ERICA

European Rare Disease Research Coordination and Support Action

WP4

Luca Sangiorgi, Ralf Dieter Hilgers

Wednesday, December 11th 2024

European Commission

ERICA has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 964908

European Reference Networks

Deliverables we are currently working on

Deliverables already completed:

D4.1 Procedure to provide ERN experts to EMA for expert opinion on RD (M6)

D4.2 Report on prepared factsheets and Youtube videos (M18)

D4.3 Report on frequency of use of the website (M24)

D4.4 Report on unmet clinical needs in ERN-overarching diseases (M24)

D4.5 Report on the outcome of clinical trial workshops (M39)

D4.6 Report on achievements of ERN-EMA dialogue (M42)

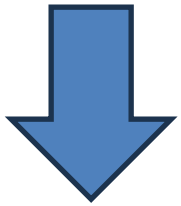
Next deliverable (February 2025):

D4.7 Report on establishing foundations for Patient Engagement Framework (M48)

Task 4.1: WP4 Expert Working Group (WP4 EWG), ERICA specific webpage on RD clinical trials, and RD Trial Workshops (IOR, UKA, EURORDIS) (M1-48)

Expert working group (EWG) manage WP4 activities, focus on stimulating the process of ERN clinical trials implementation

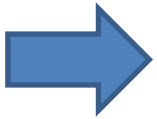
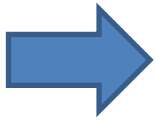
- EJP RD infrastructure
- Virtual consultation activities on Clinical Patients Management System (CPMS)
- RD Trial Workshops
- Webinar series



Inter-ERN support for RD's unmet clinical need

Work carried out

Training Program

Webinars  Factsheets  Youtube Videos

https://erica-rd.eu/work-packages/clinical-trial-support/

Webinars, Factsheets and Youtube Videos

- **Essential requirements before thinking about a clinical trial**

  Viviana Giannuzzi, Benzi Foundation

- **Definition of orphan drug by the EMA**

  Armando Magrelli, ISS

- **Feasibility for clinical trial – what Pharma Companies expect and what they require as indispensable**

  Diego Ardigò, Chiesi

Webinars, Factsheets and Youtube Videos

- **Introduction on Patient-Reported Outcomes and considerations before including them in a clinical trial. Study case from the ERN-EuroBloodNet**

Céline Desvignes-Gleizes (Mapi Research Trust), Andreas Glenthøj (Copenhagen University Hospital), Dore Peereboom (Patient advocate, Stichting Zeldzame Bloedziekten)

- **Framework for Patient Engagement in clinical trials**

Maria Cavalier, Virginie Hivert

- **REMEDI4ALL/ drug repourposing and clinical trial readiness**

Anton Ussi, EATRIS

Webinars, Factsheets and Youtube Videos

- **c4c trials, education and training**

Turner (c4c), Chloe Bickerstaff (c4c), Francesca Rocchi (INCIPIT, Bambino Gesù Children Hospital), Becca Leary (University of Newcastle)

- **c4c expert advice, patient and public involvement, data standards**

Mark Turner (c4c), Fenna Mahler (c4c), Pamela Dicks (NHS Scotland Childrens Research Network and eYPAGnet), Becca Leary (University of Newcastle)

Fondazione per la Ricerca Farmacologica Gianni Benzi Onlus

Proposal for developing 3 e-learning modules on clinical research in RDs available on ERICA website

Training activities on regulatory, ethical and methodological aspects of rare diseases clinical research:

- ✓ ICH-Good Clinical Practice (GCP)
- ✓ Ethics and regulatory issues in clinical research (use of health and genetic data)
- ✓ Clinical research methodology (data collection, reporting, management, and analysis)

Task 4.2: Interaction with stakeholders essential in facilitating ERN clinical trials (IOR, UKA) (M12-48)

Stakeholders

- EJP RD (in particular WP14)
- EMA
- BBMRI (WP4 in collaboration with WP2)
- IRDiRC

Activities with EMA

EMA expert opinion have been provided from different ERNs.

The ERN BOND coordination (ERN-EMA liaison officer), managed about 20 contacts by EMA for requesting ERN expert opinion on clinical activities, studies, registries into RD drug development, benefit/risk evaluation and monitoring.

