Tool for Registering Calcium and Phosphate Conditions.

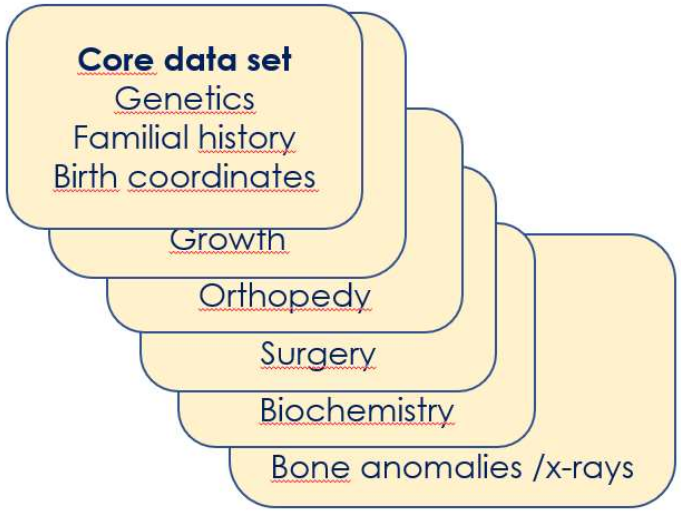
- **Developpement of the iPPSD disease specific module**
  - Step 2: Implementation of the new classification

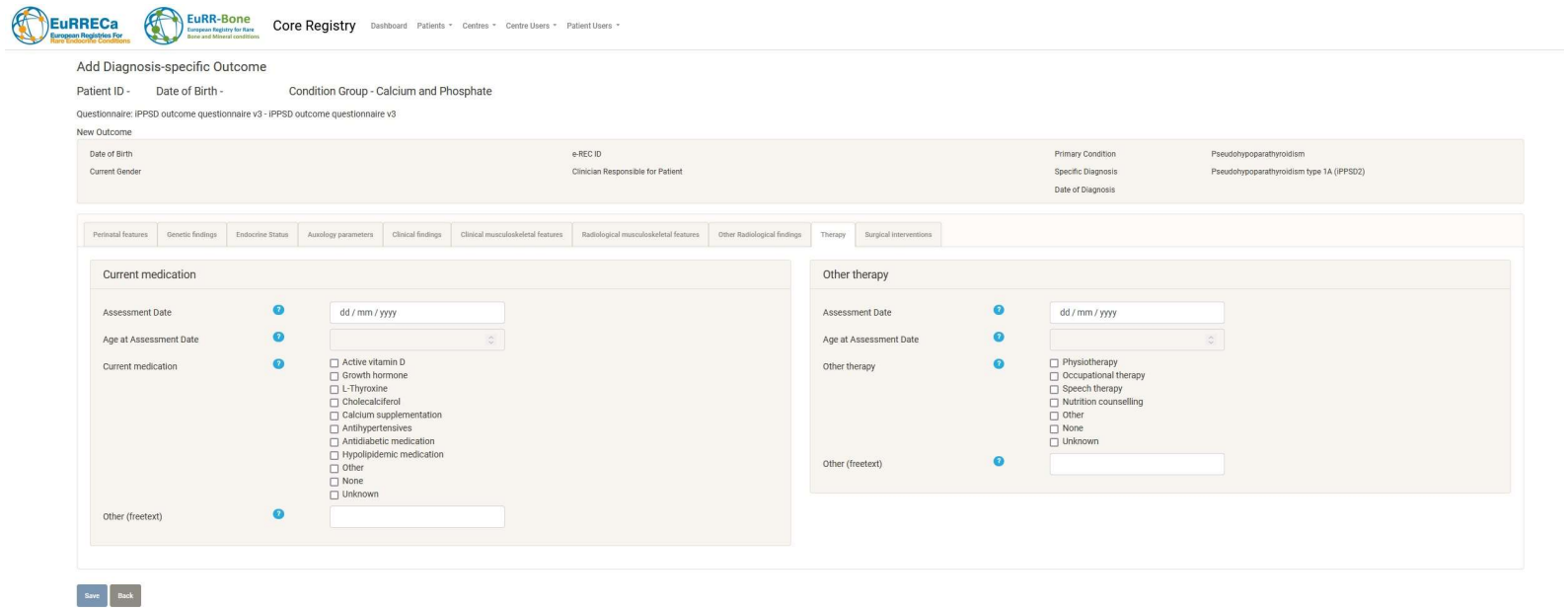
    Declaration to ORPHANET → pending

  - Step 3: generate condition specific modules for longitudinal data collection for iPPSD

Team: A. Linglart, A. Ertl, G. Peres de Nanclares, G. Mantovani

*Several meetings with the Glasgow team: **Jillian Bryce, Faisal Ahmed**
*Co-work with **EuRR-Bone Registry: Natasha Appelman-Dijkstra, Ana Luisa Priego Zurita**




EuRRECa
European Registries For Rare Endocrine Conditions
EuRR-Bone
European Registry for Rare Bone and Mineral conditions
Core Registry
Dashboard
Patients
Centres
Centre Users
Patient Users
Add Diagnosis-specific Outcome
Patient ID -
Date of Birth -
Condition Group - Calcium and Phosphate
Questionnaire: iPPSD outcome questionnaire v3 - iPPSD outcome questionnaire v3
New Outcome
Date of Birth
Current Gender
e-REC ID
Clinician Responsible for Patient
Primary Condition
Pseudohypoparathyroidism
Specific Diagnosis
Pseudohypoparathyroidism type 1A (iPPSD2)
Date of Diagnosis
Perinatal features
Genetic findings
Endocrine Status
Auxology parameters
Clinical findings
Clinical musculoskeletal features
Radiological musculoskeletal features
Other Radiological findings
Therapy
Surgical interventions
Current medication
Assessment Date
dd / mm / yyyy
Age at Assessment Date
Current medication
Active vitamin D
Growth hormone
L-Thyroxine
Cholecalciferol
Calcium supplementation
Antihypertensives
Antidiabetic medication
Hypolipidemic medication
Other
None
Unknown
Other (freetext)
Other therapy
Assessment Date
dd / mm / yyyy
Age at Assessment Date
Other therapy
Physiotherapy
Occupational therapy
Speech therapy
Nutrition counselling
Other
None
Unknown
Other (freetext)
Save
Back

EuRRECa 4th Annual Meeting – 14th February 2022

Inactivating PTH/PTHrP signaling disorder (*iPPSD)/PTH resistance*

We kindly invite you to join and share you data!

Thank you!

Disease-specific module – HypoP

EuRR-Bone
European Registries for Rare Bone and Mineral Conditions

The working team

A. Ertl
A. Raimann
G. Hauesler
R. Oheim
K. Briot
ML Brandi
C. Zillikens
J. Bauer
C. Grassemann
O. Nilsson
P. Kamenicky
G. Mindler
F. Ahmed
N. Appelman
A. Priego
J. Bryce

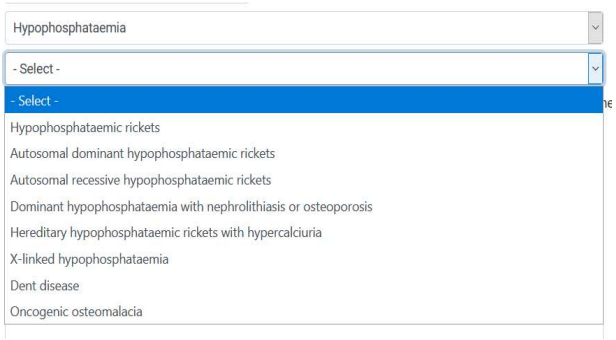
Send an e-mail to agnes.linglart@aphp.fr

Approx 1 hour meetings every 6 weeks
Review of the google sheet or registry
Implementation of the registry and patient's test

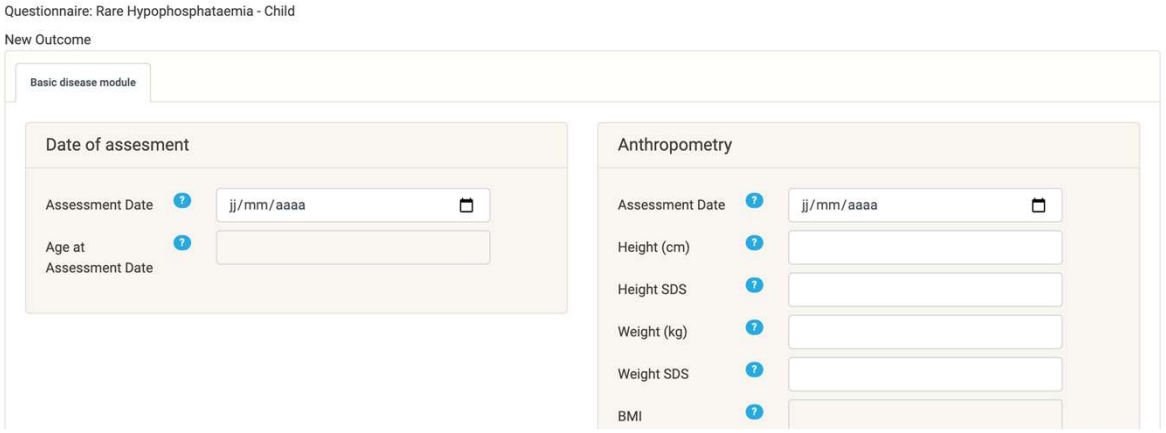
Disease-specific module – HypoP

EuRR-Bone
European Registries for Rare Bone and Mineral Conditions

- List of disorders



- Basic module



Disease-specific module – HypoP

EuRR-Bone
European Registries for Rare Bone and Mineral Conditions

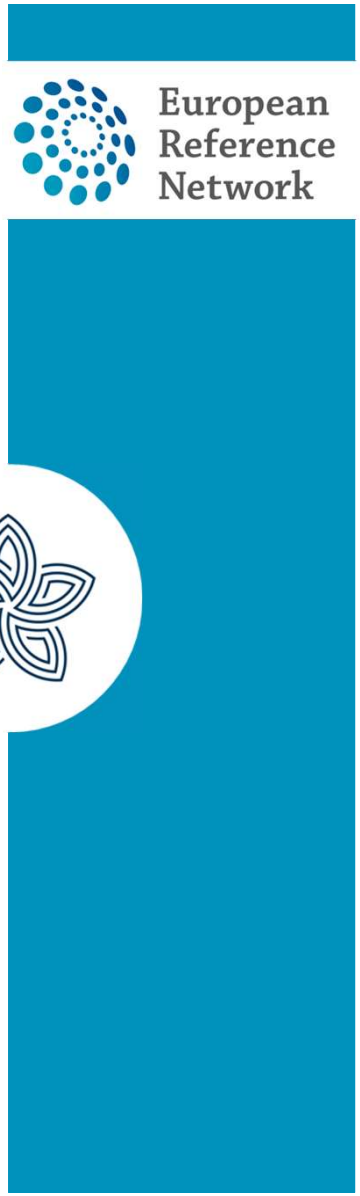
- Specific sub-modules
  - ADULT/PEDIATRICS
  - Auxology; musculoskeletal, dental, neurosurgery, orthopedic,
  - Rheumatologic ; biochemistry, genetics

- To be implemented: patients reported outcomes

[4- CPMS meetings]

Common to BOND

8 patients in 2021
2 in 2022



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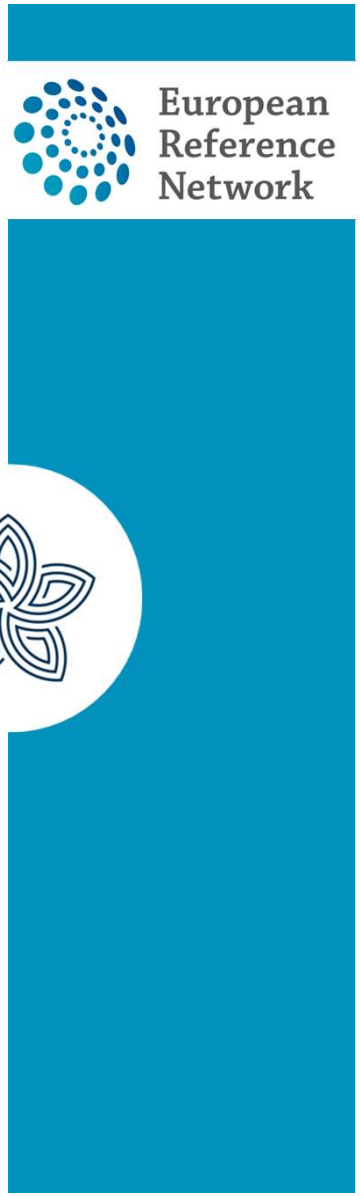
Next MTG2 meeting

13th April, 4pm CET
On zoom



THANK YOU

Endo-ERN

European Reference Network on Rare Endocrine Conditions

Genetic Disorders of Glucose and Insulin Homeostasis

MTG 3

Monday Feb 15, 2022

Prof. Dr. Thomas Danne
Hannover, Germany
Pediatric

Prof. Pietro Maffei
Padova, Italy.
Adult

Valeria Corradin
Mason Vicentino, Italy
ePAG representative
AILIP (Ass.ne Italiana Lipodistrofia)

Dr. Katharina Klee,
Hannover, Germany
Coordinator

European Commission | Endo-ERN is a European Reference Network co-funded by the European Union's Health Programme under grant agreement No 739572

European Reference Network

Adding a new ePAG Member still pending

Diese Nachricht wurde mit der Wichtigkeit "Hoch" gesendet.

Von: Klee, Katharina, Dr., Päd.III
An: 'Anne-Laure Aslanian'
Cc: Pietro Maffei; Danne,Thomas, Prof. Dr. CA Pädiatrie III
Betreff: WG: French Wolfram Association - ePAG member for ENDO ERN

Gesendet: Mo 14.02.2022 09:01

Hi Anne-Laure,

This organization wants to become an ePAG member of Endo-ERN MTG3. Can you add this organization to the ePAG group?
French Wolfram Association
Nolwen LE FLOCH
Présidente de l'Association du Syndrome de Wolfram
https://www.association-du-syndrome-de-wolfram.org/

If Nolwen is interested, he can become a ePAG representative for our group MTG3. There is a special process for this: https://endo-ern.eu/patients/how-to-become-an-endo-ern-patient-representative/

As soon as Anne-Laure has added the organization as ePAG member, I can officially ask him to become ePAG representative, if you agree.

