Challenges and solutions in the set-up of an international, cross-boundary, repurposing clinical trial for Osteogenesis Imperfecta

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INTRODUCTION

Matrix-directed therapy in older adolescents and adults with osteogenesis imperfecta – the "MOI-A" project within the REMEDi4ALL Consortium – is assessing the repurposing of losartan in adults and older adolescents with osteogenesis imperfecta, an inherited form of bone fragility caused in the majority of cases by mutations in one of the two genes encoding type I collagen. We present the challenges we have encountered during the set-up of this international study due to the variation in regulatory processes across national boundaries.

FACING CHALLENGES

RDT Meetings

- As a demonstrator project in REMEDi4ALL we have a Research Development Team (RDT) assigned to our project, including expertise across the regulatory pathway for drug development
- We presented our challenges at these meetings, detailing discussions between study team, regulators and Sponsors and they helped to facilitate solutions

Sponsorship Agreement

- We had to decide whether to have one sponsor with a legal representative or a co-sponsorship agreement
- The co-sponsorship agreement was determined to be the best practice to ensure a clear outline of responsibilities for different aspects of the study in their representative countries
- There were challenges in preparing a co-sponsorship agreement because of lack of harmonization between UK & EU regulations.

Protocol preparation and regulatory approval

We will use one master protocol across both countries ensuring the same procedures for treatment and outcome measures are followed in both countries

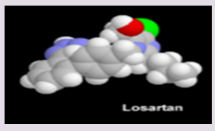
Reporting of SUSARs approaches

To ensure that we can comply with pharmacovigilance guidance we decided:

- The UK Sponsor will report all the study SUSARs to the MHRA
- The Italian Sponsor will report all the study SUSARs to EVCTM/AIFA
- Co-CIs will each inform the other immediately of any such events

Availability of the IMP

- We were unable to source one IMP product available in both countries
- Agreed to use two different IMP brands
- Agreed to use one of the SmPCs as the reference safety information in both countries



Database arrangements

- Patients will be randomised from one central randomisation system
- Data will be collected in one central database to streamline study oversight
- Having the one central database would be the best way to collate safety events centrally for reporting to the regulatory authorities

CONCLUSION

By presenting the current status of each of these areas we have demonstrated the complex regulatory environment when working cross-boundaries, and the advantages of the input of a RDT within the REMEDi4ALL Consortium. We hope that the details of the discussions between the RDT, study team, regulatory authorities and eventual solutions will help future studies to be able to proceed more swiftly.

Matrix-directed therapy in older adolescents and adults with osteogenesis imperfecta – the "MOI-A" study

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