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MEETING SUMMARY
ASBMR 2021, HYBRID MEETING

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RARE BONE DISEASE – THE PATIENT'S PERSPECTIVE

OCTOBER 2021

DISCLAIMER AND DISCLOSURES

Please note: The views expressed within this presentation are the personal opinions of the authors.

This content is supported by an independent educational grant from Ipsen, Kyowa Kirin and Ultragenyx.

SELECTED ABSTRACTS: SUMMARY OF RARE BONE DISEASES AND KEY DATA

X-LINKED HYPOPHOSPHATAEMIA (XLH)

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- **X-linked hypophosphataemia (XLH)** is a **rare inherited bone disorder** characterised by **low levels of phosphate in the blood**
  - Phosphate is abnormally processed in the kidneys, which causes a loss of phosphate in the urine and leads to rickets (soft, weak bones)
- XLH is **caused by mutations in the *PHEX*** gene on the X chromosome, and inheritance is **X-linked dominant**
- XLH is **usually diagnosed in childhood**, with symptoms becoming apparent within the first 18 months of life, when a child begins to bear weight on the legs
- **Early signs and symptoms** include **abnormal bone development** (leading to bowing or twisting of the lower legs) and **short stature or a slowing growth**. Other symptoms that may be present early or may develop include: altered gait, spontaneous tooth abscesses, bone and muscle pain, arthritis, bone spurs, and tinnitus or hearing loss
- The **symptoms of XLH can vary in severity** and some people with XLH have no apparent bone-related symptoms and only hypophosphataemia, while others have severe symptoms
- **Treatment generally involves supplements of phosphate and high-dose vitamin D**, and may also include growth hormones, corrective surgery, and dental treatment
- **The long-term outlook varies depending on severity** and whether complications arise. While some adults with XLH may have minimal medical problems, others may experience persistent discomfort or complications

PHEX, phosphate regulating endopeptidase homolog; XLH, x-linked hypophosphataemia

www.XLHNetwork.org; https://rarediseases.info.nih.gov/diseases/12943/x-linked-hypophosphatemia. Accessed 06-Oct-21

KEY XLH DATA AT ASBMR 2021

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ORAL PRESENTATION

NEUROLOGICAL AND PSYCHIATRIC MANIFESTATIONS OF XLH IN A LONGITUDINAL COHORT STUDY: XLH-DMP

- **Design: XLH-DMP** is a global, prospective, multi-centre, observational study for subjects on or off any treatment
- **Key results:** compared with general population, XLH patients had:
  - Higher prevalence of common neurological conditions
  - Higher prevalence of depression and anxiety
  - Much higher use of pain medication
- **Patient perspective:**
  - Pain management in rare bone conditions is critical and not properly cared for
  - Identification of neurological and psychological burden is key in these patients as are strategies to reduce or minimise these

POSTER

PATIENT PERSPECTIVE: XLH REQUIRES WHOLE-BODY, WHOLE-LIFE, WHOLE-FAMILY CARE

- **Design:** open, unstructured discussions with adult patients, caregivers, a representative of the XLH network and an HCP
- **Key results:**
  - Education of HCP on rare disease such as XLH is critical for correct diagnosis and treatment
  - A coordinated multidisciplinary approach to treatment is necessary
  - HCPs should ensure appropriate transition of children to adult services
  - Support networks should be offered to patients and families.
  - Open communication between HCPs and patient will help tailor treatment to patient's needs
- **Patient perspective:**
  - It is critical that HCPs understand that XLH is a whole-body, whole-life and whole-family disorder and referrals to other resources (i.e., pain management, occupational therapy, counselling) is key

DMP, disease monitoring program; HCP, health care professional; XLH, x-linked hypophosphataemia

Jan de Beur S, et al. ASBMR 2021, Abstract #1019 (oral presentation); https://clinicaltrials.gov/ct2/show/NCT03651505 ; Hamilton A, et al. ASBMR 2021, Abstract #SAT-268 (poster presentation).
https://cor2ed.com/podcast-rare-bone-disease-highlights-at-asbmr-2021/

FIBRODYSPLASIA OSSIFICANS PROGRESSIVA (FOP)

