1. PUBLISHABLE SUMMARY

Summary of the context and overall objectives of the project (For the final period, include the conclusions of the action)

EU-PEARL aims to transform the current single-treatment clinical trial approach to a platform trial approach, which can include multiple treatments sourced from different companies and organizations. To achieve this highly ambitious goal, the public and private sectors have formed a strategic alliance to develop an Integrated Research Platform (IRP) paradigm to conduct these platform trials. This IRP paradigm will be centred on a master trial protocol which can accommodate multi-sourced treatments, while using existing hospital infrastructure and federated patient data in the trial design, planning and execution. Moreover, the IRP paradigm will aim to assure an optimized regulatory pathway for these novel treatments. Altogether, EU-PEARL will develop frameworks and tools that will pave the way for more efficient development of new treatments, while also improving patient centricity in clinical trials.

For a variety of diseases, there is a clinical need for faster development of new treatments. Currently, the standard clinical trial model evaluates one drug at the time, which often results in sequential cycles of drug development and might thus not be the most efficient way of getting treatments to patients. Moreover, from a patient-centric perspective, the current trial environment often creates challenges for recruitment and patients struggle to navigate the complex trial landscape to find the optimal study.

Platform trial designs offer opportunities for more efficient drug development that could subsequently speed up the delivery of new treatments to patients. Although such multi-treatment platform trials are already being conducted, the absence of a general framework for this new clinical trial model creates hesitancy to initiate this collaborative approaches more routinely. This became again apparent during the COVID-19 response, as hundreds of individual trials were set up but many struggled to achieve meaningful outcomes quickly.

EU-PEARL is developing a framework to allow for novel treatments to be tested and developed in an IRP setting that bridges clinical care and clinical research, while involving multiple companies and organizations.

To achieve this goal EU-PEARL has 4 objectives:
1) Create an open, dynamic and patient inclusive IRP Governance structure to manage regulatory, ethical, legal, statistical and data requirements;
2) Disseminate and exploit the EU-PEARL IRP paradigm by providing the necessary common tools, procedures, expertise and operational skills that meet the highest scientific, regulatory & ethical standards and best practices. These are to be developed jointly by public and industry partners in a consensus-based approach;
3) Create site and data networks ready to execute EU-PEARL's platform master protocols, by developing 4 ready-to-go IRPs based on 4 disease areas: Major Depressive Disorder (MDD), Tuberculosis (TB), Non-Alcoholic Steatohepatitis (NASH) and Neurofibromatosis (NF). Each of these areas has its own specific challenges, which can be used as examples for other teams to build on when they are interested to initiate an IRP; and
4) Conceptualize a trusted, sustainable entity in order to sustain a generalizable IRP framework that can be used for any disease area with unmet need.

Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far (For the final period please include an overview of the results and their exploitation and dissemination)

During the first year of EU-PEARL (01/11/2019 – 31/10/2020) the project team has focused on laying a foundation for the creation of generic and disease-specific IRP frameworks and common tools, while generating awareness on the project and the advantages of adaptive platform trials.

From a disease-agnostic perspective, generic "data management and governance" guidelines have been developed for the project. Furthermore, to build and share knowledge around platform trials within the stakeholder community, EU-PEARL developed the following publicly available documents (available on EU-PEARL website: https://eu-pearl.eu/): 1) Glossary with key terminology and scenarios for platform trials; 2) Report on best practices in platform trial operational aspects. Also, several publications were developed within the project, mainly covering methodological challenges – statistics – and linking EU-PEARL to COVID-19 platform trials which are now in place.

In parallel, teams focussing on disease-specific IRPs (MDD, TB, NASH, NF) made an inventory and assessments of existing clinical trial designs and specific drug development challenges, for each specific condition. Disease-specific teams, in collaboration with expert methodologists, started to establish the foundations to address trial design challenges and master protocol development in each of the four disease areas. Additionally, a Clinical Network Working Group has been created to guide the setup of clinical site networks for each of the disease-specific IRPs with the public partners. Training and discussions were initiated with disease-specific teams to start building a federated data network and solidify the general data requirements. Patient engagement structures have been set in place to enable close collaboration with patient representatives and ensure that the patient's voice is heard throughout the design of the EU-PEARL IRP frameworks.

Within its first year, EU-PEARL also initiated efforts to make the project become widely understood: besides a communication and dissemination strategy, EU-PEARL also developed an alliance strategy which maps how EU-PEARL will promote knowledge and understanding on platform trials and introduce the concept of IRPs, launch dialogue and collaborations with relevant external expert and related on-going initiatives, and foster the sustainability and endorsement for future adoption of this innovative framework.

Furthermore, EU-PEARL organised 4 successful online Stakeholder Workshop sessions on October'20 focused on: regulatory & ethical issues, methodological challenges and patient engagement priorities for IRP development (More information: https://eu-pearl.eu/eu-pearl-stakeholder-workshop-future-clinical-trials/). The virtual environment created the opportunity to include over 600 global experts in the discussions, with significant amount of returning attendees. The increased interest might be seen against the backdrop of calls for collaborative approaches to address the challenges which healthcare is facing in a rapid response to COVID-19. Overall, the EU-PEARL Workshop created a great opportunity to interact with a variety of external stakeholders (regulators, statisticians, patients) on the concept of multi-company platform trials and the benefits of building collaborative IRPs.

Progress beyond the state of the art, expected results until the end of the project and potential impacts (including the socio-economic impact and the wider societal implications of the project so far)

Upon completion of the EU-PEARL project, frameworks for the 4 disease-specific IRPs (MDD, TB, NASH, NF) including the 4 master protocols, will be available. Additionally, more generalizable frameworks on how to set up and conduct an IRP will be written up, together with a plan on how to sustain and maintain these frameworks through a novel entity. By using these frameworks, future platform trials will be set up to generate high quality evidence that is based on strong and consistent data networks and statistical methods. These frameworks will also emphasize and provide guidance on how to embed the patient voice as a partner in the development of IRPs.

Altogether, the EU-PEARL IRP framework will lay the foundation for a clinical trial environment that enables more collaborative platform trials and creates opportunity for faster response to patient needs.

Address (URL) of the project's public website

https://eu-pearl.eu/

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