Wednesday 6 April 2022

ERN GUARD-Heart

Gateway to Uncommon And Rare Diseases of the Heart

EUROPEAN REFERENCE NETWORKS
FOR RARE, LOW-PREVALENCE AND COMPLEX DISEASES

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ERN GUARD-HEART BIMONTHLY NEWSLETTER YEAR 2022 NUMBER 3

ERNs Unite to Help Ukrainian Rare Disease Patients

Amsterdam, 23 March 2022

With the ongoing war, a large number of Ukrainian citizens have difficulty accessing care in Ukraine or are fleeing to the EU, mainly to countries in the Eastern part of Europe for the time being. Many of these refugees have, or will have, health problems. In the last few weeks, EU governments have clearly committed to ensure adequate healthcare to these refugees, including patients with rare disease and those requiring chronic treatments.

All 24 European Reference Networks (ERNs) have launched a dedicated website and a social media campaign to collect information and to help health professionals, if needed, to find support for the Ukrainian patients with rare diseases. ERN health care providers (HCPs), particularly those located in the countries currently receiving large numbers of refugees from Ukraine (i.e., Poland, Slovakia, Hungary, and Romania) have announced their readiness to help Ukrainian patients with rare or very rare diseases. These HCPs work in close collaboration with the ERNs they belong to. For more information, please visit the following website: https://www.erncare4ua.com/♥

11th Board meeting ERN GUARD-Heart

Amsterdam, 8 March 2022

On 8 March, an (online) board meeting was held for all 44 full members, 9 affiliated partners and the patient advocacy groups of ERN GUARD-Heart. With 57 participants there was time to look back at the past 5 ERN years and to present and discuss the final plans for the coming years (i.e., the bridging grant period). The slides of the meeting have been shared with all the attendees and members. ♥

Thematic area leaders

Amsterdam, 8 March 2022

For the new thematic areas Congenital Heart Diseases (thematic area 4) and Other rare heart diseases (thematic area 5) an election for leadership was organized, just before the board meeting. Thematic area 4 will be led by Prof. Nico Blom (Leiden/Utrecht) and Dr. Annemien van den Bosch (Rotterdam). They had a close finish and, together with the Coordinator (Prof. Arthur Wilde), decided to work together in this large field, to be able to coordinate the activities for both pediatric patients (Blom) and adult patients (Van den Bosch) properly. Thematic area 5 will be led by Prof. Alida Caforio (Padua).

Also thematic area 1 (familial electrical diseases in adults and children) needed a new leader, since the former leader, Dr. Carlo Napolitano decided to step back. Dr. Elena Arbelo (Barcelona) was chosen by the members as the new leader of thematic area 1. The leadership of thematic areas 2 and 3 has not been changed and will be continued by respectively Philippe Charron and Georgia Sarquella-Brugada. ♥

ESC European Society of Cardiology
Europace (2022), **00**, 1–61
https://doi.org/10.1093/europace/euac030

POSITION PAPER

European Heart Rhythm Association (EHRA)/ Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) Expert Consensus Statement on the state of genetic testing for cardiac diseases

Arthur A. M. Wilde (EHRA Chair)[1,*,†,‡,¶], Christopher Semsarian (APHRS Co-Chair)[2,*,†], Manlio F. Márquez (LAHRS Co-Chair)[3,*,†], Alireza Sepehri Shamloo[4], Michael J. Ackerman[5], Euan A. Ashley[6], Eduardo Back Sternick[7], Héctor Barajas-Martinez[8], Elijah R. Behr[9,¶], Connie R. Bezzina[11,‡], Jeroen Breckpot[12,‡], Philippe Charron[13,‡], Priya Chockalingam[14], Lia Crotti[15,16,17,‡,¶], Michael H. Gollob[18], Steven Lubitz[19], Naomasa Makita[20], Seiko Ohno[21], Martín Ortiz-Genga[22], Luciana Sacilotto[23], Eric Schulze-Bahr[24,‡,¶], Wataru Shimizu[25], Nona Sotoodehnia[26], Rafik Tadros[27], James S. Ware[28,29], David S. Winlaw[30], and Elizabeth S. Kaufman (HRS Co-Chair)[31,*,†]

Genetic testing has advanced significantly since the publication of the 2011 HRS/EHRA Expert Consensus Statement on the State of Genetic Testing for the Channelopathies and Cardiomyopathies. In addition to single-gene testing, there is now the ability to perform whole-exome sequencing (WES) and whole-genome sequencing (WGS). There is growing appreciation of oligogenic disorders, the role of modifier genes, and the use of genetic testing for risk stratification, even in common cardiac diseases such as coronary artery disease or atrial fibrillation, including a proposal for a score awaiting validation. This document, as a result of important **effort of ERN GUARD-Heart HCPs**, reviews the state of genetic testing at the present time, and addresses the questions of what tests to perform and when to perform them. Direct link to the publication:
https://academic.oup.com/europace/advance-article/doi/10.1093/europace/euac030/6562982?guestAccessKey=e2d1d4dd-4e21-4073-bda2-ae40ca006101