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- **Fibrodysplasia ossificans progressiva (FOP)** is one of the rarest, most disabling, genetic conditions known to medicine; in which **skeletal muscle and connective tissue**, such as tendons and ligaments, **are gradually replaced by bone** (ossified). This condition leads to bone formation outside the skeleton (extra-skeletal or heterotopic bone) that restricts movement
- This process **generally becomes noticeable in early childhood**, starting with the neck and shoulders and moving down the body and into the limbs
- **People with FOP are born with abnormal big toes** (hallux valgus) which can be helpful in making the diagnosis
- **Trauma, such as a fall or invasive medical procedure**, or a viral illness **may trigger episodes of muscle swelling and inflammation** (myositis). These flare-ups lasts for several days to months and often result in permanent bone growth in the injured area
- **FOP is almost always caused by a mutation at the same place in the *ACVR1* gene** and is inherited in an autosomal dominant manner. **This condition occurs in about 1 in 1,600,000 newborns and about 800 people worldwide are known to have FOP**
- **There is currently no treatment for FOP. Flare-ups are treated with high-dose corticosteroids to reduce the inflammation and swelling**

ACVR1, activin A receptor type 1; FOP, fibrodysplasia ossificans progressiva

ifopa.org; https://rarediseases.info.nih.gov/diseases/6445/fibrodysplasia-ossificans-progressiva. Accessed 06-Oct-21

KEY FOP DATA AT ASBMR 2021

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POSTER

EFFICACY OF PALOVAROTENE IN PATIENTS WHO TRANSFERRED FROM A FOP NATURAL HISTORY STUDY TO THE PHASE 3 MOVE TRIAL

Design:

- MOVE trial (NCT03312634) is a single-arm, phase 3 study, investigating efficacy and safety of palovarotene for the treatment of FOP
- Reported on FOP patients ≥4 years of age with *R206H ACVR1* mutation who were transferred from the natural history study to MOVE trial without randomisation
- 18-month post-hoc data was presented

Key results:

- 61% lower mean volume of annualised heterotopic ossifications with palovarotene treatment in the MOVE trial versus no treatment in the NHS

Patient perspective:

- A reduction in heterotopic ossification is very promising
- A new approved drug is sometime away therefore is important to focus on patient's quality of life, early referral and management of flares

ACVR1, activin A receptor type 1; FOP, fibrodysplasia ossificans progressive

Al Mukaddam M, et al. ASBMR 2021, Abstract #VPL-403; https://cor2ed.com/podcast-rare-bone-disease-highlights-at-asbmr-2021/

OSTEOGENESIS IMPERFECTA (OI)

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- **Osteogenesis imperfecta** (OI), **also referred to as brittle bone disease**, is a rare and variable genetic disorder that is **characterised by fragile bones**. People with this condition have bones that break easily, often from little or no trauma. However, the severity is different from person to person
- OI is **caused by a mutation in a gene that affects bone formation**, bone strength, and the structure of other tissues. The incidence of OI is approximately 1 in 15-20,000 live births
- There are various forms of OI which are distinguished by their features and genetic causes. OI may be inherited in an autosomal dominant (more commonly) or autosomal recessive pattern depending on the gene involved
- People with **OI experience broken bones from infancy through puberty** with the frequency decreasing in adolescents but potentially increasing again in later life
- **Other medical issues** associated with OI include: **respiratory issues** such as asthma, **hearing loss, brittle teeth, loose joints, cardiac issues, and basilar invagination**
- Treatment is focused on managing the symptoms and aims to decrease the number of fractures and disabilities

OI, osteogenesis imperfecta
https://rarediseases.info.nih.gov/diseases/1017/osteogenesis-imperfecta. Accessed 06-Oct-21

KEY OI DATA AT ASBMR 2021

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POSTER

BASELINE PATIENT DEMOGRAPHICS AND DISEASE CHARACTERISTICS IN ADULTS WITH OSTEOGENESIS IMPERFECTA (OI) IN THE PHASE

- **Design:**
  - ASTEROID was a 12-month study of setrusumab (monoclonal antibody) in adults with type I, III or IV OI who had at least 1 fracture in the past 5 years
  - This data looked at the characteristics in the patients enrolled in the study
- **Key results:** The study reinforced the diverse characteristics of patients with OI
- **Patient perspective:**
  - The results reinforced the high fracture risk in adult OI patients and therefore the need for ongoing monitoring and treatment
  - Due to the diverse nature of the different types of OI, it would be relevant to see types studied separately

