ERN Support and Training programme- WP17- EJP RD

Report Workshop "Modelling & Simulation (M&S): Research Methodologies for Small Populations in Rare Diseases"

Date/Venue/Format

4-5 July 2022, Hotel Excelsior, Bari, Italy, in person and on-line

Numbers (participants, speakers, ERNs represented, patient representatives)

Speakers - 13

Participants - 23

ERN represented - 17

Patient representatives - none

Analysis of the workshop satisfaction survey

The survey results showed a very good satisfactory rate. 59% of the participants who completed the survey evaluated it as useful while 36,4% evaluated it as extremely useful.

2-3 participants' testimonials

Antonella Potenza - Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan

'The research area I belong to is represented by rare cerebrovascular disease (VASCERN). In particular, as a biologist, I'm carrying on a research on two routes: 1) searching for novel putative and predictive biomarkers in biological samples through "omics" approaches 2) differentiation and characterization of patient blood-derived progenitor cells in order to define their molecular signatures and to recreate a cellular model. For this reason, I'm still far from the identification of a specific disease-related target, but I think that this workshop has widened my knowledge and view on disease models and the possibility to use in-silico studies and machine learning approaches for drug discovery.'

Mariapia Caputo - IRCCS, Istituto Tumori "Giovanni Paolo II", Bari

'The best aspects of this event were the practical sessions. I would carry out drug repurposing studies in oncological diseases treated in my institute.'

David Gómez Andrés - H.U. Vall d'Hebron, Spain

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'The Modelling and Simulation topic was very new for me and should be incorporated in the curricula for those who are working in rare disorders. The workshop was helpful to better understand the design of pre-clinical studies and better understanding of early phase trials I am involved in.'

If applicable a main result of the workshop (e.g. working group created to do practical sessions)

During the case study: '*A MYCN antisense PNA as a novel therapeutic strategy for the treatment of neuroblastoma in children' the* participants had the opportunity to:

- Predict overall drug properties and treatment performance in terms of:
  - PK in plasma and tumour
  - PD - MYCN Expression inhibition; Tumour viability; Tumour growth and size effects on disease progression
- Select range of doses to be used in paediatric patients (FTIH).
- Design and evaluate clinical protocol in neuroblastoma patients.

During the case study '*Machine Learning approach for prediction of developmental toxicity of chemicals'* the participants had the chance to learn why a machine learning is needed and how machine learning is implemented. Practical introduction to pharmacological prediction platforms with a focus on toxicity to assess general pharmacological friendliness of small molecules were shown and tested.

Conclusions, lessons learned, best practices to keep in mind.

The training methodology was based on **lectures, seminars, and practical sessions,** to provide concrete research skills.

Specifically, **real-life case studies** were discussed during interactive and user-friendly seminars where the attendees had the opportunity to **apply knowledge using available databases and software to consider while designing and planning a study in the field of rare diseases.**

The Workshop Agenda foresaw three main topics:

- **Paediatric toxicology** on application of web platforms for in-silico assessment of toxicity and the utility of a machine learning approach for the prediction of developmental toxicity of chemicals covered by University of Bari 'Aldo Moro' (UNIBA)
- **Regulatory part** on what is needed for translational preclinical studies covered by Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF)

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- **Clinical part** on a) the utility of PK/PD modelling and b) the simulation in drug development for small populations covered by University College London (UCL).

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