Activities with IRDiRC

Meeting with Diego Ardigò from IRDiRC to define a procedure to evaluate the feasibility of the Clinical Trial

- to increase the number of RD clinical trials in EU
- to increase the participation of ERN HCPs and patients engagment to the study design

IRDiRC Task Force Participation

2022 Shared Molecular Etiologies Underlying Multiple Rare Diseases

2022: PLUTO PROJECT – Disregarded Rare Diseases

2023: Preparing for genetic N-of-1 treatments of patients with ultra-rare mutations

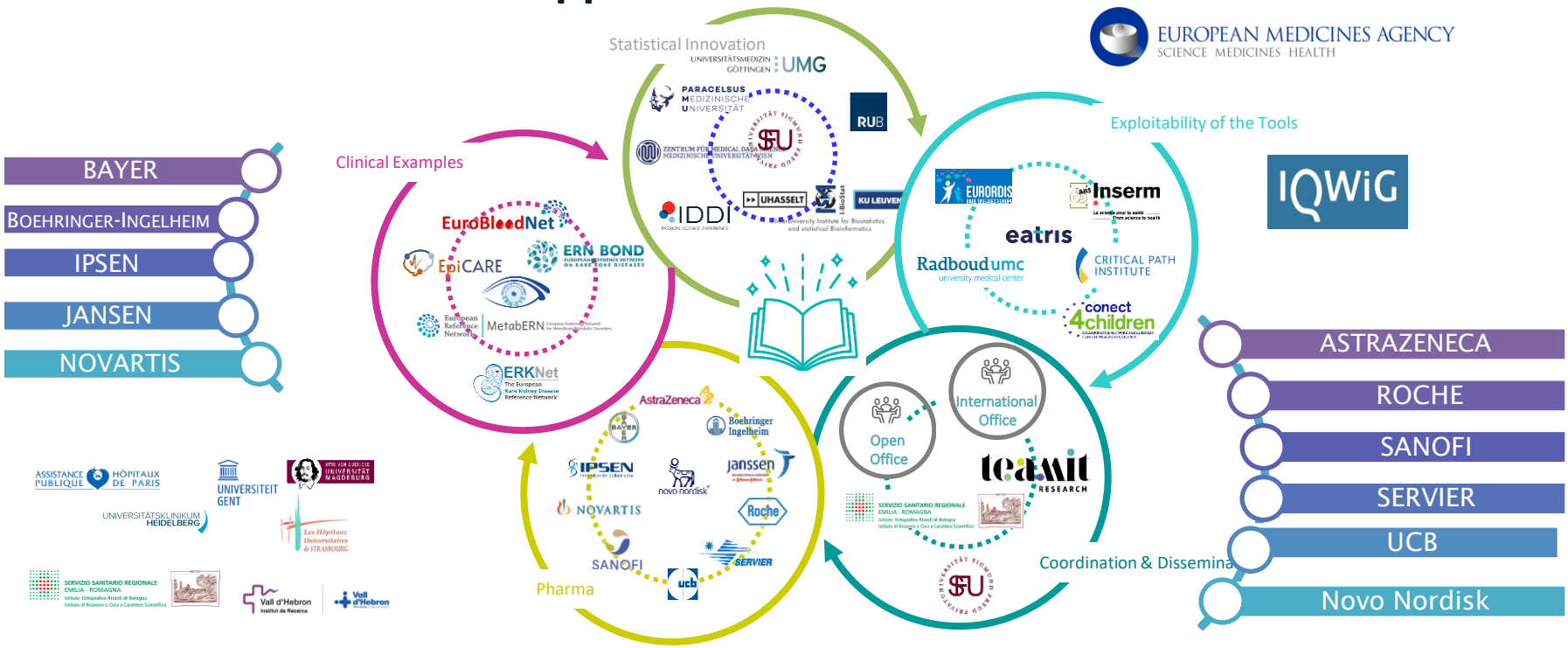
Interaction ERNs-Industry

Together For Rare Diseases (Together4RD) is a multi-stakeholder initiative aimed supporting ERNs to collaborate with stakeholders, particularly with the pharmaceutical industry, including clinical trials on rare & ultra-rare conditions.

First webinar available on ERICA Website

- to illustrate how the private industry could increase RDs research and drug development.

