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News article

1. Award nominations

15th February 2020 will be the closing date for nominations of the ECFS Award and the Gerd Döring award. More information can be found on https://www.ecfs.eu/conferences/awards.

2. Papers just published

The results of two phase 3 multi-centre clinical trials have been published in the *New England Journal of Medicine* and *The Lancet* evaluating the efficacy and safety of triple CFTR modulator treatment with elexacaftor (next-generation corrector) plus tezacaftor (corrector) and ivacaftor (potentiator) in people with CF (≥12 years) with one or two copies of the Phe508del *CFTR* mutation:

(i) *Elexacaftor–Tezacaftor–Ivacaftor for Cystic Fibrosis with a Single Phe508del Allele. New England Journal of Medicine*, DOI:10.1056/NEJMoa1908639.
(ii) *Efficacy and safety of the elexacaftor plus tezacaftor plus ivacaftor combination regimen in people with cystic fibrosis homozygous for the F508del mutation: a double-blind, randomised, phase 3 trial. Lancet*, DOI:10.1016/S0140-6736(19)32597-8.

The study published in the *NEJM* was a placebo-controlled trial conducted at 115 sites in 403 participants who harboured a single Phe508del *CFTR* mutation and a minimal function mutation. These participants either received treatment with the triple combination CFTR modulator regimen or with the placebo for a period of 24 weeks. Amongst the treatment group, improvements in clinical outcomes including an increase in lung function and patient-reported respiratory symptoms as well as reductions in pulmonary exacerbations and sweat chloride were detected when compared to the placebo group. This advance represents the first effective therapy for patients who are heterozygous for Phe508del and a minimal function mutation, which accounts for >30% of the global CF population.

The study published in *The Lancet* was an active-controlled trial conducted at 44 sites and recruited 113 participants who harboured two copies of the Phe508del *CFTR* mutation. After all participants had received tezacaftor plus ivacaftor for a period of 4 weeks, they were then assigned to receive either the triple combination regimen with elexacaftor plus tezacaftor plus ivacaftor or the dual combination regimen with tezacaftor plus ivacaftor for a further 4 weeks. Improvements in lung function, patient-reported respiratory symptoms and sweat chloride levels were observed in the elexacaftor-tezacaftor-ivacaftor group relative to the tezacaftor-ivacaftor group.

Overall, the triple CFTR modulator regimen had an acceptable safety profile and a low rate of discontinuation.

Accompanying editorial/comments highlight that further drug development is still required including for people who will not benefit from current CFTR modulator regimens due to their particular *CFTR* variants (*New England Journal of Medicine*, DOI:10.1056/NEJMe1911602; *The Lancet*, DOI:10.1016/S0140-6736(19)32676-5). The editorial in *NEJM* was written by Dr. Francis Collins, a distinguished geneticist, who is the director of the National Institutes of Health and has been integral in discovering the genes involved in various diseases including CF and also led the Human Genome project.

Pulmonary Outcomes Associated with Long-Term Azithromycin Therapy in Cystic Fibrosis. Azithromycin is used as a chronic treatment in people with CF; but the long-term health outcomes are unclear. This retrospective cohort study based on the CF Foundation Patient Registry investigated pulmonary outcomes in those receiving chronic azithromycin treatment compared to matched controls. Results included that in people with *Pseudomonas aeruginosa* infection, lung function decline was slower over a 3-year period with azithromycin treatment. Conversely, in people without *P. aeruginosa* infection, no impact on lung function decline was observed with azithromycin use. Furthermore, azithromycin was not associated with a reduced requirement for intravenous antibiotics for treatment of pulmonary exacerbations. *American Journal of Respiratory and Critical Care Medicine*, DOI:10.1164/rccm.201906-1206OC.

