Disease Registry & Biobank, Patient Association and Biopharmaceutical Company: a successful work in concert for Multiple Osteochondromas disease

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MULTIPLE OSTEOCHONDROMAS

Multiple Osteochondromas (MO) is an autosomal dominant rare skeletal disorder whose key clinical features are benign cartilage-capped bone tumors arising from the growth plates of long bones called osteochondromas (OCs). MO is caused in 90% of patients by heterozygous mutations in the heparan sulphate (HS)-synthesizing enzymes EXT1/EXT2, implicated in the cartilage growth during endochondral ossification. OCs are rarely present at birth and grow in size and number until skeletal maturity, producing pain and resulting in various deformities and functional limitations. There are currently no effective therapeutic options to prevent OCs formation. Serial x-ray evaluations are the most common method to monitor OC growth and deformities with surgery as the only available treatment for OC excision and deformity correction. MO patients have multiple surgeries during their lifetime. The most serious complication in adults is the malignant transformation of OCs into secondary peripheral chondrosarcomas (1-5%).

REGISTRY DEFINITION

A patient registry is an organized system that uses observational study methods to collect uniform data to evaluate specified outcomes for a population defined by a particular disease, or exposure, and that serves one or more predetermined scientific, clinical or policy purposes

BIOBANK DEFINITION

A collection of biological material and the associated data and information stored in an organised system, for a population or a large subset of a population

REGISTRY OF MULTIPLE OSTEOCONDROMAS (REM) & BIOBANK OF GENETIC SAMPLE (BIOGEN)

To improve diagnosis, research and development of personalized treatments in rare disease, the Medical Genetic Department (MGD) of Istituto Ortopedico Rizzoli created 4 diseases registries, including for MO, and a strictly interconnected biobank aiming to collect high quality data & biological materials of patients. Since 2003, MGD has initiated a collection process for patient information, implemented a data standardization process and established in 2013 the Registry for Multiple Osteochondromas Disease (REM). A comparable process has been performed for biosample storage and maintenance, leading to the Biobank for Genetic Samples (BIOGEN) in 2013. Since the beginning, these two entities have worked in concert to provide high quality data linked to high quality biosamples.

The procedures for collection and governance of all data and specimens according to the ELSI standards have been implemented and supported by the cooperation among clinicians, geneticists, and researchers. In addition, a strong collaboration with ACAR Onlus, the Italian MO patients' association has been active for many years to support REM implementation. This model, presented in ECRD2016, has been very productive. ACAR with an effective patient empowerment is actively involved in REM & BIOGEN governance and participated as a member of the Advisory Board.

With the support and collaboration of Clementia Pharmaceuticals, a biopharmaceutical company dedicated to developing treatments for rare bone diseases, extensive analyses were performed on data from children <18 years old. These iterative analyses were essential to provide information on natural history of MO and facilitate design of a clinical trial for treatment of MO patients with palovarotene (PVO), a retinoic acid receptor gamma (RARγ) agonist. This clinical trial will evaluate the efficacy and safety of PVO treatment to prevent new OC, reduce morbidity and deformity, and preserve functionality in patients affected by MO.

The phase 2 clinical trial PVO-2A-201 has been opened with an IND at the FDA and has commenced enrolling MO paediatric patients. The protocol is currently being reviewed by the Paediatric Committee at EMA to support recruitment of European patients. REM & BIOGEN data are still contributing to support this process. ACAR provided a forum for patient outreach and for information sharing. Collaboration between patients' association, healthcare provider and pharmaceutical company allow longitudinal patient data (diagnosis, disease features and outcomes) to rationally guide clinical trial design with the goal of improving patient's health and quality of life by preventing invasive surgical treatment with pharmacological therapy.

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