European Reference Network for rare, low prevalence, or complex diseases of the heart (ERN GUARD-Heart): 5 year anniversary

Amsterdam, March 2022

On 8 march 2022, a short manuscript has been published in the European Heart Journal to provide an overview of the activities of the ERN GUARD-Heart in the first 5 years of its existence. The manuscript has been published in the category CardioPulse (maximum 4 authors), co-authoring Arthur Wilde and Ahmad Amin (ERN Coordination team), Philippe Charron (leader of the thematic area familial cardiomyopathies in adults and children), and Ruth Biller (chair of the Patient Advocacy Board in the ERN GUARD-Heart). ♥
Free-access link: https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehac117/6543968?guestAccessKey=805b3968-b5ee-49dc-aec6-409bc2fc850b

ERN Workshop in Lyon: open for registration!

European Reference Network
for rare or low prevalence complex diseases

Network
Heart Diseases
(ERN GUARD-HEART)

Member
Hospices Civils de Lyon — France

Within the context of EJP Rare Diseases' ERN Workshops, a face-to-face workshop entitled "*Functional exploration of genetic variants in cardiac diseases*", will be organized by Philippe Chevalier of the Hospices Civils de Lyon. The workshop aims to focus on functional explorations of genetic variants using Drosophila, C. elegans, Zebrafish and iPSc models to better understand the molecular bases of genetic diseases, in particular heart and muscle diseases,
The in-person event will take place over two days on **June 14th – 15th** at the Hospices Civils de Lyon in Lyon, France.

The workshop is open, by prior registration, to cardiologists, molecular biologists, post-docs, medical fellows, and PhD students and persons who are employees of or affiliated to an ERN Full Member or affiliated Partner institution.

The training workshop is free of charge and consists of interactive presentations and discussions.
Registration closes on 1 May 2022, and those selected to participate from among the applicants will be informed by 9 May 20202 of their selection.

More information, draft program and registration here:

https://www.ejpraremdiseases.org/event/ejp-rd-ern-workshop-functional-exploration-of-genetic-variants-in-cardiac-diseases/ ♥

Scientific Network Session focused on Lamin A/C Cardiomyopathy

Register (for free) via https://www.lmnacardiac.org/research-meeting/

Soest, 30 March 2022

LMNAcardiac.org is a relatively new network with special focus on LMNA-linked cardiac diseases. They are one of the European Patient Advocacy Groups (ePAGs) of the ERN GUARD-Heart. They aim to provide a platform for both patients and experts to find information and help to speed up research and developments in LMNA-related cardiac diseases. Their focus is on networking and making connections between the researchers, experts, companies and patients. In an effort to further strengthen this network, LMNAcardiac.org together with the Netherlands Heart Institute, will organize a scientific session focused on Lamin A/C Cardiomyopathy. ♥

Survey from Working Group Pregnancy and Family Planning

Pisa, 1 March 2022

The ERN Working Group Pregnancy and Family Planning is very glad to inform you that the surveys developed by this Working Group have been finalized, with a considerable effort of both the translators and the Working Group Team, All the 8 versions of the surveys have been uploaded in the EU Survey platform (1 survey for healthcare professionals and 7 survey versions for the patients). It would be great if all members, affiliated partners and patients would fill in one of the survey's below:

1) Survey for healthcare professionals:
https://ec.europa.eu/eusurvey/runner/ERN_PregnancyFamilyPlanning_HCPs

2) Survey for patients and caregivers:

Language	Short Link
Bulgarian	https://bit.ly/preg_bg
Dutch	https://bit.ly/preg_nl
Italian	https://bit.ly/preg_ita
French	https://bit.ly/preg_fra
German	https://bit.ly/preg_de
English	https://bit.ly/preg_eng
Spanish	https://bit.ly/preg_es

We would suggest to leave the surveys open until 15th April 2022. ♥

Dutch ePAGs participation in the ESC position paper: their experience

Amsterdam, 7 March 2022

At the end of 2019, Patricia Vlasman (former ERN GUARD-Heart patient representative) and Dayenne Zwaagman (current ERN patient representative) were requested by Prof. Jolanda van der Velden, Chair of the Department of Physiology and Director of Amsterdam Cardiovasular Sciences Institute, to participate in a position paper on animal modals and animal-free innovations in cardiovascular research. Her specific wish was to contribute in describing and highlighting the role and the added value of patient participation in scientific research.