Kind regards,
Katharina

Work in progress…

HORIZON-HLTH-2022-DISEASE-06-04-two-stage: Development of new effective therapies for rare diseases

Specific conditions	
Expected EU contribution per project	The EU estimates that an EU contribution of around EUR 8.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 60.00 million.
Type of Action	Research and Innovation Actions

Call: HORIZON-HLTH-2022-DISEASE-06-two-stage

(Tackling diseases (Two Stage - 2022))

Topic: HORIZON-HLTH-2022-DISEASE-06-04-two-stage

Type of action: HORIZON-RIA

Type of Model Grant Agreement: HORIZON Action Grant Budget-Based

Proposal number: 101080948-1

Proposal acronym: REDIRECT

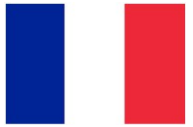
REDIRECT: REPURPOSING DRUGS FOR NEW EFFECTIVE THERAPIES IN RARE MONOGENIC DIABETES

List of participants

Participant No. *	Participant organisation name	Country
1 (Coordinator)	University of Padua	Italy
2	ALMS Therapeutics	France
3	Azienda Ospedale-Università Padova	Italy
4	University of Lisbon	Portugal
5	Hannoversche Kinderheilanstalt	Germany
6	University of Birmigham	UK
7	University of Vigo	Spain
8	Institut National de la Sante Et de la Recherche Medicale	France
9 Affiliated entity to 8	University of Strasbourg	France

Thomas Danne

Vincent Marion



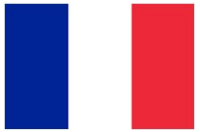
Tim Barrett

Monica Mazzucato

Diana Valverde

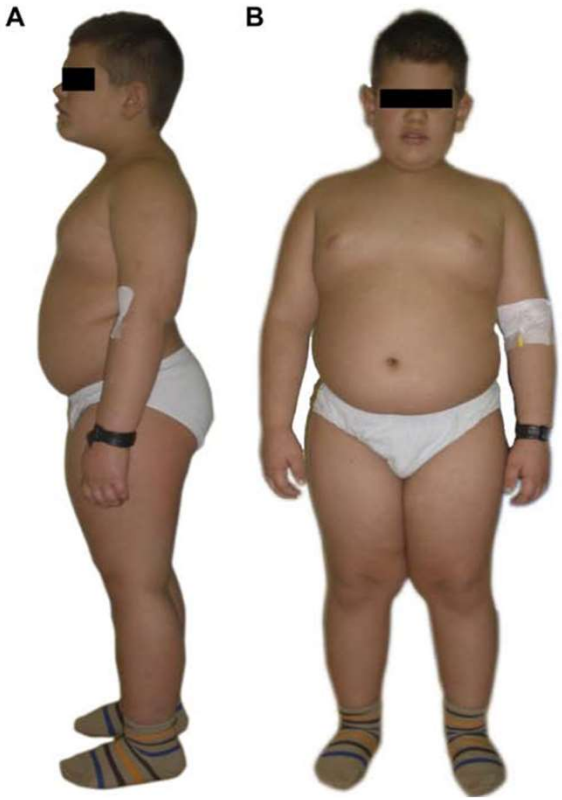
Caterina Limbert

Helen Dollfuss



Pietro Maffei

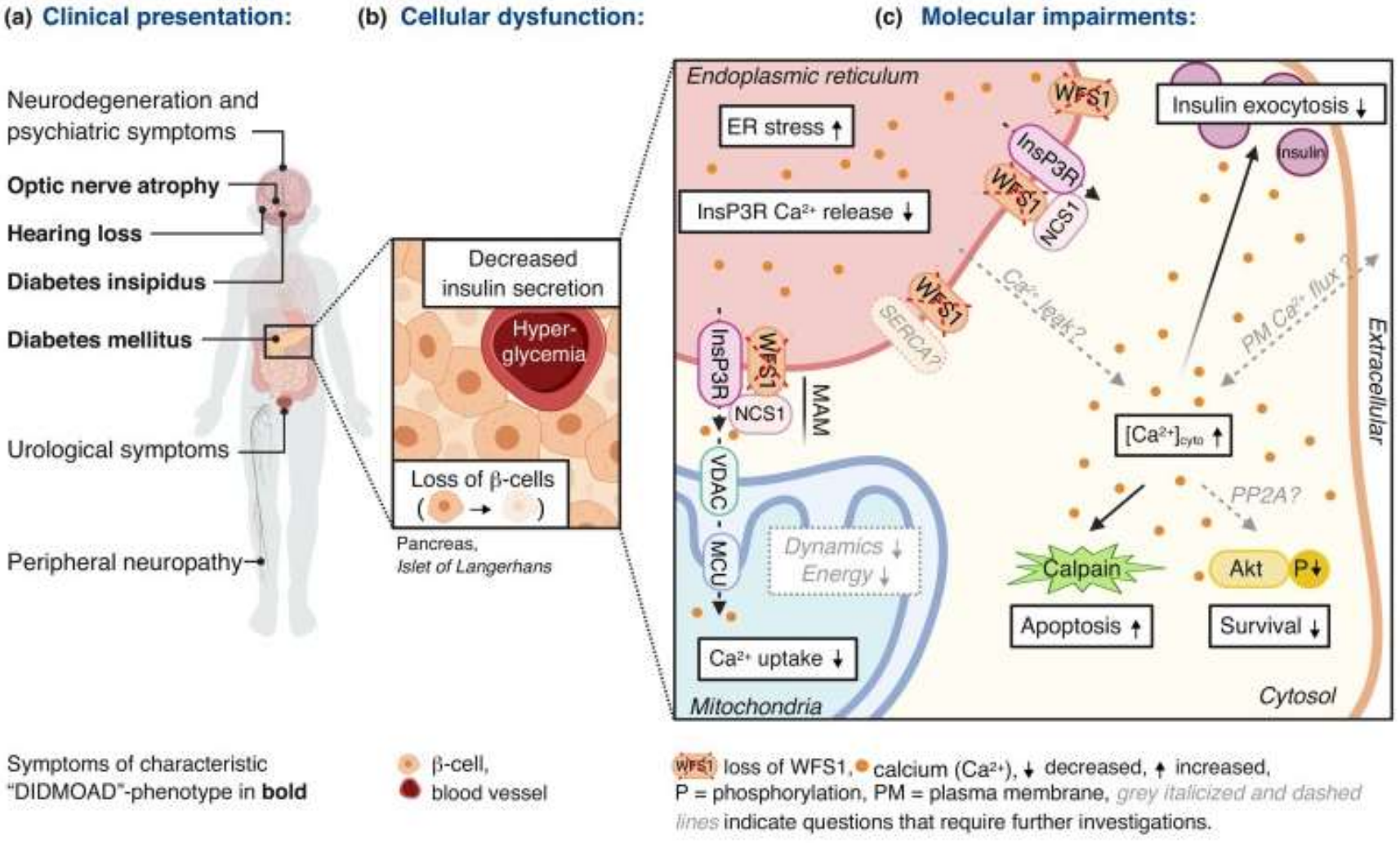
Alström Syndrome Phenotype



6-year-old

- Autosomal recessive
- Prevalence < 1:1.000.000
- Cone-rod dystrophy
- Hearing loss
- Obesity
- Hyperinsulinemia, T2DM
- Hypertriglyceridemia
- DCM, Liver, kidney failure
- Systemic fibrosis

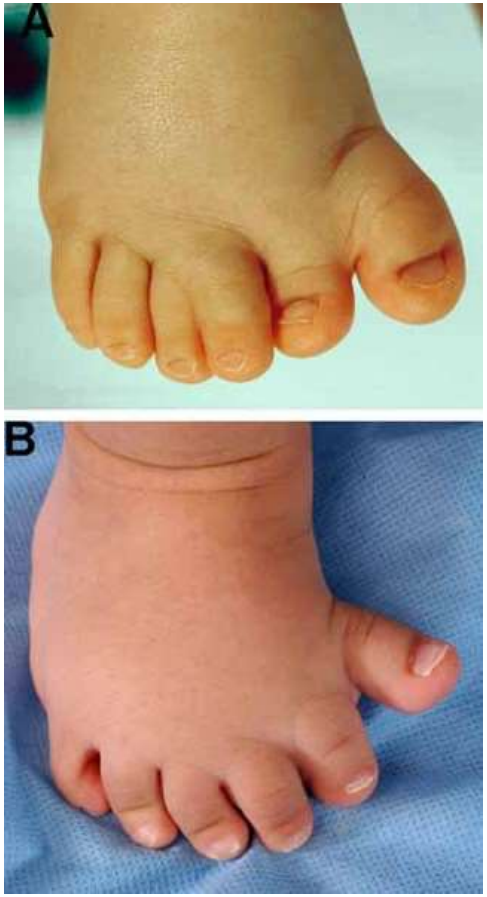
Wolfram syndrome



Fisher & Ehrlich, Current Opinion in Physiology 2020

ii. Diagnostic features

Primary features	*Frequency*
Rod-cone dystrophy	93%
Polydactyly	63–81%
All four limbs:	21%
Upper limbs only:	9%
Lower limbs only:	21%
Obesity	72–92%
Genital anomalies	59–98%
Renal anomalies	53%
Learning difficulties	61%
Secondary features	
Speech delay	54–81%
Developmental delay	50–91%
Diabetes mellitus	6–48%
Dental anomalies	51%
Congenital heart disease	7%
Brachydactyly/ syndactyly	46–100%/8–95%
Ataxia/ poor coordination	40–86%
Anosmia/hyposmia	60%



Forsythe et al, Frontiers in Pediatrics, 2018

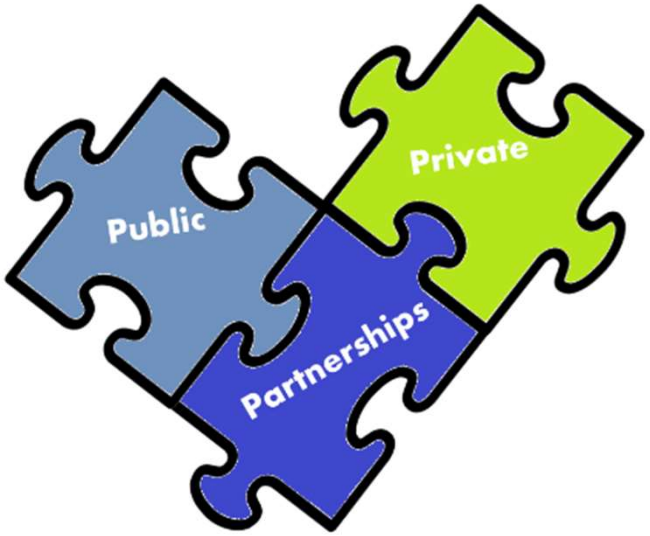
1.1 Objectives and ambition

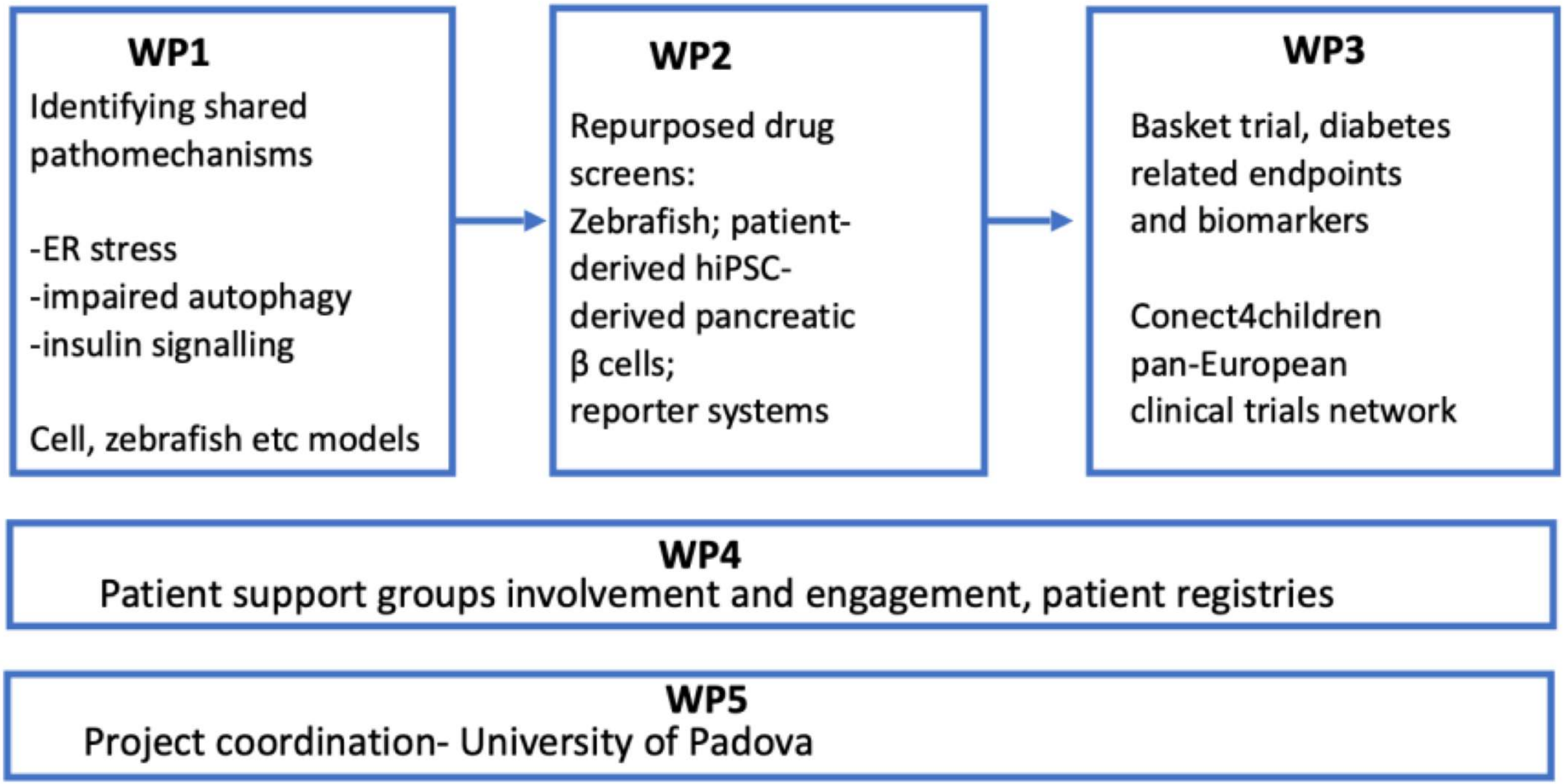
Diabetes mellitus with metabolic syndrome and and their systemic complications, are major health issues of rare monogenic diabetes disorders, and are caused by a combination of insulin resistance and beta cell failure. **We aim to work on a new therapeutic approach for monogenic rare diabetic disease (RDS) syndromes by repurposing existing therapies in order to prevent or slow-down the progress of diabetes, obesity and their systemic complications.** We will address the disconnect between basic science discoveries about the mechanisms of these diseases and the care of patients by linking preclinical data on therapy to early phase clinical trials.