Losartan Rescues Inflammation-Related Mucociliary Dysfunction in Relevant Models of Cystic Fibrosis. Currently used anti-inflammatory treatments in CF, *e.g.* steroids, are limited by their side-effect profile. Losartan is an angiotensin receptor blocker used to treat cardiovascular disease but also has anti-inflammatory activity. This study investigated the effect of losartan *in vitro* using human airway epithelial cells with two copies of the Phe508del *CFTR* mutation exposed to TGF-β1, which is increased in the CF airways. The activity of losartan was also investigated *in vivo* using a CF-like sheep model. The findings included that losartan improved ciliary beat frequency and airway surface liquid volume and decreased mucus concentration and inflammation *in vitro*. *In vivo*, losartan also improved mucus properties and reduced TGF-β1 levels. *American Journal of Respiratory and Critical Care Medicine,* DOI:10.1164/rccm.201905-0990OC.

3. Upcoming events

- 14th European CF Young Investigators Meeting: 26th to 28th February 2020, Paris, France
- 17th ECFS Basic Science Conference: 25th to 28th March 2020, Albufeira, Portugal
- American Thoracic Society International Conference: 15th to 20th May 2020, Philadelphia, Pennsylvania, USA

https://doi.org/10.1016/j.jcf.2019.12.003
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- 43rd ECFS European CF Conference: 3rd to 6th June 2020, Lyon, France
- 34th North American CF Conference: 22nd to 24th October 2020, Phoenix, Arizona, USA

4. People

Dr. Michael Boyle has been appointed as the next president and CEO of the Cystic Fibrosis Foundation and will succeed Dr. Preston Campbell following his retirement (effective January 2020). Here we acknowledge Drs. Campbell and Boyle and for their contribution to the Cystic Fibrosis Foundation.

Dr. Preston Campbell

It is my privilege to share my deep gratitude to a dear friend, a special friend, and long-time colleague whose exceptional leadership and commitment has brought us to this exciting time in the history of CF.

As you know, Dr. Preston Campbell has retired as president and CEO of the Cystic Fibrosis Foundation, following more than thirty years of service to people with CF and their families. Preston has brought the thoughtfulness of a devoted physician and the resolve of a seasoned innovator to every challenge he has tackled.

Though he is always the last to take credit, Preston helped drive unprecedented advances in CF treatment and care, drug discovery and development, and has led the way in bringing the essential voice of individuals with CF into everything we do.

As a CF parent, a long-time volunteer, and the leader of the Foundation's Board, I have always felt that he walked hand in hand with me and with the entire CF community. Preston has always kept us focused on the future and has always given us hope.

I am happy to share with you that we will not be saying goodbye to Preston. He will continue to play an important role improving the lives of people with CF. He will be a strategic advisor to the Foundation team and focus on a number of issues, including learning more about the needs of our international CF community, especially in developing countries.

Preston has enriched us and made a difference in our lives. Because of him, our steward leader, we remain fiercely focused and more determined than ever to advance the mission we share.

Cam McLoud, Chair, Board of Trustees

Dr. Preston Campbell

Dr. Michael Boyle

Dr. Michael Boyle is an adjunct professor of medicine at The Johns Hopkins Hospital, USA, and in his current role at the Cystic Fibrosis Foundation as the senior vice president of therapeutics development he oversees the clinical development programs of new treatments for the Cystic Fibrosis Foundation, as well as the Foundation's Therapeutic Development Network of 82 academic research centers.

Dr. Boyle completed his medical training at Johns Hopkins, including a fellowship in pulmonary and critical care medicine and then joined the medical faculty in 1999. Importantly, he founded and subsequently directed the Johns Hopkins Adult CF Program, one of the largest programs in the USA, between 1999 and 2015. He has dedicated his career to improving the care of people with CF for ~20 years and he is also internationally recognised for his clinical research including in CFTR modulator regimens and lung infections that are challenging to treat. He has been the recipient of many honors during his career including the American Lung Association's George Comstock Career Achievement Award, American Federation of Clinical Research Achievement Award, "Patient's Choice Award", "Best Teacher", and "Best Doctors in America".

Dr. Michael Boyle