RealiseD - Succesfull Application



Networking – Talks - Publications

RD Trial Workshops

- 2021: **ERN Skin** Scientic Day 2021" 19.2.21
- 2021: **ERN Liver** Membership Meeting 3.6.21
- 2022 **ERN-RND**
- 2023 ***Endo ERN* – GA Meeting**
- 2023 May: ***ERN BOND* – GA Meeting**
- 2023 June. ***ERN Liver*** – Workshop
- 2023 ***ERN EpiCare together with Rima Nabbout***
- 2024 May: ***ERKnet*– Webinar**
- 2024 June: ***ERN Blood***
- 2024 November: ***ERN Blood***
- 2024 November: ***MetabERN***

Reached 9 ERN's
Story continues

ERN CT Awareness 2023

2021: Webinar: Does Randomization matter in RD clinical trials

2024: Webinar: Webinar for Modelling natural history in longitudinal data- Challenges and Solutions

2023 November: **IQWiG Herbstsymposium**

‚Methodische Lösungsansätze zur Generierung belastbarer(er) Evidenz bei seltenen Erkrankungen' - 25.11.2023

Publications

2021: Traschütz et al. *Neurology*. Natural History, Phenotypic, Spectrum and Discriminatave Features of Multisystem RFC1 Disease

2021: Rückbeil, M. V., Manolov, M., & Hilgers, R. D. (2021). The Choice of a Randomization Procedure in Survival Studies with Nonproportional Hazards. Statistics in Biopharmaceutical Research, 15(2), 323–331. https://doi.org/10.1080/19466315.2021.1952894

2022: Römer, T.; Franzen, S.; Kravets, H.; Farrag, A.; Makowska, A.; Christiansen, H.; Eble, M.J.; Timmermann, B.; Staatz, G.; Mottaghy, F.M.; et al. Multimodal Treatment of **Nasopharyngeal Carcinoma in Children**, Adolescents and Young Adults-Extended Follow-Up of the NPC-2003-GPOH Study Cohort and Patients of the Interim Cohort. Cancers 2022, 14, 1261. https://doi.org/10.3390/cancers14051261

2023: Verbeeck, J., Dirani, M., Bauer, J.W. et al. **Composite endpoints**, including patient reported outcomes, in rare diseases. Orphanet J Rare Dis 18, 262 (2023). https://doi.org/10.1186/s13023-023-02819-x

2023: Bülow T, Hilgers R-D, Heussen N (2023) Confidence interval comparison: **Precision of maximum likelihood estimates in LLOQ** affected data. PLoS ONE 18(11): e0293640. https://doi.org/10.1371/journal.pone.0293640

2024: **Schoenen, S., Heussen, N., Verbeeck, J. and Hilgers R-D. The impact of allocation bias on test decisions in clinical trials with multiple endpoints using multiple testing strategies. BMC Med Res Methodol 24, 223 (2024). https://doi.org/10.1186/s12874-024-02335-x**

2024: **Wied S, Hilgers R-D, Heussen N, Kotulska K, Dirani M, Kuchenbuch M, et al. (2024) Methodological insights from the EPISTOP trial to designing clinical trials in rare diseases—A secondary analysis of a randomized clinical trial. PLoS ONE 19(12): e0312936. https://doi.org/10.1371/journal.pone.0312936**

2024: Hilgers, Ralf-Dieter, Heussen Nicole. Methodological approaches for generating robust evidence from trials in rare diseases Zeitschrift für Evidenz, Fortbildung und Qualität im Gesundheitswesen, Volume 189, 66 - 72

Publications

2021: Ott et al. *Hepatology*. Designing Clinical Trials in Wilson's Disease

2024: Keith Smart; Victoria Abbott-Fleming; Frank Birklein; Stephen Bruehl; Erica Corcoran; Simon Day; Michael C Ferraro; Sharon Grieve; Ralf-Dieter Hilgers; Carolyn Ingram; David J Keene; Franz König; Candida McCabe; Stavros Nikolakopoulos; Neil E O'Connell. Optimising clinical trial methods for complex regional pain syndrome (CRPS): a methodological framework (OptiMeth-CRPS). Submitted.

2025: ERN Guard. Clinical, genetic and methodological considerations for the design and execution of interventional studies in rare cardiac diseases. In prep

2025: EJP-RD. Added Value of transversal developments to innovative trials methodologies in rare disease clinical studies. In prep

Thank you!