1) Set-up a knowledge and research hub
2) Identifying shared pathomechanisms
3) Repurposed drug screen in pre-clinical models
4) Patient recruitment in clinical trials and access to tissue samples through registries
5) Patients advocacy group
6) Pivotal trial exemplar
7) Legacy therapeutic discovery and development pipeline

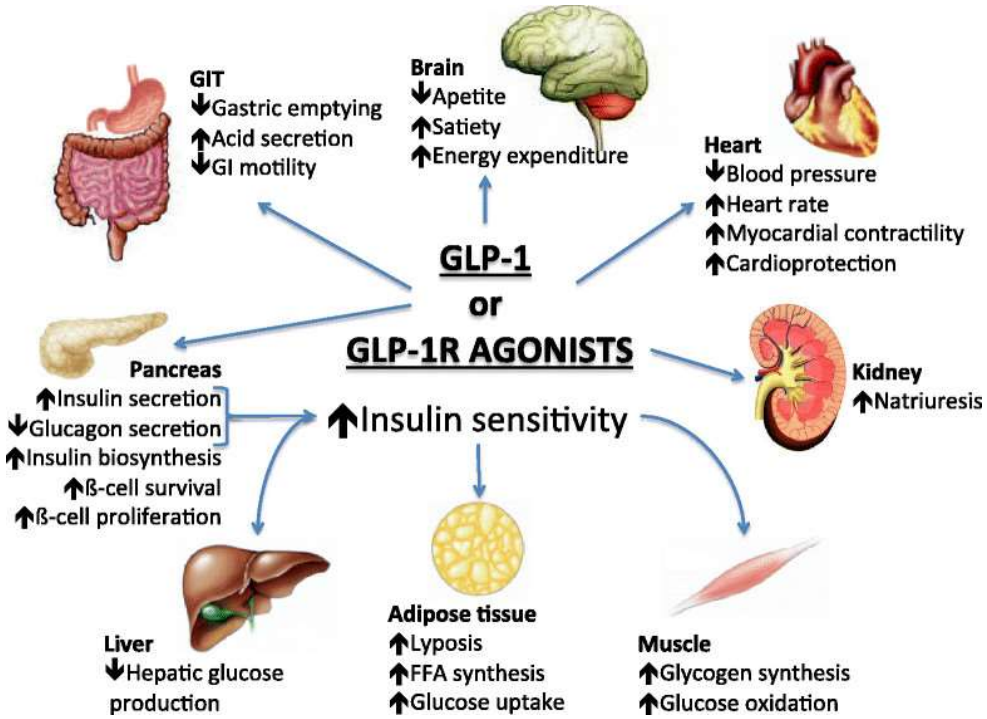

EUROPEAN REFERENCE NETWORK
DEDICATED TO RARE EYE DISEASES
ERN-EYE

Endo-ERN


Public
Private
Partnerships


WP1
Identifying shared pathomechanisms
-ER stress
-impaired autophagy
-insulin signalling
Cell, zebrafish etc models
WP2
Repurposed drug screens:
Zebrafish; patient-derived hiPSC-derived pancreatic β cells;
reporter systems
WP3
Basket trial, diabetes related endpoints and biomarkers
Conect4children pan-European clinical trials network
WP4
Patient support groups involvement and engagement, patient registries
WP5
Project coordination- University of Padova

WP3. Pivotal trial exemplar. Rationale: Currently, no drugs are globally approved for the treatment of WS, AS or BBS. First-line therapy of metabolic complications are lifestyle intervention (especially diet and physical exercise), insulin, and treatment of comorbidities. Evidence supports a role of the GLP-1 agonists to control diabetes, obesity and their systemic complications. Name of the investigational product: Liraglutide (human glucagon-like peptide-1 (GLP-1) analogue produced by recombinant DNA technology in Saccharomyces cerevisiae). Pharmaceutical form: Solution for injection. Pivotal treatment indication: treatment of pre-diabetes, diabetes, and/or overweight WS, AS, BBS. Objectives: *Primary end point*: mean change from baseline in HbA1c, glycated albumin, BMI SDS, at week 24. 2) *Secondary end point*: to evaluate the safety and tolerability. 3) *Exploratory end points*: to assess the effect of



The proposals should involve group(s) of rare diseases (i.e. a rare disease being individually defined in the European Union as affecting not more than five in 10.000 persons). Proposals that plan to run clinical trials should demonstrate that they have already taken into account scientific advice[84] or protocol assistance from EMA. In particular, the proposals planning the clinical development of orphan medicinal products should demonstrate that they have been granted approval for an orphan designation at the latest on the date of the call deadline.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 April 2021
EMADOC-628903358-2283
Human Medicines - Scientific Evidence Generation

Deadlines for submission of applications for orphan medicinal product designation to the EMA and corresponding COMP timetable for valid applications

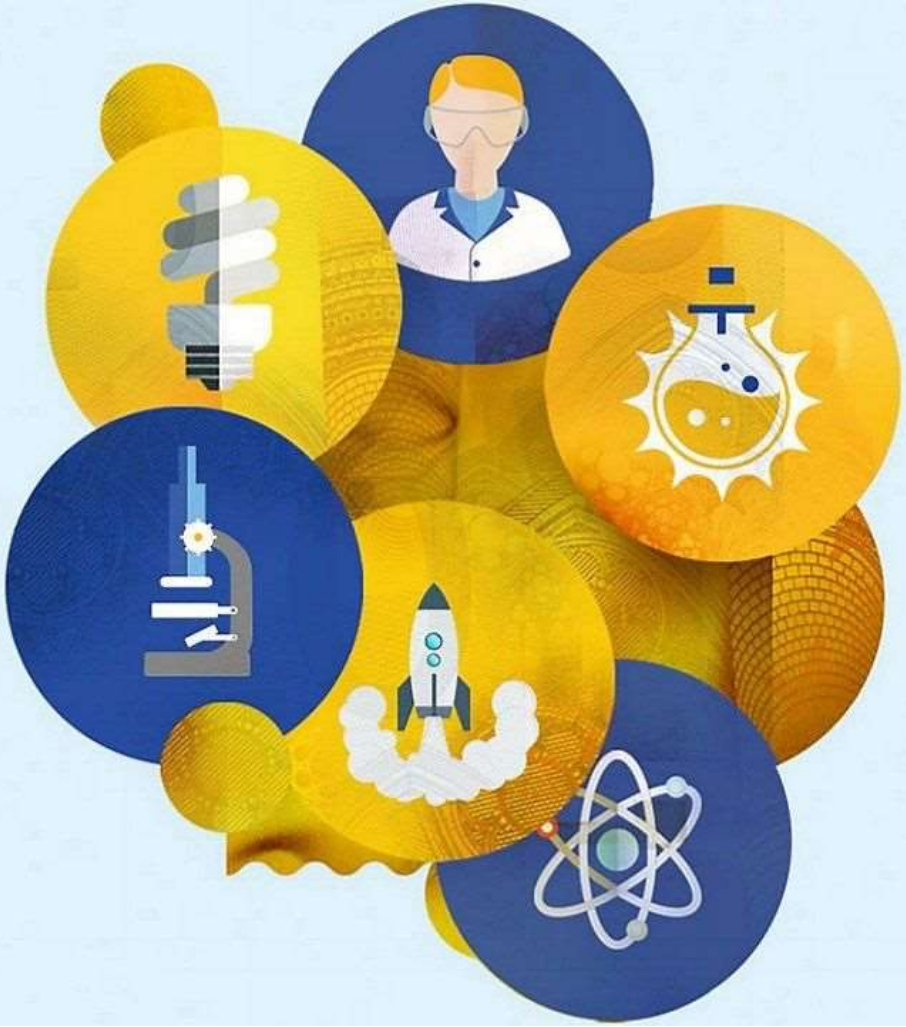
2021/2022

Submission deadline	Start of procedure Day 1	COMP meeting Day 60 (1st discussion)	COMP meeting* Day 90 (2nd discussion)
25/02/2022	25 March 2022	10-12 May 2022	14-16 June 2022
24/03/2022	19 April 2022	14-16 June 2022	12-14 July 2022

Next projects ?

Horizon Europe

THE NEXT EU RESEARCH & INNOVATION PROGRAMME (2021 – 2027)



Endo-ERN

European Reference Network on Rare Endocrine Conditions

MTG 4 - Genetic Endocrine Tumour Syndromes

Dr. Antje Redlich
University Magdeburg

Prof. Attila Patocs
Semmelweis University

Petra Brügmann
ePAG, EMENA

European Commission | Endo-ERN is a European Reference Network co-funded by the European Union's Health Programme under grant agreement No 739572

European Reference Network

Agenda MTG 4 meeting 15 february 2022 / 15.30 – 16.00

1. Introduction – current HCP ´s and new members
   What do you expect ? Ideas ? Contribution ?

2. Ongoing projects
   - 2.1. Submissions / Publications/Grant applications
   - 2.2.Trials
   - 2.3. Recommendations / guidelines
   - 2.4. Endo – ERN Webinars
3. Registries

4. Collaboration with patients´s advocacy groups

1. Introduction

Current HCPs and New members

Expectations ? Ideas ? Contribution ?

43 HCPs

Belgium	4
Bulgaria	1
Denmark	3
Finland	2
France	3
Germany	4
Greece	1
Hungary	1
Ireland	1
Italy	11
Latvia	1
Malta	1
Netherlands	4
Norway	1
Spain	2
Sweden	2

2.1. Publications in 2021
Endocrine, Special Endo-ERN issue

Molecular genetic testing strategies used in diagnostic flow for hereditary endocrine tumour syndromes
Butz H, Blair J, & Patócs A.(Endocrine., 2021(2).)

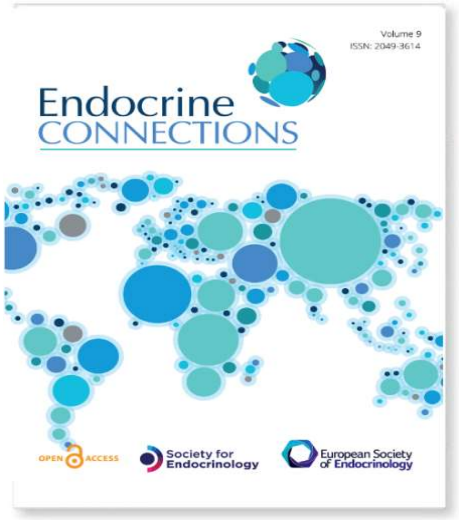
Patients' perception on the quality of care for multiple endocrine neoplasia disorders in Europe: an online survey from a patient support group
Drewitz KP, Grey J, Brügmann P, Pichl J, Sammarco M, Aarts M, … Schaaf L.(Endocrine., 2021(2).)

Cancers, Special issue of thyroid cancer
Epidemiology and Survival Analysis of MTC:20 years experience in Hungary

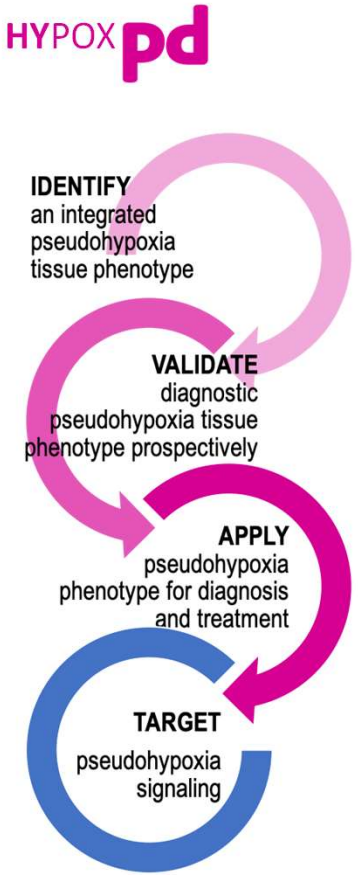
2.1. Submissions in 2022

Endocrine Connections, Special Endo-ERN issue

Epidemiology of Endocrine Tumour Syndromes in Children and Adults.



2.2. Grant proposal



European Joint Programme on Rare Diseases (EJP RD)
Call for Proposals 2022
"Development of new analytic tools and pathways to accelerate diagnosis and facilitate diagnostic monitoring of rare diseases"

Hypo PD: Rare tumor predisposition (PD) syndromes that converge on activated hypoxia signaling (HYPOX)

Principal investigator: Matthias Kroiss (LMU München)

Participants:

ENDO-ERN Main Thematic Group (MTG) 4:
Reference Centers (RC) involved and representative of each RC involved in the project:
- Ludwig-Maximilians-University Munich, DE: Matthias Kroiß
- University Medical Center Utrecht, NL: Ronald de Krijger
- Semmelweis University Budapest, HU: Attila Patocs

VHL PHEO (n=131)

SDHx PPGL (n=521)

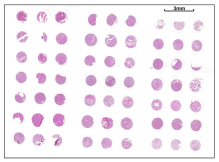
non-HYPOX PD PPGL (n=229)

oncocytic thyroid cancer (n=49)

oncocytic tumors (n=74)*

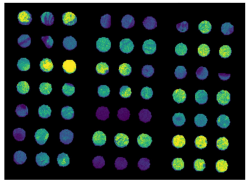
control tumors (n=199)

available tumor MS data (n>1000)



