ECFS Diagnostic Network Working Group
Meeting Report

DNWG virtual meeting during ECFS Digital Conference 2020 - September 23th 2020

Webinar via Zoom

The virtual meeting started with welcome words by the coordinator of the ECFS Diagnostic Network Working Group, giving an overview of the content of the meeting.

Part 1

Chair: Elke De Wachter (Brussels, Belgium)

The first presentation was held by Isabelle Sermet (Paris, France) about the variability of nasal potential difference (NPD) as a biomarker of CFTR activity in clinical trials. Intrasubject and intersubject variability of NPD measurements in the placebo-arm of the earlier phase 3 PTC trial were highlighted. Strategies to minimize the test variability were discussed.

Lutz Naehrlich (Giessen, Germany) stressed in his talk that it is wise to still invest in NPD and ICM as a diagnostic tool, despite the intra-and intersubject variability, highlighted by the first speaker. NPD and intestinal current measurement (ICM) have been demonstrated previously to be informative in cases with an unclear CF diagnosis. To date, it is too early to replace these *in vivo* and *ex-vivo* measurements for CFTR-function by the intestinal organoid model, for which the availibility for clinicians is even more limited than NDP and ICM.

Both presentations gave enough input for a lively discussion chaired by Carlo Castellani (Genua, Italy). Dr Castellani opened the discussion by addressing his thoughts and concerns on NPD and ICM. He highlighted the entity of CFTR-RD as an entity that does not completely fulfill the CF-diagnostic criteria, and for which we may be forced to use a more sensitive tool (as NPD/ICM) than the sweat test to measure CFTR activity. However, still many questions remain unresolved.

The next speaker, Audrey Reynaerts (Brussels, Belgium), presented the first selected abstract in the diagnostic field (ECFS 2020 WS09.2). Instead of the earlier described β-adrenergic sweat test, for which intradermal injections with 3 consecutive substances are needed in order to promote sweat stimulation in a CFTR-dependent way, the investigators applied the 3 different

substances by iontophoresis. This method is much less invasive than the original method described by the group of Paul Quinton. First data of the validation study, comparing healthy controls with CF patients, were shared. Further studies are needed in order to find out if this variant on the original beta-adrenergic sweat test may be an alternative to NPD and ICM in difficult CF diagnosis.

Part 2:

Chair: Nicholas Simmonds (London, UK)

The second poster presenter was Emmanuelle Girodon (Paris, France), studying the penetrance of certain CFTR variants, in order to better identify their disease liability. The investigators used data from CFTR2 and genetics population data in the general population, as well as data from the French newborn screening database in order to get the best insights in their penetrance. This study showed important differences compared to CFTR2 data in the disease liability of certain variants. (ECFS 2020 WS09.5)

The coordinator of the newborn screening working group, Jürg Barben (St Gallen, Switzerland), gave an update on the newest guidance of the management of children with CFSPID, recently submitted for publication in JCF. During his presentation, he gave an overview of the main reasons for a subsequent CF diagnosis after CFSPID. He also highlighted the way in which communication of a CFSPID diagnosis to the parents should be done, according to the expert-group.

The third abstract "Symptoms at diagnosis and genotype of false negatives in newborn screening in Tuscany: experience over 26 years" was presented by Giovanni Taccetti (Florence, Italy). His study aimed to evaluate clinical and genotypical features of false negatives of NBS over 26 years in the region of Tuscany. Details on the 18 false negative subjects were shared. This presentation highlighted the importance of maintaining a careful surveillance for CF even in a region with a NBS program. (ECFS 2020 P018)

Eirini Bourgani (Athens, Greece) presented the last selected abstract (ECFS 2020 P27) of the meeting. An increasing group of CF patients is diagnosed during adulthood. Eirini and her team investigated the clinical characteristics and symptoms of late diagnosed patients, collecting data such as FEV1, BMI, clinical and microbiological characteristics at the time of the CF-diagnosis. This study showed that clinical manifestation is very diverse at presentation in

adulthood compared to diagnosis in early childhood. Specialties other than pulmonology should be aware of a missed diagnosis of CF in adulthood.

Nicholas Simmonds, the vice-coordinator of the working group, closed the first virtual DNWG meeting after summarizing the meeting and giving future perspectives for the next DNWG meeting.

We thank all speakers and participants for their fantastic contribution to make this first virtual ECFS Diagnostic Network Working Group Meeting a great success!

We would also like to thank Helen Chadwick (ECFS Education Coordinator) for her support in organizing the webinar.

We are looking forward to meeting you at our next ECFS DNWG Meeting.

22nd November 2020

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