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Results of Triple Drug Trial for Progeria Published

PRF Continues Aggressive Research Agenda

BOSTON, MA (July 11, 2016) Results from the fourth Progeria clinical trial – the triple drug trial – were published online by the journal *Circulation* today. Building on the success of the lonafarnib monotherapy trial, investigators sought to understand if a combination therapy of lonafarnib, pravastatin and zoledronic acid would provide further disease improvement.

The 37-patient study, which was co-funded by The Progeria Research Foundation (PRF) and the National Institutes of Health (NIH), found increased bone mineral density, but no other improvements (weight gain or cardiovascular variables) were noted beyond the earlier lonafarnib trial. No patients withdrew due to side effects.

"The results of the triple drug trial demonstrate the need for us to continue an aggressive study protocol as we search for additional treatments and a cure. It is vital to continue to identify treatments with the most promise to offer these children longer, healthier lives," said Dr. Leslie Gordon, Medical Director of The Progeria Research Foundation (PRF). "PRF continues to fund promising research and clinical trials aimed at curing Progeria. PRF is currently funding and co-coordinating a promising new two-drug trial to assess lonafarnib plus everolimus, at Boston Children's Hospital (https://clinicaltrials.gov/ct2/show/NCT02579044?term=progeria+everolimus&rank=1). Children are enrolling from the USA and countries throughout the world"

In an editorial about the triple trial results, NIH Director and study author Francis Collins, MD PhD, wrote in *Circulation*, "To proceed from gene discovery to the first molecularly driven clinical trial in less than five years was unusually rapid, and might have been considered a paradigm for translational medicine for rare diseases… additional therapeutic options are emerging, and there is more momentum than ever in the basic and clinical research communities."

Progeria

Hutchinson-Gilford Progeria Syndrome (Progeria) is an extremely rare, fatal, segmental premature aging syndrome caused by a genetic mutation. Without treatment, death occurs at an average age of 14.6 years. The Progeria Research

Foundation has funded four clinical trials and 62 scientific studies in an effort to identify life-saving treatments and a cure for Progeria. In May of 2016, PRF held an international scientific meeting where researchers from 14 countries gathered and presented at least 17 new potential treatment strategies for Progeria under development (http://www.progeriaresearch.org/prfs-2016-scientific-workshop/).

2012 Monotherapy Trial

In 2012 the lonafarnib study results were published (http://www.pnas.org/content/109/41/16666), demonstrating that every child in the study experienced improvement in one or more areas, including the vital cardiovascular system. In May 2014, further study revealed lonafarnib and possibly the other 2 drugs tested in the Triple Trial increased estimated lifespan.

2016 Everolimus Trial

PRF is now funding and co-coordinating a new clinical trial, which will assess a two-drug combination of lonafarnib plus everolimus. Everolimus is a form of the FDA-approved drug rapamycin, but everolimus can be more easily given to the children with Progeria because it requires fewer blood draws to measure drug levels. While lonafarnib may block progerin from developing, rapamycin appears to allow cells to more rapidly clear out the toxic progerin protein. Thus with everolimus targeting a different pathway than lonafarnib, the combination may prove to be a "one-two punch" to Progeria - hopefully a better treatment than lonafarnib on its own.

More information on all PRF-funded clinical trials can be found here.

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