TMA construction

MALDI-MSI



full slide image

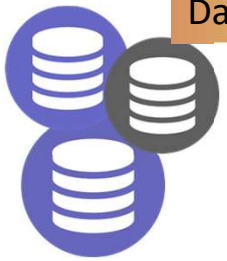
feature selection

Metabolome

Morphology

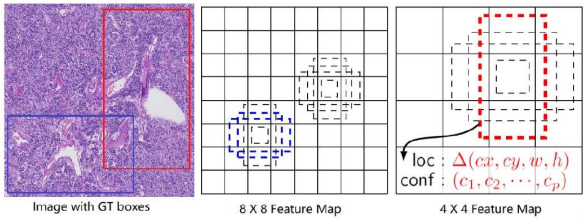
Genetics

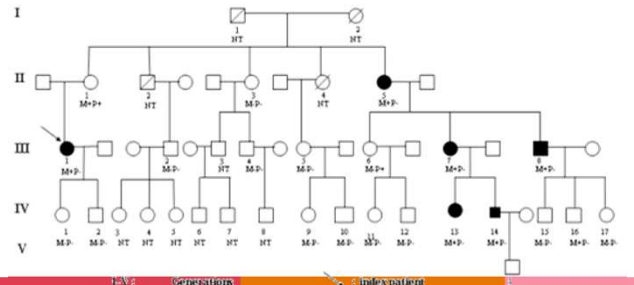
Data integration

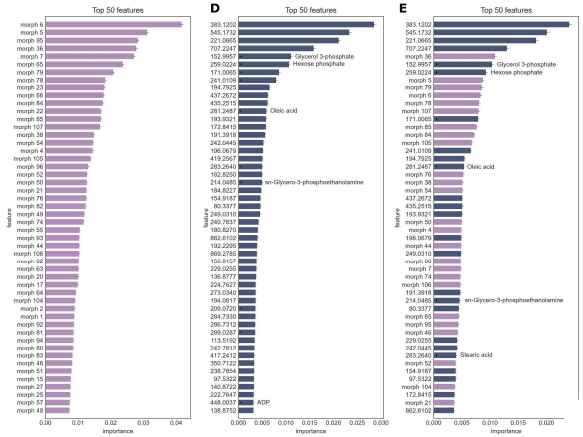


neuronal networks

AI Biomarker







2.3. Recommendations / Guidelines

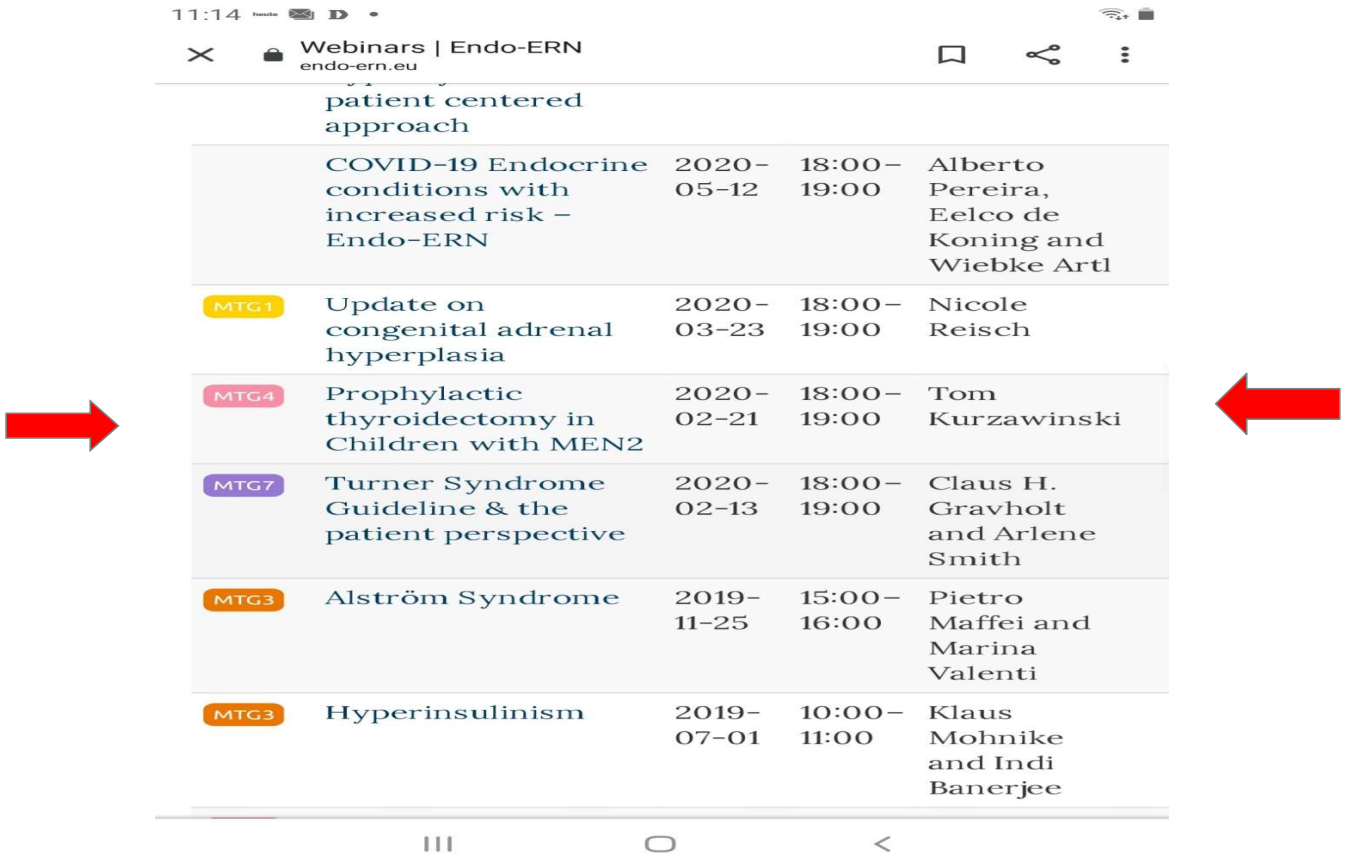
- MEN 1 Guideline - global expert group
- M.L.Brandi/G.Valk/R.Thakker ongoing

Pediatric:

- Neuroendocrine Tumors of the appendix
  EXPeRT (European Cooperative Study Group for Pediatric Rare Tumors)

2.4. Endo – ERN Webinars

Please consider contributing a webinar to one of the disease groups of MTG 4 – thanks for the presentation in february 2020 !



	patient centered approach			
	COVID-19 Endocrine conditions with increased risk – Endo-ERN	2020-05-12	18:00–19:00	Alberto Pereira, Eelco de Koning and Wiebke Artl
MTG1	Update on congenital adrenal hyperplasia	2020-03-23	18:00–19:00	Nicole Reisch
MTG4	Prophylactic thyroidectomy in Children with MEN2	2020-02-21	18:00–19:00	Tom Kurzawinski
MTG7	Turner Syndrome Guideline & the patient perspective	2020-02-13	18:00–19:00	Claus H. Gravholt and Arlene Smith
MTG3	Alström Syndrome	2019-11-25	15:00–16:00	Pietro Maffei and Marina Valenti
MTG3	Hyperinsulinism	2019-07-01	10:00–11:00	Klaus Mohnike and Indi Banerjee

Webinars planned in 2022

Multiple endocrine neoplasia type 2B: diagnosis before development of advanced medullary thyroid carcinoma

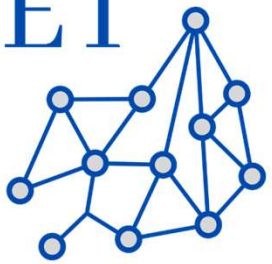
Dermatological aspects of hereditary endocrine tumors (M Medvecz, Semmelweis University)

3. Registries

EuRRECa

European Registries For Rare Endocrine Conditions

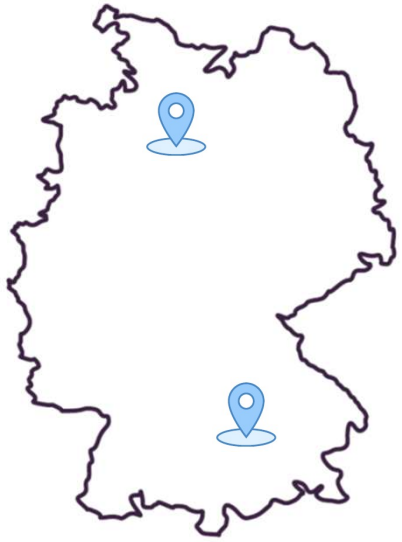
GPOH-MET Registry



Antje Redlich

Trials and registries in pediatric oncology in Germany

Pediatric Oncology



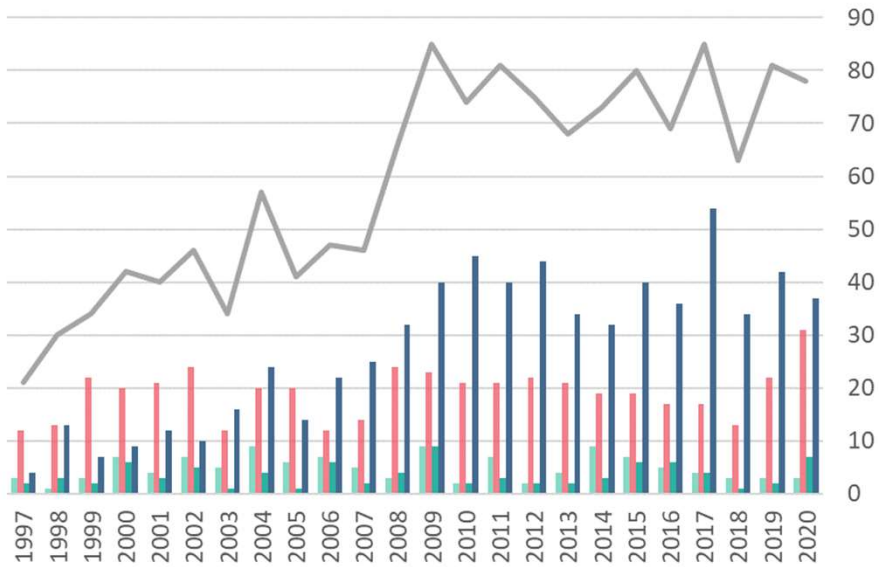
National study center

- Collects data and samples of all affected children in Germany
- Reference institutions (pathology, imaging etc.) and scientific projects
- Recommendations regarding diagnostics, therapy and follow up
- Multidisciplinary study commission with experts on the field

Malignant endocrine tumors in children

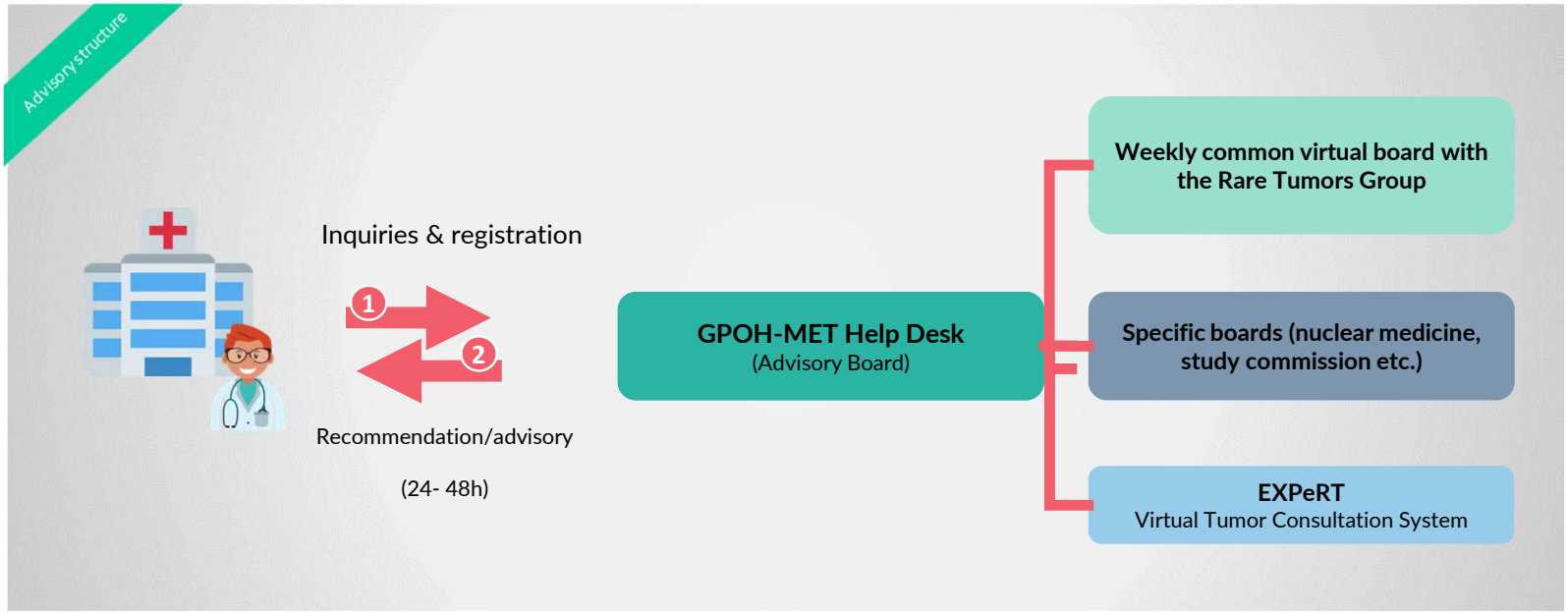
Registered patients per years in Germany

- Thyroid carcinomas
- Adrenocortical tumors
- Pheochromocytoma/ paraganglioma
- Gastrointestinal NET



GPOH-MET Registry

Easy accessible and powerful advisory



GPOH-MET Registry

Pediatric oncology

Redlich, Antje	Investigator, EXPeRT	Magdeburg
Kuhlen, Michaela	Co-Investigator	Augsburg
Schneider, Dominik	STEP-Registry, EXPeRT	Dortmund
Brecht, Ines	STEP-Registry, EXPeRT	Tübingen
Kratz, Christian	Cancer predisposition registry	Hannover
Langer, Thorsten	LESS Project	Lübeck
Pfister, Stefan	INFORM Registry	Heidelberg
Frühwald, Michael	EU-RHAB Registry	Augsburg

Pediatric endocrinology

Hübner, Angela	Adrenal research CRC	Dresden
Rohrer, Tilman		Homburg
Palm, Katja		Magdeburg

Endocrine surgery

Lorenz, Kerstin	CAEK	Halle
Musholt, Thomas	Registry Eurocrine	Mainz

Human genetics

Zenker, Martin		Magdeburg

Internal medicine/Endocrinology/Clin. chemistry

Faßnacht, Martin	Adrenal research CRC	Würzburg
Pape, Ulrich-Frank	NET-Registry	Hamburg
Eisenhofer, Graeme	Adrenal research CRC	Dresden

Nuclear medicine

Luster, Markus	Reference center RIT	Marburg
Kreißl, Michael		Magdeburg

Pathology

Vokuhl, Christian	Bonn
Schmid, Kurt Werner	Essen

Pediatric surgery

Seitz, Guido	Marburg
Fitze, Guido	Dresden

Statistics

Hering, Thomas	Stendal

4. Collaboration with patients´s advocacy groups

The current Endo-ERN
European Patient Advocacy Group likes to get in contact with groups in South European and East European countries.

If you collaborate with a patients´groups in your country, please contact the office in Leiden or one of the members of the Endo-ERN patient advocacy group.

Furthermore: we like to improve the website and are looking for **patient materials** connected with the MTG 4 disease aera in different languages.

Endo-ERN

European Reference Network on Rare Endocrine Conditions

MTG 5 - Growth and genetic obesity syndromes

European Commission | Endo-ERN is a European Reference Network co-funded by the European Union's Health Programme under grant agreement No 739572

European Reference Network

Prof. Irène Netchine, MD, PhD
Pediatric Endocrinology
Trousseau Children Hospital
Pierre et Marie Curie School
of Medicine Paris,
France

Prof. Gudmundur Johannsson,
MD, Ph.D
Endocrinology
Sahlgrenska university hospital
Gothenburg
Sweden

Elisabetta Freo, ePAG chair, A Fa DOC, Italy

Patricia Carl, ePAG chair, BKMF, Germany

Nathalie Ferard, ePAG chair, Ass. Grandir, France

Berit Otterlei, ePAG chair, Landsforeningen for PWS, Norway

The Stearing Group	
Erika van den Akker	NE
Maité Tauber	FR
Thomas Eggermann	GE
Anita Hokken Koelega	NE
Christine Poitou	FR

Activities 2020-2022

Webinars:

2020 - Genetic Obesity Disorders caused by Leptin-melanocortin Pathway Defects- Erica van den Akker

2020 - Prader Willi Syndrome - Anita Hokken-Koelega (SG-ESPE)

2020 - Clinical guidelines on Silver Russles syndrome – Iréne Netchine

2020 - Webinar Molecular diagnosis of imprinting and growth disorders- Thomas Eggermann

2021 - Clinical trials with new drugs in PWS - Maithe Tauber

2021- Beckwith Wiedemann Syndrome – Frederic Brioude

2021 – PWS syndrome and transition of care a MTG 5 Symposia

MTG5 online meetings- 2 monthly

CPMS Panel

- Recurrent time slots every 2 months (limited activity)

Registry EuRReCa contribution

- Registry of patients (some centres)
- Survey genetic obesity
- Survey COVID and Growth & Obesity disorders

2022 - Planned

Noonan syndrome – clinical and genetic features?