'I have never done anything like this and have no knowledge about cells or other body tissue, but I think I can help with a patient perspective view', Dayenne replied. She acknowledged that the offer of Prof. van der Velden was a wonderful opportunity for her as a patient to work closely together with experts and researchers. Dayenne: 'I was aware of the fact that my input for this paper would be minimum, but I felt honored to participate and I see a future role in any other patient who is willing to work in a the co-creation (on equivalent level) with a researcher, nurse and doctor.'

Patricia agrees with Dayenne. Especially in a paper dealing with fundamental research, the view of the patient does not seem very obvious, but according to Patricia it certainly is.

'Behind the tissue or cells in a dish hides the life of real people. Keeping this in the minds of the researchers is a challenge but ultimately, also fundamental research has the same goal and that is to improve the quality of the life of patients. The social impact of research can only be measured if it is visible to the general public. To contribute in a scientific paper as a patient representative is a great step in that direction.'

The paper has been published on 6 January, 2022 in *Cardiovascular Research*, entitled: "Animal models and animal-free innovations for cardiovascular research: current status and routes to be explored. Consensus document of the ESC Working Group on Myocardial Function and the ESC Working Group on Cellular Biology of the Heart."
https://doi.org/10.1093/cvr/cvab370 ♥

Dayenne Zwaagman

Patricia Vlasman

The **Exchange Programme** resumed on 1 April 2022. The programme will run until the end of the year (31 December 2022). So, it's time to create exchange plans! Please use the following link: https://guardheart.ern-net.eu/experts/ern-exchange-programme/

The next ERN GUARD-Heart board meeting will be held in Barcelona, during the ESC congress, on Tuesday 30 August 2022.

European Conference on Rare diseases and Orphan Products

Amsterdam, 8 March 2022

The European Conference on Rare Diseases & Orphan Products (ECRD) is recognised globally as the largest, patient-led rare disease event in which collaborative dialogue, learning and conversation takes place, forming the groundwork to shape goal-driven rare disease policies and allow for important and innovative discussions on a national and an international level to take place.

ECRD 2022 will take place online on 27 June - 1 July.

Leading, inspiring and engaging all stakeholders to take action, the Conference is an unrivalled opportunity to network and exchange invaluable knowledge with over 1500 stakeholders in the rare disease community – patient advocates, policy makers, researchers, clinicians, healthcare professionals, healthcare industry representatives, academics, payers, regulators and Member State representatives. This 11th edition follows a pivotal two-year Rare 2030 Foresight Study, supported by the European Parliament and European Commission, that guided a large-scale and multi-stakeholder reflection on rare disease policy in Europe through 2030.

The concluding recommendation of Rare2030 was the need for a new European policy framework on rare diseases with measurable and actionable goals. Current actions at Member State level alone, or legislative changes in specific areas are not enough. We need a new European collective strategy for rare diseases to bring Member States' commitment to rare diseases under a common umbrella and mark a step forward in the post-COVID world. This ECRD will be a critical opportunity for all stakeholders to consider how to transform this exhaustive review of the strategy on rare diseases into a proposal of concrete actions ultimately creating the ecosystem required to address the unmet needs and persisting inequalities across Europe. ♥

See the full ECRD programme: https://www.rare-diseases.eu/programme/

ECRD REGISTRATIONS -> https://www.rare-diseases.eu/register/

Latest ERN GUARD-Heart Publication(s)

1. Outcomes of Patients With Catecholaminergic Polymorphic Ventricular Tachycardia Treated With β-Blockers. Mazzanti A, Kukavica D, Trancuccio A, Memmi M, Bloise R, Gambelli P, Marino M, Ortíz-Genga M, Morini M, Monteforte N, Giordano U, Keegan R, Tomasi L, Anastasakis A, Davis AM, Shimizu W, Blom NA, Santiago DJ, Napolitano C, Monserrat L, Priori SG. JAMA Cardiol. 2022 Mar 30. doi: 10.1001/jamacardio.2022.0219. Online ahead of print. PMID: 35353122.