POSTER

THE PATIENT CLINICAL JOURNEY AND SOCIOECONOMIC IMPACT OF OSTEOGENESIS IMPERFECTA: A SYSTEMATIC REVIEW

- **Design:**
  - A review of OI-related publications from Jan 1995-Dec 2020
- **Key results:** Few studies reported on:
  - Standard of OI care, diagnosis and monitoring, interactions with the healthcare system and transition of care from child to adult services or, the social and economic impact of OI on patients and caregivers
- **Patient perspective:**
  - Ongoing monitoring of patients through their lifetime of OI is critical
  - Adult patients often don't receive appropriate follow-up because they were diagnosed with OI as a child and they haven't been transitioned to adult services, which is a transversal issue among other rare bone diseases

OI, osteogenesis imperfecta

Javaid M, et al. ASBMR 2021, Abstract #VPP-688; Javaid K, et al. ASBMR 2021, Abstract #1016; Rauch F, et al. ASBMR 2021, Abstract #SUN-280;
https://cor2ed.com/podcast-rare-bone-disease-highlights-at-asbmr-2021/

FIBROUS DYSPLASIA (FD) AND MCCUNE-ALBRIGHT SYNDROME (MAS)

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- **Fibrous dysplasia (FD) and McCune-Albright syndrome (MAS)** are **not inherited conditions** but are **caused by a mutation of the *GNAS1* gene**
- **Fibrous dysplasia is a skeletal disorder**, characterised by the **replacement of normal bone with fibrous bone tissue**. It presents as soft bones susceptible to fracture, chronic bone pain, and deformity
- **FD may involve one or multiple bones** and can affect any bone in the body. The most common sites are the bones in the skull and face, the long bones in the arms and legs, the pelvis, and the ribs
- Patients can experience **symptoms such as chronic pain, hormonal abnormalities, and restricted mobility, vision, and hearing**
- **McCune-Albright syndrome is the combination of FD and abnormal hormone levels**, rare benign tumour of the musculoskeletal system and/or cafe-au-lait birthmarks. Features resulting from abnormal hormone levels may include precocious puberty especially in girls, excess growth hormone; thyroid lesions with possible hyperthyroidism; renal phosphate wasting, and, rarely, Cushing syndrome caused by an excess of the hormone cortisol produced by the adrenal glands of the kidney
- **There is no known cure for FD**. Medications known as bisphosphonates can help reduce pain and surgery may be used to treat fractures or to correct misshapen bones

FD, fibrous dysplasia; GNAS1, guanine nucleotide-binding protein, alpha-stimulating activity polypeptide 1; MAS, McCune-Albright syndrome

info@fibrousdyplasia.org; https://rarediseases.info.nih.gov/diseases/6444/fibrous-dysplasia. Accessed 06-Oct-21

KEY FD/MAS DATA AT ASBMR 2021

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POSTER

EFFECT OF A MULTIDISCIPLINARY CARE PATHWAY ON QUALITY OF LIFE AND PAIN FOR PATIENTS WITH FD/MAS: A PROSPECTIVE OBSERVATIONAL STUDY

Design:

- This study assessed the effect of extensive counselling and multi-disciplinary care on quality of life and pain using diverse patients' questionnaires

Key results:

- Additional patient information and a multidisciplinary care adds to treatment success for patients with FD/MAS
- Patients treated with bisphosphonates had a significant reduction in pain and an improvement in physical function

Patient perspective:

- Counselling and follow-up of patients affected by FD/MAS led to a significant improvement in quality of life
- Multidisciplinary care is absolutely key for FD/MAS as for all rare bone conditions

FD, fibrous dysplasia; MAS, McCune-Albright syndrome
Meier M, et al. ASBMR 2021, Abstract #VPL-407; https://cor2ed.com/podcast-rare-bone-disease-highlights-at-asbmr-2021/

TAKE HOME MESSAGES

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FROM: CHARLENE WALDMAN AND INÊS ALVES