Best management of adolescents and young adults with genetic obesity (syndromic and non-syndromic)

Craniopharyngioma and obesity (together with MTG6)

Achondroplasia and novel treatments

MTG 5 SYMPOSIUM 16 November 2021

Prader Willi Syndrome (PWS) Clinical management of transition of care

2:00 – 2:30	Introduction - PWS and transition of care – the paediatric aspects (Maithé Tauber- FR)
2:30 – 3:00	PWS and transition of care - focus on psychology (Tony Holland - UK)
3:00 – 3:45	PWS and transition of care – endocrine care of the young adults
	Adrenal insufficiency and hypogonadism (Laura De Graaf - NL)
	Growth hormone treatment (Charlotte Højbye – SE)
3:45 – 4:00	Break "Learning from People with Prader-Willi Syndrome" a video from International PWS Organisation
4:00 – 4:20	Coordination of transition and management of transitional care for patients with rare endocrine disorders (Christine Poitou and Sandrine Bottius)
4:20 – 4:50	Patient's and parent's view on transition of care
	The parent's view "Thank you for listening" (Berit Otterlei – NO)
	The patient's view (pre-recorded – 27 years with PWS)

Publications

ERN Publications

Clinical management of patients with genetic obesity during COVID-19 pandemic: position paper of the ESE Growth & Genetic Obesity COVID-19 Study Group and Rare Endo-ERN main thematic group on Growth and Obesity. de Groot et al. *Endocrine* jan 2021.

Growth restriction and genomic imprinting - overlapping phenotypes support the concept of an imprinting networkAuthors: Eggermann et al. *Genes* 2021

The EuRRECa Project as a Model for Data Access and Governance Policies for Rare Disease Registries That Collect Clinical Outcomes. Ali et al*. Int. J. Environ. Res. Public Health* 2020

Genetic testing in inherited endocrine disorders: joint position paper of the European reference network on rare endocrine conditions (Endo-ERN) Eggermann et al. *Orphaned journal of rare diseases 2020*

Endo-ERN
European Reference Network on Rare Endocrine Conditions

European Reference Network

MTG6 – Pituitary

Evangelia Charmandari
Pediatric Chair

Nienke Biermasz
Adult Chair

Johan de Graaf
ePAG

Diana Vitali
ePAG

Update MTG 6 Pituitary

Registries (EuRRECa)

- E-Rec registration
- E-Rec COVID registrations (in collaboration with ESE) / core registry
- Disease specific modules (EuRRECa: 1) aggressive pituitary tumors; working group established, 2) additional modules.

Guidelines

Pregnancy and pituitary adenoma (ESE guideline, EndoERN collaborated through participation of Susan Webb), finalized

Congenital hypopituitarism, in preparation, request support if possible otherwise continue with the guideline group composed prior to covid

Papers

An overview of clinical activities in Endo-ERN: the need for alignment of future network criteria (published EJE)

Outcomes of pituitary surgery within the Endo-ERN (in preparation)

Endocrine Minireviews (in preparation), please let us know ideas for future ideas

Patient care (CPMS)

Several cases discussed but: please consider to discuss your interesting cases!

Webinars (MTG6)

Daly (Liege, genetic pituitary disease); Trotsenburg/Zwaveling-Soonawala/Naafs (Amsterdam, congenital central hypothyroidism); de Vries/ Biermasz/ Pereira (Leiden, Value based health care in pituitary disease)

Please bring your ideas

Surveys and patient journeys

Cushing (cardiovascular), SOD, Transition, Craniopharyngeoma

Examples of (future) activities

Ana Priego - Update on pituitary module of EuRRECa (5 min)

Carla Scaroni- Mapping the current clinical practice in prevention and treatment of cardiovascular risk in patients with Cushing's syndrome across center of Endo ERN (5 min)

Johan de Graaf- A proposal to make a survey for craniopharyngioma care (5 min)

Savi Shishkov- Evaluation of exchange program and survey of transitional care in pituitary (5 min)

Endo-ERN
European Reference Network on Rare Endocrine Conditions

EuRRECa
European Registries for Rare Endocrine Conditions

The Pituitary Tumour Module

Ana Luisa Priego
EuRRECa and EuRR-Bone Fellow

Pituitary Tumour Study Group

European Society of Endocrinology

EuRR-Bone
European Registries for Rare Bone and Mineral Conditions

ESPE
European Society for Paediatric Endocrinology

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European Reference Network

Ana Luisa Priego Zur

Pediatric Endocrinologist

EuRRECa and EuRR-Bone Fellow

Endo-ERN
European Reference Network on Rare Endocrine Conditions

EuRRECa
European Registries for Rare Endocrine Conditions

LUMC Leids Universitair Medisch Centrum

EuRR-Bone
European Registries for Rare Bone and Mineral Conditions

Pituitary Tumour Study Group

Faisal Ahmed

Natasha Appelman-Dijkstra

Nienke Biermasz

Pia Burman

Luis Castano

Mehul Dattani

Olaf Dekkers

Benedetta Fibbi

Hoong-Wei Gan

Sonia Gaztambide

Harshini Katugampola

Helene Lasolle

Hermann Müller

Alberto Pereira

Ana Luisa Priego Zurita

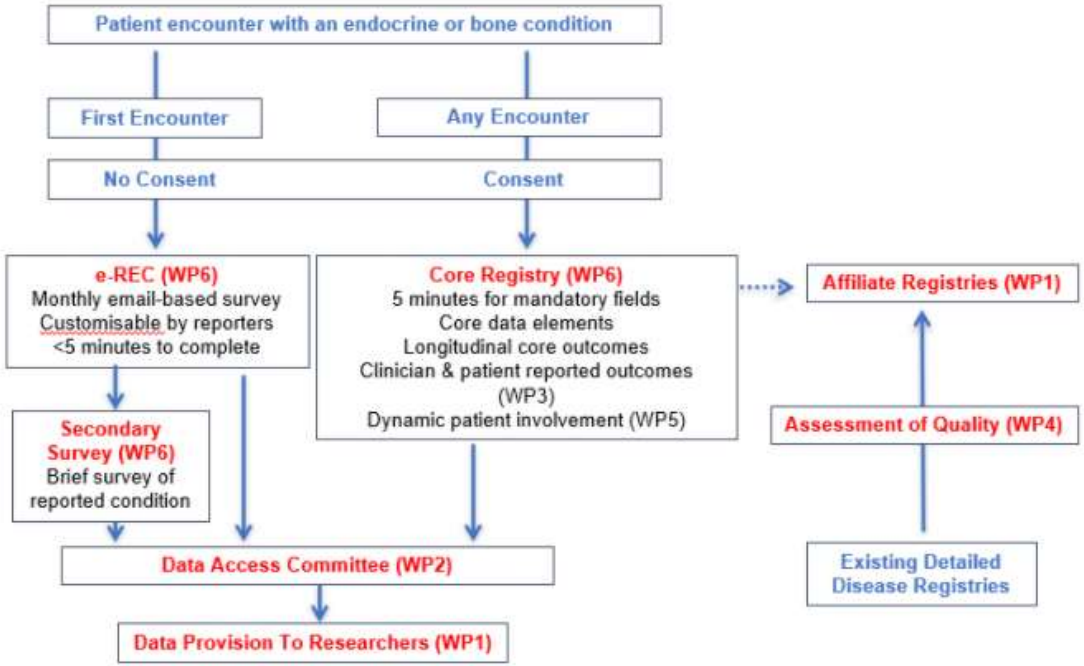
Gerald Raverot

Itxaso Rica

Friso de Vries

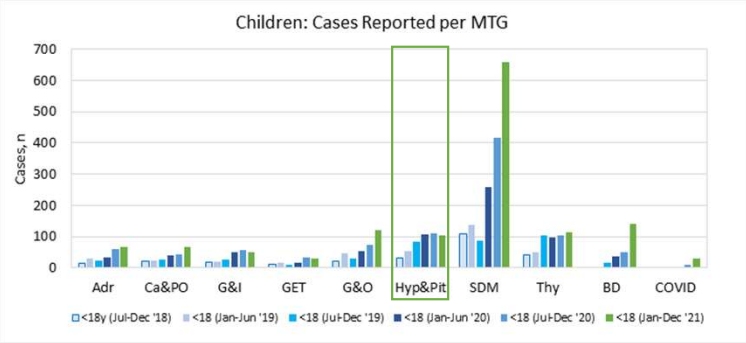
Amir Zamanipoor Najafabadi

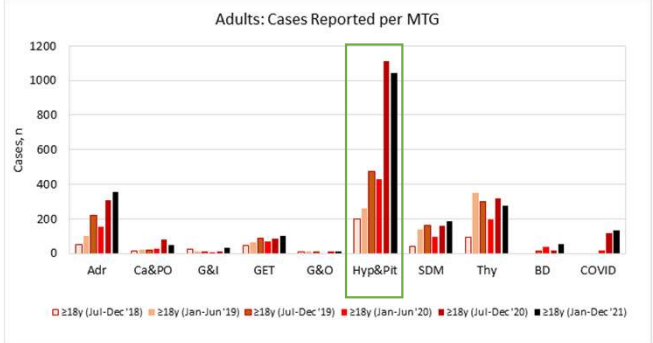
EuRRECa Platforms



https://eurreca.net/

Pituitary Tumours in e-REC



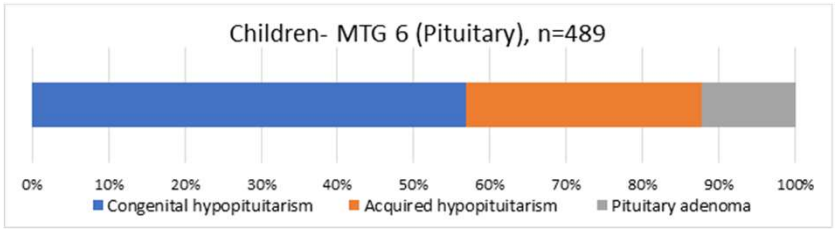


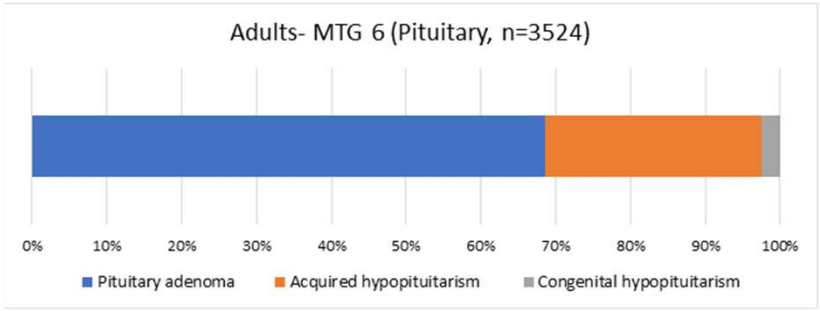
https://eurreca.files.wordpress.com/2021/10/e-rec-report-october-2021-v1.5.pdf

Pituitary Tumours in e-REC

Amongst adults, pituitary adenoma is the most reported condition

34 centres





>2400 cases

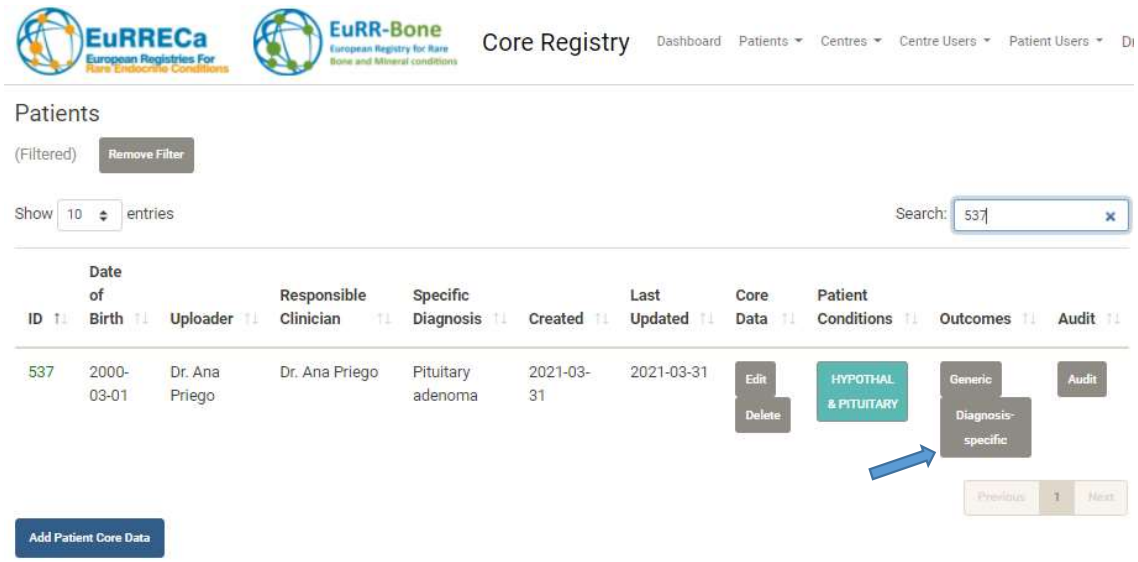
https://eurreca.files.wordpress.com/2021/10/e-rec-report-october-2021-v1.5.pdf

Developing the Pituitary Tumour Module

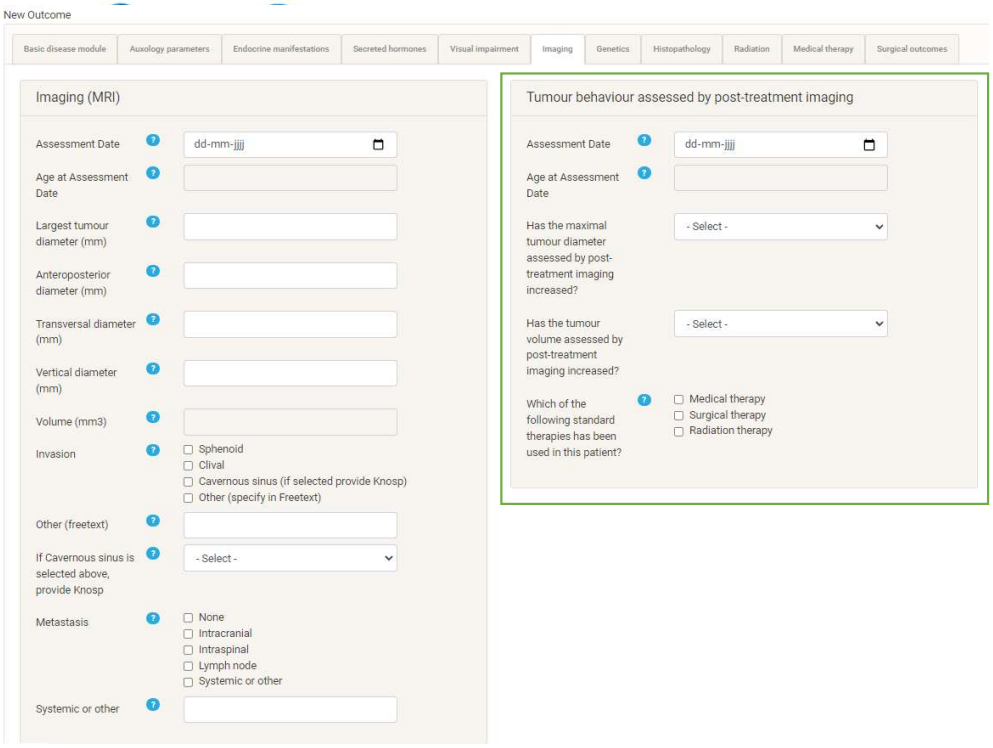
Pituitary tumour study group

Objective: to collect longitudinal data on pituitary tumours; identify tumours with aggressive behaviour