2. European Reference Network for rare, low prevalence, or complex diseases of the heart (ERN GUARD-Heart): 5 year anniversary. Amin AS, Biller R, Charron P, Wilde AAM. Eur Heart J. 2022 Mar 8:ehac117. doi: 10.1093/eurheartj/ehac117. Online ahead of print. PMID: 35257167 *(see direct link on page 5)*

3. Genome-wide association analyses identify new Brugada syndrome risk loci and highlight a new mechanism of sodium channel regulation in disease susceptibility. Barc J, Tadros R, Glinge C, Chiang DY, Jouni M, Simonet F, Jurgens SJ, Baudic M, Nicastro M, Potet F, Offerhaus JA, Walsh R, Choi SH, Verkerk AO, Mizusawa Y, Anys S, Minois D, Arnaud M, Duchateau J, Wijeyeratne YD, Muir A, Papadakis M, Castelletti S, Torchio M, Ortuño CG, Lacunza J, Giachino DF, Cerrato N, Martins RP, Campuzano O, Van Dooren S, Thollet A, Kyndt F, Mazzanti A, Clémenty N, Bisson A, Corveleyn A, Stallmeyer B, Dittmann S, Saenen J, Noël A, Honarbakhsh S, Rudic B, Marzak H, Rowe MK, Federspiel C, Le Page S, Placide L, Milhem A, Barajas-Martinez H, Beckmann BM, Krapels IP, Steinfurt J, Winkel BG, Jabbari R, Shoemaker MB, Boukens BJ, Škorić-Milosavljević D, Bikker H, Manevy FC, Lichtner P, Ribasés M, Meitinger T, Müller-Nurasyid M; KORA-Study Group, Veldink JH, van den Berg LH, Van Damme P, Cusi D, Lanzani C, Rigade S, Charpentier E, Baron E, Bonnaud S, Lecointe S, Donnart A, Le Marec H, Chatel S, Karakachoff M, Bézieau S, London B, Tfelt-Hansen J, Roden D, Odening KE, Cerrone M, Chinitz LA, Volders PG, van de Berg MP, Laurent G, Faivre L, Antzelevitch C, Kääb S, Arnaout AA, Dupuis JM, Pasquie JL, Billon O, Roberts JD, Jesel L, Borggrefe M, Lambiase PD, Mansourati J, Loeys B, Leenhardt A, Guicheney P, Maury P, Schulze-Bahr E, Robyns T, Breckpot J, Babuty D, Priori SG, Napolitano C; Nantes Referral Center for inherited cardiac arrhythmia, de Asmundis C, Brugada P, Brugada R, Arbelo E, Brugada J, Mabo P, Behar N, Giustetto C, Molina MS, Gimeno JR, Hasdemir C, Schwartz PJ, Crotti L, McKeown PP, Sharma S, Behr ER, Haissaguerre M, Sacher F, Rooryck C, Tan HL, Remme CA, Postema PG, Delmar M, Ellinor PT, Lubitz SA, Gourraud JB, Tanck MW, George AL Jr, MacRae CA, Burridge PW, Dina C, Probst V, Wilde AA, Schott JJ, Redon R, Bezzina CR. Nat Genet. 2022 Mar;54(3):232-239. doi: 10.1038/s41588-021-01007-6. Epub 2022 Feb 24. PMID: 35210625.

4. An International Multicenter Cohort Study on β-Blockers for the Treatment of Symptomatic Children With Catecholaminergic Polymorphic Ventricular Tachycardia. Peltenburg PJ, Kallas D, Bos JM, Lieve KVV, Franciosi S, Roston TM, Denjoy I, Sorensen KB, Ohno S, Roses-Noguer F, Aiba T, Maltret A, LaPage MJ, Atallah J, Giudicessi JR, Clur SB, Blom NA, Tanck M, Extramiana F, Kato K, Barc J, Borggrefe M, Behr ER, Sarquella-Brugada G, Tfelt-Hansen J, Zorio E, Swan H, Kammeraad JAE, Krahn AD, Davis A, Sacher F, Schwartz PJ, Roberts JD, Skinner JR, van den Berg MP, Kannankeril PJ, Drago F, Robyns T, Haugaa K, Tavacova T, Semsarian C, Till J, Probst V, Brugada R, Shimizu W, Horie M, Leenhardt A, Ackerman MJ, Sanatani S, van der Werf C, Wilde AAM. Circulation. 2022 Feb;145(5):333-344. doi: 10.1161/CIRCULATIONAHA.121.056018. Epub 2021 Dec 7. PMID: 34874747

5. Clinical and Functional Characterization of Ryanodine Receptor 2 Variants Implicated in Calcium-Release Deficiency Syndrome. Roston TM, Wei J, Guo W, Li Y, Zhong X, Wang R, Estillore JP, Peltenburg PJ, Noguer FRI, Till J, Eckhardt LL, Orland KM, Hamilton R, LaPage MJ, Krahn AD, Tadros R, Vinocur JM, Kallas D, Franciosi S, Roberts JD, Wilde AAM, Jensen HK, Sanatani S, Chen SRW. JAMA Cardiol. 2022 Jan 1;7(1):84-92. doi: 10.1001/jamacardio.2021.4458. PMID: 34730774

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