- There were a large number of abstracts related to rare bone disease presented at the ASMBR 2021
- It is very encouraging that the scientific community are researching these rare and ultra-rare conditions
- There are many stakeholders involved in managing patients with rare bone disease and it is key that all stakeholders continue to collaborate
- Patient experts and patient organisations play a key role in raising awareness of these diseases and ensuring that research into them remains high on the agenda and focused of unmet needs

https://cor2ed.com/podcast-rare-bone-disease-highlights-at-asbmr-2021/

RARE BONE DISEASE ORGANIZATIONS

REPRESENTED BY CHARLENE WALDMAN & INÊS ALVES

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RARE BONE DISEASE ALLIANCE

RBDA
RARE BONE DISEASE ALLIANCE

For more information:
https://rbdalliance.org/

EUROPEAN RARE BONE FORUM

ERBF
European Rare Bone Forum

For more information:
https://rarebone.org/

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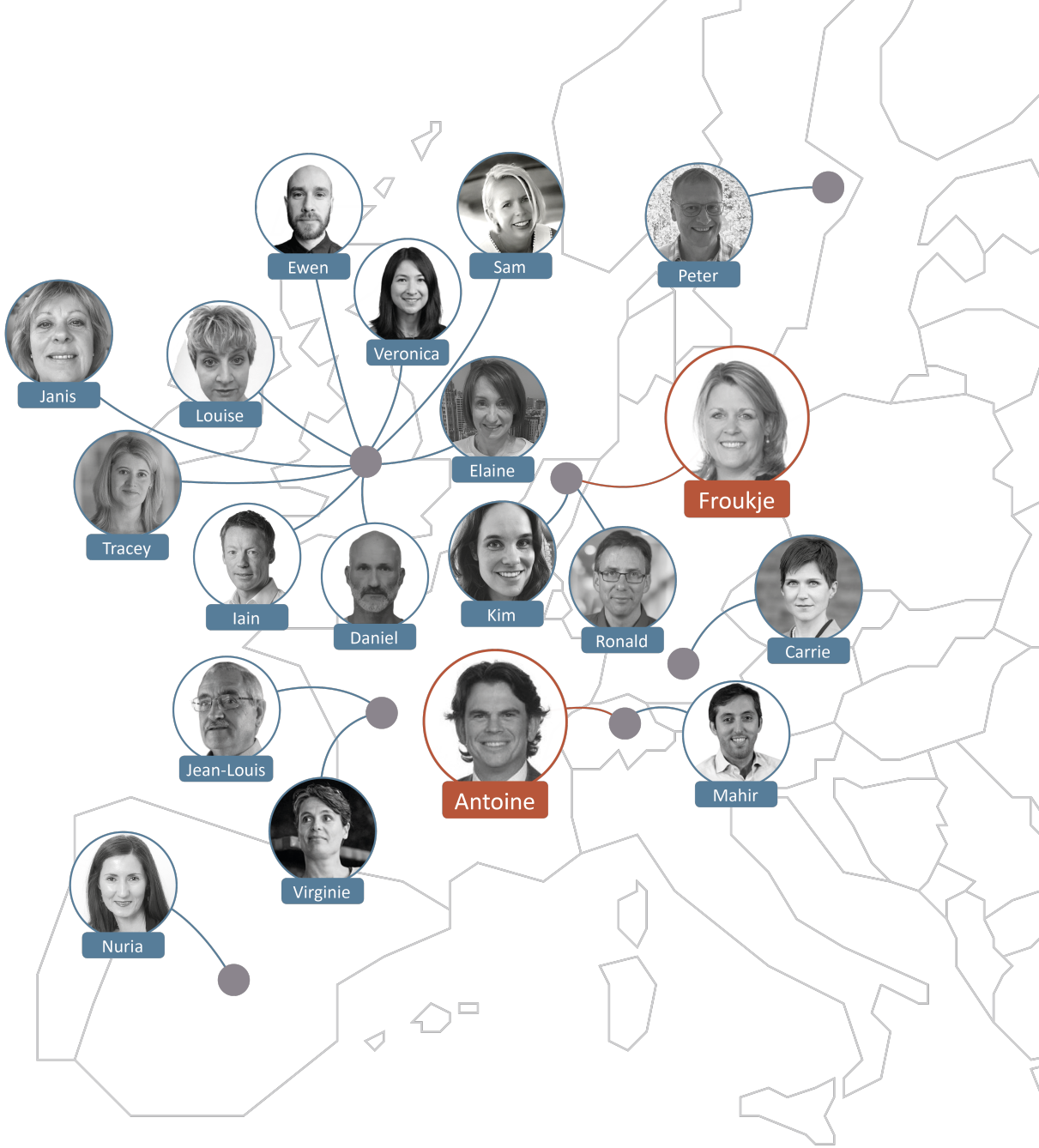

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