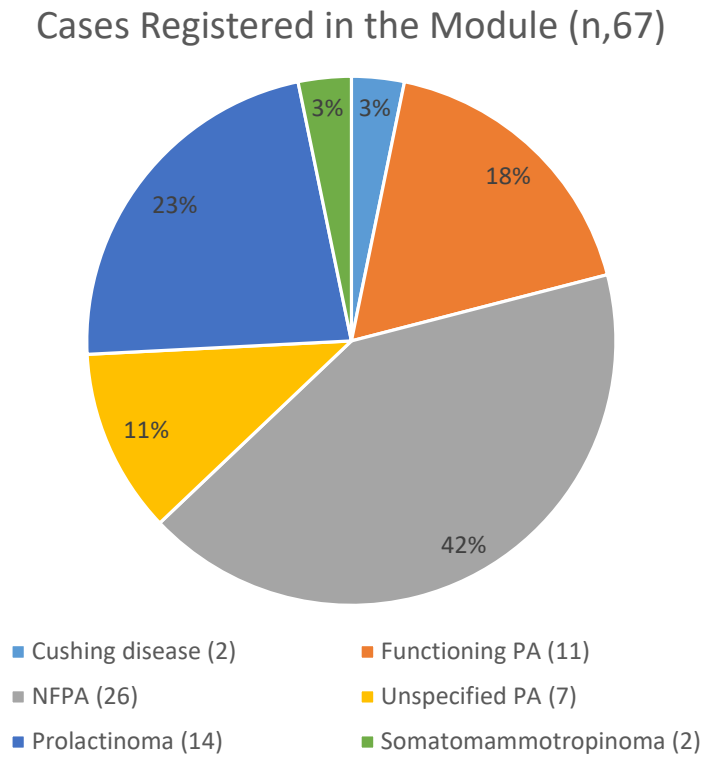
The Module in the Core Registry



The Module in the Core Registry



Activity in the Module



To find out more…

Visit our website

https://eurreca.net/

Join our drop in sessions

Contact us by email

info@eurreca.net
a.l.priego_zurita@lumc.nl

PROMs are questionnaires used to study how patients feel about their own health status and well-being

If you are part of the endocrine or bone community, you can help the registries understand your needs regarding Patient Reported Outcome Measures (PROMs)

Participate in this survey before February 21, 2022

https://eurreca.net/
https://eurr-bone.com/

Patients

SCAN ME

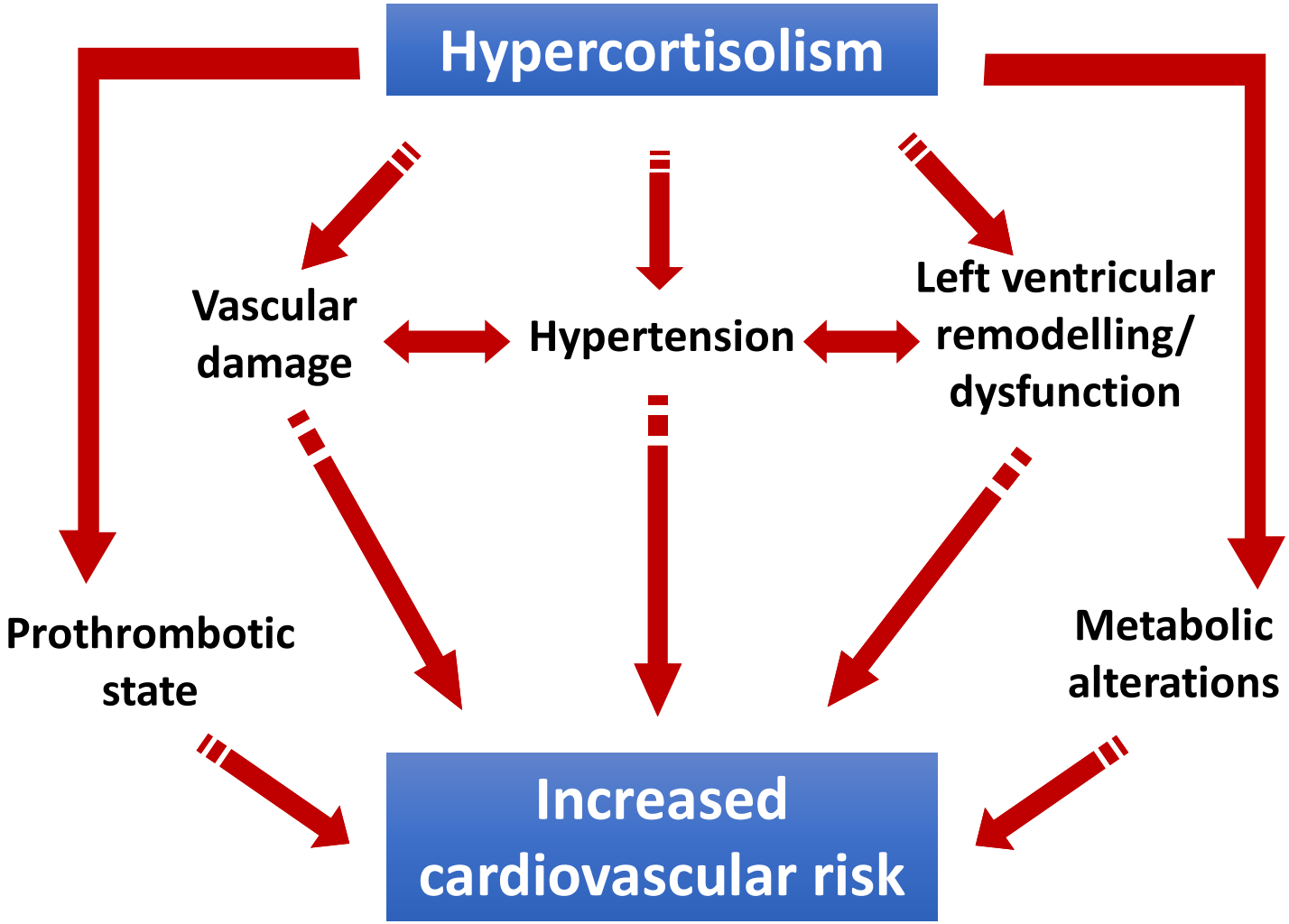
Health care staff

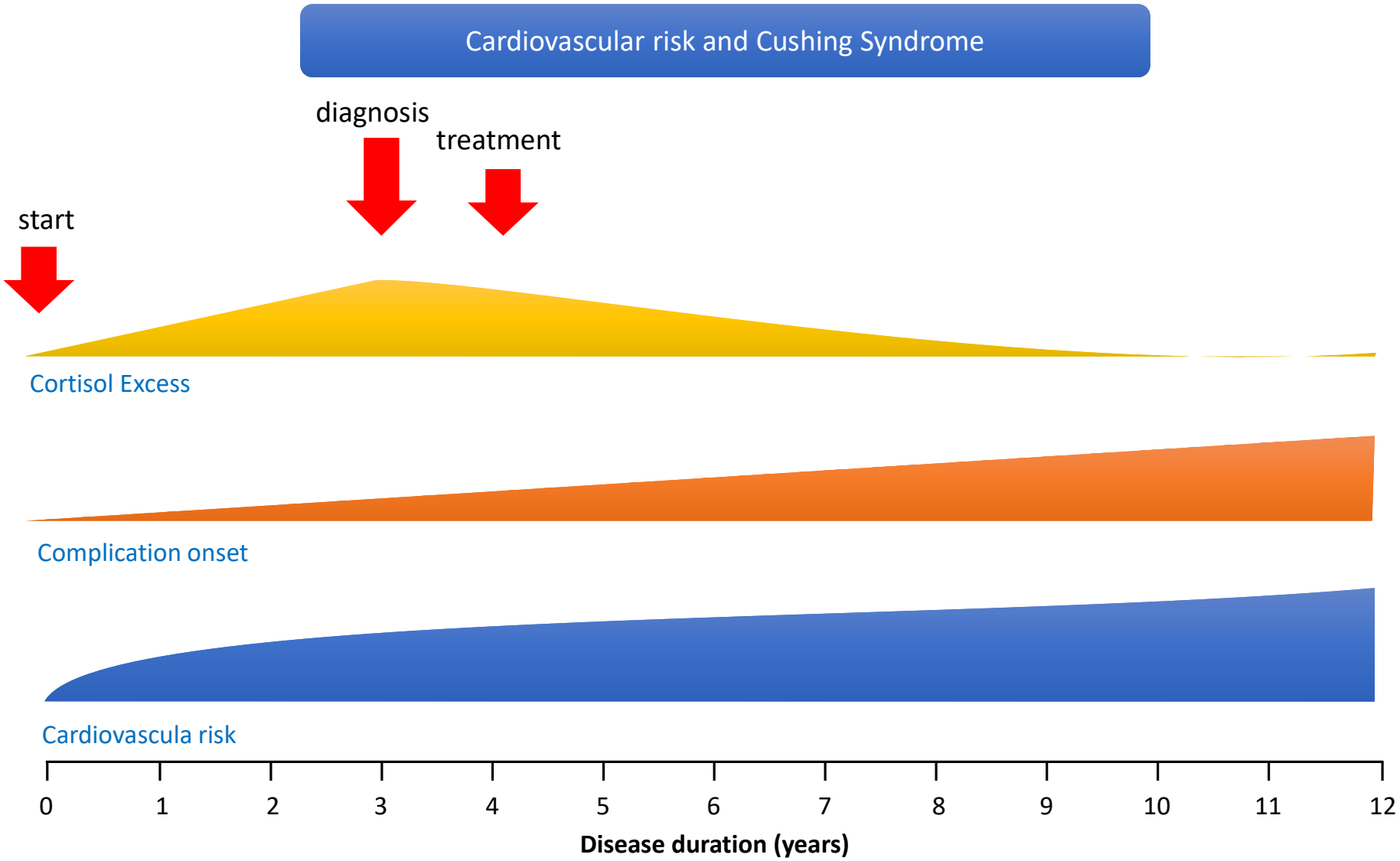
SCAN ME

EuRR-Bone
European Registries for Rare Bone and Mineral Conditions

EuRRECa
European Registries For Rare Endocrine Conditions

Carla Scaroni


Hypercortisolism
Vascular damage
Hypertension
Left ventricular remodelling/ dysfunction
Prothrombotic state
Metabolic alterations
Increased cardiovascular risk


Cardiovascular risk and Cushing Syndrome
diagnosis
treatment
start
Cortisol Excess
Complication onset
Cardiovascula risk
0
1
2
3
4
5
6
7
8
9
10
11
12
Disease duration (years)

Mortality in active and remission CS

Multisystem Morbidity and Mortality in Cushing's Syndrome: A Cohort Study

- 343 CS
- 34300 matched controls

Table 2. Rates and Hazard Ratios With 95% Confidence Intervals (95% CI) for the Risk of VTE, AMI, Stroke, Heart Failure, Infections, Ulcers, and Fractures in Patients With CS, Stratified by Follow-up Time

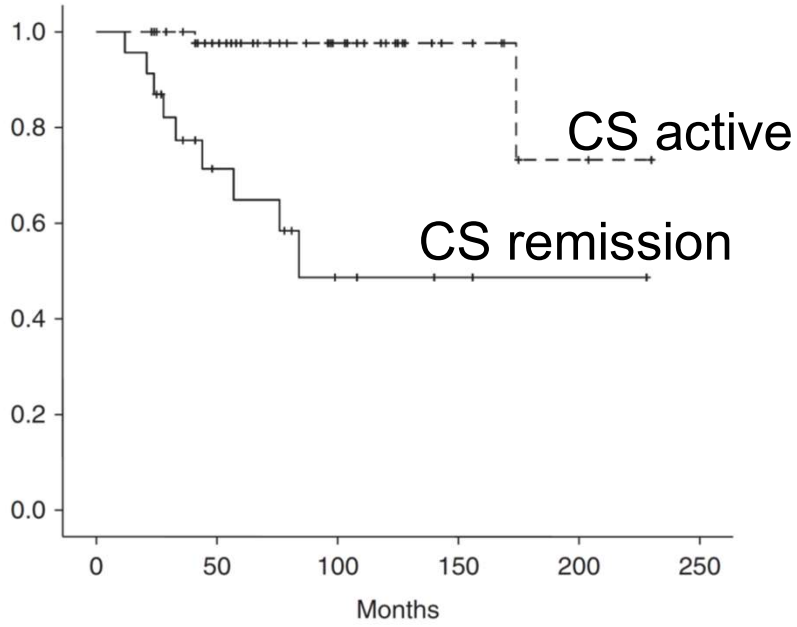
Outcome	Period (y before/ after diagnosis)	Rate (95% CI) per 1000 Person-years in CS Cohort	Rate (95% CI) per 1000 Person-years in Control Cohort	Hazard Ratio (95% CI), Age- and Sex-adjusted Model	Hazard Ratio (95% CI), Fully Adjusted Model[a]
VTE	3 y before	4.3 (1.1–9.3)	0.5 (0.4–0.7)	8.4 (3.0–23.4)	6.8 (2.4–19.3)
	1 y after	15.3 (4.9–31.4)	0.9 (0.6–1.2)	20.6 (7.8–53.9)	17.1 (6.4–45.8)
	>1 to 30 y after	1.9 (0.8–3.6)	1.3 (1.2–1.4)	1.6 (0.8–3.4)	1.4 (0.6–2.9)
AMI	3 y before	2.1 (0.2–5.9)	0.9 (0.8–1.2)	2.2 (0.5–8.9)	2.1 (0.5–8.6)
	1 y after	6.1 (0.7–16.9)	1.4 (1.0–1.8)	4.5 (1.1–18.4)	3.5 (0.8–14.7)
	>1 to 30 y after	6.0 (3.8–8.8)	1.9 (1.8–2.1)	3.6 (2.4–5.5)	2.8 (1.8–4.4)
Stroke	3 y before	5.3 (1.7–10.9)	1.1 (0.9–1.3)	5.0 (2.1–12.4)	4.5 (1.8–11.1)
	1 y after	9.1 (1.8–22.0)	1.4 (1.1–1.9)	6.5 (2.0–21.0)	4.3 (1.3–14.2)
	>1 to 30 y after	4.3 (2.5–6.7)	2.7 (2.5–2.8)	1.8 (1.1–3.0)	1.5 (0.9–2.5)
Heart failure	3 y before	4.3 (1.1–9.3)	0.6 (0.5–0.8)	6.8 (2.5–18.6)	6.0 (2.1–17.1)
	1 y after	6.1 (0.7–17.0)	0.9 (0.6–1.3)	6.7 (1.6–28.1)	3.1 (0.7–14.2)
	>1 to 30 y after	1.6 (0.6–3.1)	1.9 (1.8–2.0)	1.0 (0.4–2.2)	0.8 (0.3–1.7)
Fractures	3 y before	14.9 (7.9–24.0)	4.2 (3.8–4.7)	3.4 (2.0–6.0)	3.2 (1.9–5.6)
					–8.7)
					–1.6)
Infections					–5.9)
					.1–31.3)
					–4.1)
Peptic ulcers					–13.9)
					–26.3)
	>1 to 30 y after	1.9 (0.8–3.6)	1.6 (1.5–1.7)	1.3 (0.6–2.8)	1.1 (0.5–2.2)

Mortality risk increased 3 yrs before, and 1→30 years after CS diagnosis and remission

Dekkers OM, JCEM 2013

Surgical remission of Cushing's syndrome reduces cardiovascular risk

- 51 CS remission (5 years)
- 24 CS with active hypercortisolism
- 60 pituitry incidentaloma (controls)



Terzolo M, EJE 2014

Survey development

- ✓ Steering Committee, composed of members of the endoERN, develop the study objectives and the statement questions

- ✓ Delphi process via email survey

- ✓ panelists will use Likert- type scale as follows: 1 (“complete disagreement”), 2 (“some disagreement”), 3 (“disagreement”), 4 (“neither disagree- ment nor agreement”), 5 (“agreement”), 6 (“some agree- ment”) to 7 (“complete agreement”).

