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STUDY FINDS TRIAL MEDICATIONS INCREASE LIFESPAN FOR CHILDREN WITH PROGERIA

*First-Ever Study of Progeria Children Drug Treatments Shows
Protein Farnesylation Inhibition Increased Lifespan*

BOSTON, MA (May 6, 2014) – A new study demonstrates there is evidence that a drug originally developed to treat cancer can extend the lives of children with Progeria, a rare, fatal “rapid-aging” disease, by at least one-and-a-half years, according to [The Progeria Research Foundation \(PRF\)](#). The study, published this month in *Circulation* (Epub ahead of print) showed an extension of mean survival of 1.6 years during the six years following initiation of treatment with a farnesyltransferase inhibitor (FTI). Two additional drugs added later in the trials, pravastatin and zoledronate, may also contribute to this finding. This is the first evidence of treatments influencing survival for this fatal disease.

A link to the article, “Impact of Farnesylation Inhibitors on Survival in Hutchinson-Gilford Progeria Syndrome,” can be found on The Progeria Research Foundation [website](#).

Progeria, also known as Hutchinson-Gilford Progeria Syndrome (HGPS), is a rare, fatal genetic disease characterized by an appearance of accelerated aging in children. All children with Progeria die of the same heart disease that affects millions of normal aging adults (atherosclerosis), but instead of occurring at 60 or 70 years of age, these children may suffer heart attacks and strokes as early as 5 years old.

The study, a collaborative effort between The Progeria Research Foundation, Brown University, Hasbro Children’s Hospital, Boston University and Boston Children’s Hospital, began by re-defining the natural history of lifespan for children with Progeria, by tracking 204 children, most of the world’s population with Progeria, primarily through the PRF patient registry. Once that was achieved, comparison with lifespan of children on therapy in clinical trials at Boston Children’s Hospital showed extension of lifespan for the treated children.

“This is the first study to assess whether treatments influence patient survival, and thanks to a robust PRF registry and the clinical trials, we have been able to conclude that lifespan extension is possible for children with Progeria. Moreover, the study provides parameters for future assessments of changes in survival with other potential treatments for Progeria, as we continue working to discover drugs that extend life even further,” said Leslie Gordon, M.D., Ph.D., lead and corresponding author of the study, and Medical Director for PRF. In addition, Dr. Gordon is a staff scientist at Boston Children’s Hospital and Harvard Medical School, and Associate Professor at Hasbro Children’s Hospital and Alpert Medical School of Brown University.

First PRF Clinical Trial Tested FTI

PRF sponsored an [initial Progeria treatment study](#) in 2007 with 28 children from 13 countries. Treatment consisted of the FTI lonafarnib, supplied by Merck & Co., under the supervision of principal investigator Mark Kieran, M.D., Ph.D., director of pediatric medical neuro-oncology at the Dana-Farber/Children's Hospital Cancer Center. Children in the study showed improvement in an ability to gain additional weight, increased flexibility of blood vessels or improved bone structure, all conditions impacted by Progeria.

In 2009, PRF and the National Heart, Lung and Blood Institute co-funded another trial, adding two drugs, pravastatin and zoledronate, to the FTI treatment. The study is still underway, with results currently being analyzed. The 45 children from 24 different countries in the "triple drug" trial included children enrolled in the FTI-only study. The children travel to Boston periodically to receive comprehensive medical testing at Boston Children's Hospital.

While children in the study were treated with the three drugs, the FTI lonafarnib is the drug to which all subjects were exposed, and has shown cardiovascular benefit in Progeria. The study concludes that lonafarnib likely has the largest influence on increased estimated lifespan.

Children with Progeria have a genetic mutation that leads to the production of the protein progerin, which is responsible for Progeria. Progerin blocks normal cell function and part of its toxic effect on the body is caused by a molecule called a "farnesyl group," which attaches to the progerin protein. FTIs act by blocking the attachment of the farnesyl group onto progerin. The drugs FTI lonafarnib, pravastatin, usually used for lowering cholesterol and preventing cardiovascular disease, and zoledronic acid, used to improve bone strength, are all considered farnesylation inhibitors, and work in different ways.

Evaluation of Survival

To evaluate how the treatment impacted survival among the children with Progeria in the study, researchers first analyzed an untreated Progeria population for comparison. Using records from The Progeria Research Foundation International Registry, published scientific news articles and publicly available databases, each child in the treatment trial was matched with an untreated child of the same gender, from the same continent, and who was alive when the treated child began treatment.

Study results showed that children with Progeria receiving lonafarnib treatment had an 80 percent lower risk of death compared to the untreated cohort. In the treated group, 5 of 43 children died, compared with 21 of 43 in an untreated matched comparison group, both with a median follow up of 5.3 years. Children in the treatment group included those of different ages, with varying durations of treatment and at varying stages of disease upon treatment initiation. Repeat evaluation of lifespan after children are treated for a longer period of time will be needed to evaluate whether lifespan is further extended with long-term treatment.

"These findings give hope to the children and families who face this incurable and fatal disease. Through the support of The Progeria Research Foundation, these researchers have taken one more step in the process of finding a treatment and a cure for this disease," said Elizabeth G. Nabel, President of Brigham and Women's Hospital, and former Director of the National Heart, Lung and Blood Institute. "As further research evaluates the impact that progerin-reducing therapies may have, we have the potential to not only discover effective treatments for Progeria, but also to illuminate some of the fundamental biological questions about the aging process, including heart disease and stroke."

Progeria Linked to Normal Aging Process

In an editorial accompanying the *Circulation* paper, Drs. Junko Oshima, Fuki M. Hisama and George M. Martin note the observations in the study raise an important question about the extent to which progerin – a protein involved in Progeria – is associated with aging and age-related disorders such as atherogenesis. The authors of the editorial, “An Encouraging Progress Report on the Treatment of Progeria and its Implications for Atherogenesis,” praised PRF for leading research efforts in this area.

Previous research shows that progerin is also produced in the general population and increases in blood vessels with age. A number of studies successfully linked progerin with normal aging, including a causal link between progerin and genetic instability, specifically telomere dysfunction in the aging process. Researchers plan to continue exploring the effect of FTIs, which may help scientists learn more about cardiovascular disease in the general population that affects millions, as well as the normal aging process

“This is an historic finding in our quest to improve health and extend the lives of children with Progeria,” said [Audrey Gordon](#), Executive Director of PRF. “We continue to be immeasurably grateful to our supporters who provide funding for the research and drug trials that make such progress possible.”

About The Progeria Research Foundation (PRF)

[The Progeria Research Foundation \(PRF\)](#) was established in 1999 to find the cause, treatment and cure for Progeria – a rapid aging disease that causes children to die from heart disease or stroke at an average age of 13 years. In the past 15 years, research conducted in partnership with PRF has identified the gene that causes Progeria, and the first-ever drug treatment. PRF continues to identify more children who can benefit from the programs and services that it provides while helping advance research towards treatment and cure. To learn more about Progeria and what you can do to help, please visit www.progeriaresearch.org.

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