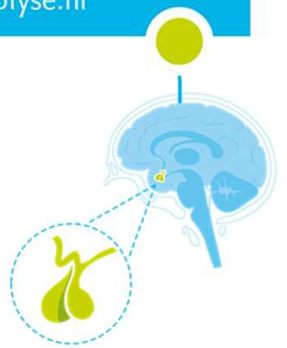
- ✓ Key question will cover areas as
  - Number of patients with Cushing
  - Type if treatment used (surgery, drugs, RT)
  - Definition of remission
  - Diagnosis of CV comorbidities (diabetes, hypertension, dyslipidemia, carotid US and so on) at diagnosis, at remission, and which follow up in active-remission patients? Those under medical treatment?

Proposed questions

- Which tools/score are used in your center to stratify CV risk?
- Do you assess at diagnosis and during follow up ECGs, carotid US, echocardiogram?
- Do you measure blood glucose,lipid profile, high sensitivity C-reactive protein?
- Which cholesterol target do you consider?
- Which blood pressure target do you consider?
- Which fasting glucose / HbA1c levels do you consider?
- Do you consider anti-platelet therapy during active hypercortisolism? And before surgery?
- Patient with medical-controlled hypercortisolism is a high-risk patient?
- Is Cushing at high-risk for CV disease? Do you consider useful a strict glucose-lipid-presure target as in patients with diabetes?
- Early statin treatment?

Dutch Pituitary Foundation

www.hypofyse.nl



- Chair Dutch Pituitary Foundation (2015), Founded 1996, 2.200+ members, 50+ volunteers
- Mission: Shortening the diagnostic delay by creating awareness
- Full colour patients' magazine 4x per year, Recently updated website with summaries in English, Turkish and Arabic
- Working together will all relevant centres (mostly academic) in the Netherlands
- Webinars on both general as specific subjects; 18th June 2022: Jubilee congress, 700-900 guests expected

- ePAG/Steering Committee member MTG 6 Pituitary and WP3 Research and Science
- Active in EuRRECa, EJP-RD, EMA, Eurordis, Dutch Brain Foundation
- Eupati Fellow
- Main motive: Rare pituitary disorders don't stop at the borders of the Netherlands; since becoming chair of my organisation I've tried to widen the focus both geographically as professionally
- Resulting in: benficial (inter)national contacts, participation in scientific research, strong member growth, attracting volunteers with professional backgrounds

nederlandse hypofyse stichting

Johan de Graaf – j.degraaf@hypofyse.nl

Unmet need craniopharyngeoma patients

In cooperation with the Wilhelmina Childrens' Hospital Utrecht (dr. Hanneke van Santen)

- Creating a survey targetting patients livings with a craniopharyngeoma diagnoses
  - Children above 12 independently
  - Parents if the child is younger than 12
  - Adults with a childhood diagnoses of a cranio
  - Craniopharyngeomas diagnosed in adults are excluded
- Available languages: Dutch, German, French, English, Italian and Portuguese
- Translations through Deepl.com and corrected by native speakers
- Dissemination through HCPs and patient organisations

Johan de Graaf – j.degraaf@hypofyse.nl

nederlandse hypofyse stichting

Survey contents

General data on the medical condtion and bio-statistical data

Inventory of medical and social care received or wanted to have received

Unmet medical need

Unmet social need

Suggestions from patients on future medical research

Draft finished, final check and ready for translation

Johan de Graaf – j.degraaf@hypofyse.nl

nederlandse hypofyse stichting

DIANA VITALI

- **ENDO ERN ePAG member since 2017**

- **ePAG Steering Committe MTG6**
- **ePAG Steering Committee WP4**

- **Mother of Carolina, with SOD PLUS**

- **President of SOD ITALIA ONLUS/APS**
- *Italian Patient Organization for Septo Optic Dysplasia and other Neuroendocrine Disorders*

- **Board of ePAG Italia**

- **In normal life Diana works as a sports technician of horse riding and sailing specialized in disabled people.**

Current practice in transition of patients with pituitary disease

Endo-ERN
European Reference Network on Rare Endocrine Conditions

European Reference Networks

Exchange Programme 2021-2022

European Reference Networks

Exchange Programme 2021-2022

Savi Shishkov, MD
Endocrinologist
UMHAT St. Marina Varna
Bulgaria

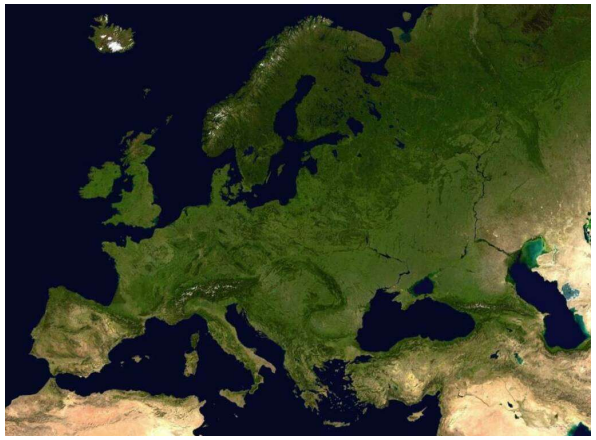
Luigi Tuccillo, MD
University of Naples
Federico II
Italy

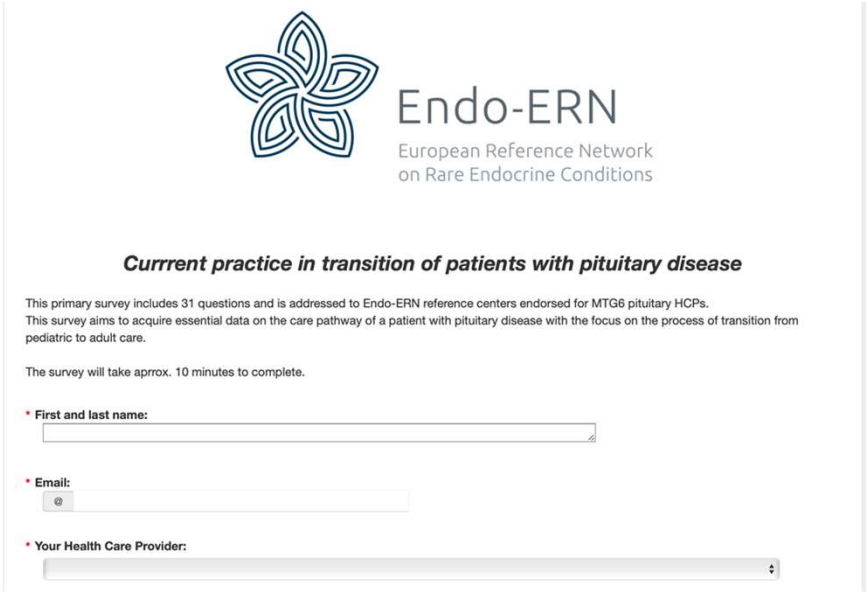
Leiden University Medical Center
Netherlands

Endo-ERN
European Reference Network on Rare Endocrine Conditions

Current practice in transition of patients with pituitary disease

- Response from 30 Reference centers out of 43 endorsed for MTG6
- **69% response rate**





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European Reference Network on Rare Endocrine Conditions

Currrent practice in transition of patients with pituitary disease

This primary survey includes 31 questions and is addressed to Endo-ERN reference centers endorsed for MTG6 pituitary HCPs.
This survey aims to acquire essential data on the care pathway of a patient with pituitary disease with the focus on the process of transition from pediatric to adult care.

The survey will take aprrox. 10 minutes to complete.

* **First and last name:**

* **Email:**

* **Your Health Care Provider:**

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European Reference Network on Rare Endocrine Conditions

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Results

I. 75% physicians do not evaluate the success of the transition process.

I. 81% of all endocrinologists do not evaluate clinical outcomes for their patients.

I. 50% of physicians and 50% of RCs do not have an established protocol for transition. None of the currently existing are tailored for pituitary disease.

I. PROMs are not regularly used in the transition process.

Future plans

Short term goals:

- Publication of current results
- Systematic review on pituitary transition

Long term goals:

- Transition protocol

Endo-ERN
European Reference Network on Rare Endocrine Conditions

European Reference Networks

Exchange Programme 2021-2022

MTG7 – Rare disorders of sex development and maturation

Luca Persani
Adult co-chair

Olaf Hiort
Pediatric co-chair

Manuela Brösamle
ePAG co-chair

Arlene Smythe
ePAG co-chair

European Reference Network

Endo-ERN
European Reference Network on Rare Endocrine Conditions

Manuela Brösamle

Member of Bord of AGS-Eltern- und Patienteninitiative e.V. in Germany

E-mail: geschaeftsstelle@ags-initiative.de https://www.ags-initiative.de

Mother of an adult daughter (without CAH) and a son at the age of 17 with salt wasting CAH

ERN ePAG of MTG1
Adrenal

ERN ePAG of MTG7

Sex development and Maturation

ERN ePAG of WP1

Education & Training

Member of the I-DSD/I-CAH Scientific Panel

I am grateful for the chance to be accepted as an ePag in Endo-ERN. This has not only given me the opportunity to share information with other ePags, but also to expand my knowledge and awareness of other rare diseases and to become actively involved.

European Reference Network

www.endo-ern.eu

Arlene Smyth

Executive Officer of Turner Syndrome Support Society [UK]

E-mail:- Turner.syndrome@tss.org.uk https://tss.org.uk/

Mother to an adult daughter with Turner Syndrome [TS] and founding member

With over 30 years experience and expertise

President of Turner Syndrome International Group

Email:TSI2020@tss.org.uk https;//tsint.org

ERN ePAG co-Chair of MTG7

Sex development and Maturation

EuRRECa Board member and part of work package 5

(Patients, parents and ethics) & data access committee

I-TS data registry board member

I am proud to be part of The Office for Rare Condition in Glasgow

Board member & chair of our Patient advisory Group speaking to families and helping, supporting them and raising awareness about Rare Conditions.

https://officeforrareconditions.org

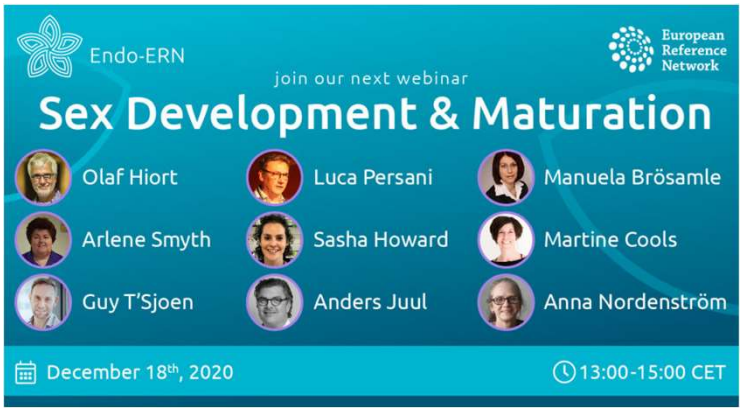
Patient information materials

- Update:
- Sex chromosome DSD: Turner syndrome: published since 2021
- 46,XX-DSD / Congenital adrenal hyperplasia (CAH): published since 2021
- 46,XY-DSD: reviewed, sent to Office in Leiden, will be published 02/2022
- Kallmann syndrome and other CHH syndromes: in preparation for review
- Gender Dysphoria: less information, in preparation for review

First Workshop of MTG 7

First Workshop of MTG 7

MTG7 WEBINARS



Webinar	Turner Syndrome Guideline & the patient perspective
Date	February 13th, 2020
Speakers	Claus H. Gravholt, Arlene Smyth

15/16 Febr. 2022

MTG7 event

ESPE Science Symposium 2021

Congenital adrenal hyperplasia: from molecular medical research to clinical application

Radboudumc, Nijmegen, the Netherlands
October 29th – 30th, 2021

MTG7 PUBLICATION ACTIVITIES

MTG7 articles in Endocrine – ENDO-ERN special issue 2021

1. Jürgensen M, Rapp M, Döhnert U, Frielitz F, Ahmed F, Cools M, … Hiort O. Assessing the health-related management of people with differences of sex development. (Endocrine., 2021(2).)
2. Persani L, Bonomi M, Cools M, Dattani M, Dunkel L, Gravholt CH, & Juul A. ENDO-ERN expert opinion on the differential diagnosis of pubertal delay. (Endocrine., 2021(2).)
3. Johannsen TH, Ljubicic ML, Young J, Trabado S, Petersen JH, Linneberg A, … Juul A. Serum insulin-like factor 3 quantification by LC–MS/MS in male patients with hypogonadotropic hypogonadism and Klinefelter syndrome. (Endocrine., 2021(2).)

MTG7 PUBLICATION ACTIVITIES

1: Claahsen-van der Grinten HL, Speiser PW, Ahmed SF, Arlt W, Auchus RJ, Falhammar H, Flück CE, Guasti L, Huebner A, Kortmann BBM, Krone N, Merke DP, Miller WL, Nordenström A, Reisch N, Sandberg DE, Stikkelbroeck NMML, Touraine P, Utari A, Wudy SA, White PC. Congenital Adrenal Hyperplasia-Current Insights in Pathophysiology, Diagnostics, and Management. **Endocr Rev. 2022**

2: Lucas-Herald AK, Bryce J, Kyriakou A, Ljubicic ML, Arlt W, Audi L, Balsamo A, Baronio F, Bertelloni S, Bettendorf M, Brooke A, Claahsen van der Grinten HL, Davies JH, Hermann G, de Vries L, Hughes IA, Tadokoro-Cuccaro R, Darendeliler F, Poyrazoglu S, Ellaithi M, Evliyaoglu O, Fica S, Nedelea L, Gawlik A, Globa E, Zelinska N, Guran T, Güven A, Hannema SE, Hiort O, Holterhus PM, Iotova V, Mladenov V, Jain V, Sharma R, Jennane F, Johnston C, Guerra Junior G, Konrad D, Gaisl O, Krone N, Krone R, Lachlan K, Li D, Lichiardopol C, Lisa L, Markosyan R, Mazen I, Mohnike K, Niedziela M, Nordenstrom A, Rey R, Skaeil M, Tack LJW, Tomlinson J, Weintrob N, Cools M, Ahmed SF. Gonadectomy in conditions affecting sex development: a registry-based cohort study. **Eur J Endocrinol. 2021**

3: Ali SR, Bryce J, Haghpanahan H, Lewsey JD, Tan LE, Atapattu N, Birkebaek NH, Blankenstein O, Neumann U, Balsamo A, Ortolano R, Bonfig W, Claahsen-van der Grinten HL, Cools M, Costa EC, Darendeliler F, Poyrazoglu S, Elsedfy H, Finken MJJ, Fluck CE, Gevers E, Korbonits M, Guaragna-Filho G, Guran T, Guven A, Hannema SE, Higham C, Hughes IA, Tadokoro-Cuccaro R, Thankamony A, Iotova V, Krone NP, Krone R, Lichiardopol C, Luczay A, Mendonca BB, Bachega TASS, Miranda MC, Milenkovic T, Mohnike K, Nordenstrom A, Einaudi S, van der Kamp H, Vieites A, de Vries L, Ross RJM, Ahmed SF. Real-World Estimates of Adrenal Insufficiency-Related Adverse Events in Children With Congenital Adrenal Hyperplasia. **J Clin Endocrinol Metab. 2021**

4. Galazzi E, Improda N, Cerbone M, Soranna D, Moro M, Fatti LM, Zambon A, Bonomi M, Salerno M, Dattani M, Persani L. Clinical benefits of sex steroids given as a priming prior to GH provocative test or as a growth-promoting therapy in peripubertal growth delays: Results of a retrospective study among ENDO-ERN centres. **Clin Endocrinol (Oxf). 2021**

5: Eggermann T, Elbracht M, Kurth I, Juul A, Johannsen TH, Netchine I, Mastorakos G, Johannsson G, Musholt TJ, Zenker M, Prawitt D, Pereira AM, Hiort O; European Reference Network on Rare Endocrine Conditions (ENDO-ERN). Genetic testing in inherited endocrine disorders: joint position paper of the European reference network on rare endocrine conditions (Endo-ERN). **Orphanet J Rare Dis. 2020**

15/16 Febr. 2022

MTG7 PUBLICATION ACTIVITIES

6: van der Straaten S, Springer A, Zecic A, Hebenstreit D, Tonnhofer U, Gawlik A, Baumert M, Szeliga K, Debulpaep S, Desloovere A, Tack L, Smets K, Wasniewska M, Corica D, Calafiore M, Ljubicic ML, Busch AS, Juul A, Nordenström A, Sigurdsson J, Flück CE, Haamberg T, Graf S, Hannema SE, Wolffenbuttel KP, Hiort O, Ahmed SF, Cools M. The External Genitalia Score (EGS): A European Multicenter Validation Study. J Clin Endocrinol Metab. 2020

7. Ali SR, Bryce J, Tan LE, Hiort O, Pereira AM, van den Akker ELT, Appelman-Dijkstra NM, Bertherat J, Cools M, Dekkers OM, Kodra Y, Persani L, Smyth A Smythe C, Taruscio D, Ahmed SF. The EuRRECa Project as a Model for Data Access and Governance Policies for Rare Disease Registries That Collect Clinical Outcomes. Int J Environ Res Public Health. 2020

8: Flück C, Nordenström A, Ahmed SF, Ali SR, Berra M, Hall J, Köhler B, Pasterski V, Robeva R, Schweizer K, Springer A, Westerveld P, Hiort O, Cools M. Standardised data collection for clinical follow-up and assessment of outcomes in differences of sex development (DSD): recommendations from the COST action DSDnet. Eur J Endocrinol. 2019

9: Hiort O, Cools M, Springer A, McElreavey K, Greenfield A, Wudy SA, Kulle A, Ahmed SF, Dessens A, Balsamo A, Maghnie M, Bonomi M, Dattani M, Persani L, Audi L; COST Actions DSDnet and GnRH Network as well as the European Reference Network for Rare Endocrine Conditions (Endo–ERN). Addressing gaps in care of people with conditions affecting sex development and maturation. Nat Rev Endocrinol. 2019

10: Ali SR, Bryce J, Cools M, Korbonits M, Beun JG, Taruscio D, Danne T, Dattani M, Dekkers OM, Linglart A, Netchine I, Nordenstrom A, Patocs A, Persani L, Reisch N, Smyth A, Sumnik Z, Visser WE, Hiort O, Pereira AM, Ahmed SF. The current landscape of European registries for rare endocrine conditions. Eur J Endocrinol. 2019

11. Tack LJW, Maris E, Looijenga LHJ, Hannema SE, Audi L, Köhler B, Holterhus PM, Riedl S, Wisniewski A, Flück CE, Davies JH, T'Sjoen G, Lucas-Herald AK, Evliyaoglu O, Krone N, Iotova V, Marginean O, Balsamo A, Verkauskas G, Weintrob N, Ellaithi M, Nordenström A, Verrijn Stuart A, Kluivers KB, Wolffenbuttel KP, Ahmed SF, Cools M. Management of Gonads in Adults with Androgen Insensitivity: An International Survey. Horm Res Paediatr. 2018

12: Cools M, Nordenström A, Robeva R, Hall J, Westerveld P, Flück C, Köhler B, Berra M, Springer A, Schweizer K, Pasterski V; COST Action BM1303 working group1. Caring for individuals with a difference of sex development (DSD): a Consensus Statement. Nat Rev Endocrinol. 2018

MTG7 current and future PUBLICATION ACTIVITIES

ENDO-ERN/ESE/ESPE Guidelines on Sex Hormone Replacement submitted to Eur J Endocrinol (end of 2021) with contribution by several MTG7 experts!

ENDOCRINE CONNECTION ENDO-ERN special Issue 2022

Variable genetic approaches to the diagnosis of DSD and CHH across Europe (results of an ENDO-ERN survey among ENDO-ERN centers): 16 centers form Belgium, Cyprus, Denmark, Germany, Italy, Netherlands, Slovenija so far gave feedback and data; we will circulate again the survey @old/new members

Long term outcomes of CAH Patients (focusing on bone, fertility or cardiovascular outcomes in male and female patients) (topic in potential sharing with MTG1-Adrenal)

MTG7 current and future ACTIVITIES

- **Survey on transgender care** across Europe (M Cools/G T'sjoen)
- Launched **project on the LC/MS determination of INSL3** in DSD together with WP3 (A Juul)
- **Inclusion of Primary Ovarian Insufficiency (idiopathic POI <25 yrs of age)** among the rare diseases covered by ENDO-ERN and defintion of the specific criteria (MDTs, number of cases, etc)
- **15-20 MTG7 CPMS sessions, so far:** but there is need to stimulate the HCPs to create/ join a CPMS meeting: DG Health during 2022 are offering some workshops for our team and members that are mainly aimed at better understanding your environment, the "real clinical world" in which you manage rare disease patients. Those workshops will be ERN-specific and aimed to tackle ERNs specific needs and update the CPMS. They wish to tackle here some technical barriers to using CPMS in the HCPs..... Please indicate if you are interested to participate in these workshops by replying to this email by 21st February.
- Many proposals for **webinars**, in particular several on CAH (proposal of joint event with MTG1)
- Effort to be done for the organization of **clinical trials**

15/16 Febr. 2022

International ePAG Collaboration on CAH

- Initiators: Manuela Brösamle (Germany), Marika Mayerdorfer-Muhr (Austria)

- First International Kickoff Meeting:
- 29.01.2022: 12 countries (Germany, Austria, UK, USA, Canada, Zimbabwe, Denmark, Finland, Netherlands, Spain, Italy, Bulgaria): 26 participants
- 12.02.2022: 9 countries (Germany, Austria, Switzerland, France, Australia, Indonesia, India, Vietnam, Philippines): 19 participants, IFCAH, CLAN

International ePAG Collaboration on CAH

- <u>AIM/Main topics (result of the questionnaire and Kickoff):</u>
- Establish an international CAH Community/Improve the life of CAH patients
- Surgery, Classification of CAH/DSD/Intersex, Standard of Care/Best Practice Sharing/Research, International Contact Network, Education

- The theme classification DSD is particularly significant in the USA and Western/Southern Europe and shows how important it was to set up the working group in MTG 7 on this topic.

MTG7 subgroup meeting: re-defining DSD and organising of DSD care

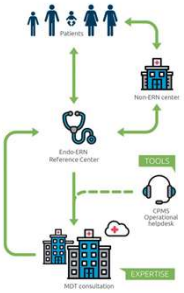
- Participants:
- Olaf Hiort, Luca Persani, Hedi Claahsen, Arlene Smith, Stefan Riedl, M. Brösamle

- Agenda:
- Classification DSD: Is there a need to re-define DSD terminology?
- The position of CAH within the spectrum of DSD
- Development of Quality standards of care
- Condition specific quality indicators

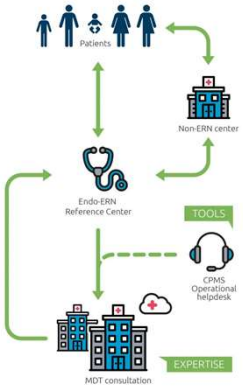
MTG7 subgroup meeting: re-defining DSD and organising of DSD care

- Plan
- To work out new classification system based on proposal Stefan Riedl
- To perform a digital survey among European DSD related patient organizations about their opinion about the current DSD classification
- To define condition specific quality indicators for all DSD related conditions, financial support to be clarified
- Proposal to discuss the topic during the I-DSD meeting in Bern
- Next meeting of the subgroup: March 2nd, 2.30 CET

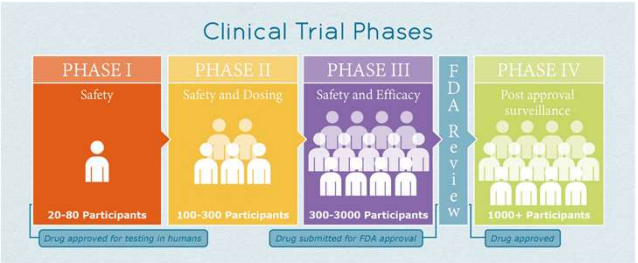
MTG7 current and future ACTIVITIES



MTG7 current and future ACTIVITIES



EuRRECa
European Registries For
Rare Endocrine Conditions



Endo-ERN

European Reference Network on Rare Endocrine Conditions

MTG8

Thyroid Group

Juliane Léger
(ped endo)

Edward Visser
(adult endo)

Beate Bartès
(ePAG)

European Commission | Endo-ERN is a European Reference Network co-funded by the European Union's Health Programme under grant agreement No 739572

European Reference Network

Endo-ERN

European Reference Network
on Rare Endocrine Conditions

Subtheme 1
Thyroid hormone signalling disorders

Subtheme 2
Congenital hypothyroidism & hyperthyroidism

Subtheme 3
Thyroid cancer

European Commission | Endo-ERN is a European Reference Network co-funded by the European Union's Health Programme under grant agreement No 739572

European Reference Network

2021

New in subtheme 2

Pediatric hyperthyroidism

Webinars

Jolante Krajewska (cancer)

Erik Verburg (radioactive iodine)

Registry: disease specific registries.

MCT8 deficiency. RTHa, RTHb: active discussions to get started

Publications

1- Ferdy van Geest et al. Long-term efficacy of T3 analogue Triac in children and adults with MCT8 deficiency: a real-life retrospective cohort study. JCEM 2021 acknowledgements: the centers in Rotterdam, Bucharest, Paris, and Angers are part of the Endo-ERN. The center in Rome is a HCP member of the ERN for Rare Neurological Disorders (ERN RND) and the center in Naples is part of the ERN ITHACA.

2- Van Trotsenburg et al. Thyroid 2021; consensus guideline on congenital hypothyroidism

CPMS: we are doing bad

2021

Project: Congenital hypothyroidism: Educational material for patients/families

We collected links and brochures from various patient associations:

Denmark, France, Italy, Spain, United Kingdom, Canada.

Some associations have booklets and films for children, others have leaflets for parents, or dedicated websites.

How to continue in 2022?

>> We must decide on the format, on the style, compare and harmonize the existing texts with the content of the recently published 2020-2021 Consensus Guidelines Update for congenital hypothyroidism…

https://pubmed.ncbi.nlm.nih.gov/33272083/

>> How? Team? Who?

2021/2022

Ongoing interaction Eurordis – ERNs (ePAGs)

PaedCan, EURACAN, EuroBloodNet, GENTURIS and Endo-ERN

EURACAN endocrine domain leader (G6)

Robin Peeters

>> opportunities for interaction on thyroid cancer

2022

CPMS ideas to improve?

New guidelines in preparation:

Diagnosis and treatment of *NKX2-1*-related disorder . Collaboration ERN-RND (neuro), ENDO-ERN, ERN-LUNG, ERN-GENTURIS (genetic)

Webinars: Luca Persani (RTH vs TSHoma)

(we will proceed with the shortlist arranged before)

Publications 2022

1- Mooij C et al. Eur Thyroid J 2022 European Thyroid Association for the management of pediatric Graves'disease : ENDO-ERN HCP members from the Netherlands (Amsterdam, Rotterdam), Paris (France) and members from UK, Germany.

Guidelines for Congenital Hypothyroidism, published in March 2021: "*Congenital Hypothyroidism: A 2020–2021 Consensus Guidelines Update—An ENDO-European Reference Network Initiative Endorsed by the European Society for Pediatric Endocrinology and the European Society for Endocrinology*"

https://www.liebertpub.com/doi/10.1089/thy.2020.0333

These guidelines are for **medical professionals**. The MTG8 wants to issue updated **information material for parents.**

We asked Endo-ERN members and various thyroid associations to send us the educational material they already have.

Italy: booklet for families received from Luisa de Sanctis : Opuscolo_Ipotiroidismo_congenito.pdf

Luca Persani sent some **Italian** links:

https://www.iss.it/documents/20126/0/Iodio+e+Salute+web.pdf/f485018e-5f6a-e450-3de4-28c79324a491?t=1582211499025
https://www.iss.it/registro-nazionale-ipotiroidei-congeniti
https://www.auxologico.it/centro-tiroide#description
https://www.capeitalia.org/chi-2

The **British** Thyroid Foundation has 2 leaflets about congenital hypo and a film for children:

https://www.btf-thyroid.org/congenital-hypothyroidism
https://www.btf-thyroid.org/your-thyroid-broke-but-we-can-fix-it

The Thyroid Foundation of **Canada** has a section "neonatal hypothyroidism" in their general information on hypothyroidism (but no special educational material): https://thyroid.ca/resource-material/information-on-thyroid-disease/hypothyroidism/

The **Danish** thyroid association has made a leaflet for parents : STOFSKIFTEFORENINGEN_HAEFTE_BORN_LOW.pdf

Spain: Diego Yeste sent a guide on congenital hypo for families in Spanish (and proposes to translate it to English if necessary): guia-hipo-ESP.pdf

In **France**, there is a guide (AFDPHE) on "how to raise a child with congenital hypo" (in French): http://www.tousalecole.fr/sites/default/files/medias/integrascol/documents/hypothyroidie_AFDPHE.pdf

Some years ago, during the International Thyroid Awareness Week in May, Merck, together with the Thyroid Federation International, elaborated a video and booklet for children, with "hypo and hyper butterflies": https://youtu.be/6F7yWItmv3Y There is also a brochure for parents, and a quiz on thyroid disorders in children: https://www.thyroidaware.com/en/forparents.html

Question: How can we translate this material into an informative, up-to-date, official European "guideline for patients & parents"? Who can help?