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Clinical Trials in which main indication is Progeria

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Abstract

Progeria is a disorder, known as progeroid syndrome, which is also known as Hutchinson-Gilford syndrome or Hutchinson-Gilford progeroid syndrome. A mutation on a single gene is causing this disease. The mutation that is causing it is on the LMNA (Lamina A) gene, the function of this gene is to make proteins that are needed to hold the nucleus cells together. The mutation is causing new protein called Progerin, which is causing the individuals who have this mutation to age faster than the persons who does not have this mutation. The people with this mutation looks a lot older than their actual age, and in most cases live until late-teen years or some of the persons with this mutation live up until early twenties. Usually there are cardiovascular problems with severe grading, starting to develop in the puberty of the people with these syndromes. In later stages these complications lead to death of the patients with Progeria.

Key Words: Progeria, Progerin, Hutchinson-Gilford Syndrome, LMNA, Gene mutation

Introduction

Progeria is a rare disease which is causing premature aging of the people with this disease, starting from early months of life of the people after their birth.
The classic type is the Hutchinson-Gilford Progeria Syndrome (HGPS), which was first described in England in 1886 by Dr. Jonathan Hutchinson and again in 1904 by Dr. Hastings Gilford. [1]
The children born with this disease appear normal at their birth, however after a couple of months in their life the first symptom of the disease appeared. First symptoms that occurred as result of this disease may be but are not limited to only these symptoms are scleroderma, it is usually localized. Another known symptom that can occur is a failure to thrive. As time is passing by, by 2 years symptoms like alopecia and changes in the look of the person can be seen, the face of the patient is small and looks shallow, the mandibula is recessed and the nose is pinched. These all are some of the typical symptoms that occur at persons with progeria. As the child ages, the symptoms become more and more visible, Later, the condition causes wrinkled skin, kidney failure, loss of eyesight, and atherosclerosis and other cardiovascular problems [2].
The syndrome is caused by rare autosomal dominant genetic disorder, this results to a germline mutation which is a detectable variant of a mutation on the germ cells. The mutated gene cause progerin, progerin leads to disruption of the nuclear architecture.

The nuclear changes are the reason for acceleration of aging related processes, damage in DNA, telomerase shortening and cellular senescence.
As a result of the mentioned processes, the signs and symptoms of progeria appear.
The known signs and symptoms and the collected information for the disease has been reason for organizing clinical trials in which a medication for the disease is examined. Overall reported are 11 clinical trials organized in which the main indication is Progeria, couple of the clinical trials have some promising results. The most promising clinical trial is regarding the medication Lonafarnib, which after the approval is sold under the brand name Zokinvy.
In November 2020, the U.S. Food and Drug Administration approved lonafarnib, which helps prevent buildup of defective progerin and similar proteins [3]. In phase 2 the clinical trial for Lonafarnib showed safety and some efficacy for treatment of cardiovascular problems at patients with Progeria. In phase 3 the clinical trial for the same medication has shown some promising results in increase of the median survival of patients with Progeria. These results are promising and are showing that there are some possibilities for finding medication for the disease.

Another Clinical Trial related to the medication Rapamycin, which is a mTOR Inhibitor, has shown some promising results is slowing the aging process as a result of this disease. The medication is improving the vascular function of patients who are affected with this disease, however additional studies are needed to show the long-term efficacy of the medication. So far, the results look promising.
Another Clinical Trial that is worth to be mentioned is related to a gene therapy, the goal of this therapy is to correct the mutated LMNA gene, so the production of normal protein can continue, and progerin won't be produced. This trials have shown some positive results in trials in which animals are treated, the clinical trials inn which treatment on humans is applied are still in early stages.
Other therapies that are investigated for treatment of Progeria are treatments with small molecules and also a treatment with stem cells, however additional information should be collected for both the disease and the treatments of it.
The most challenging part of the clinical trials for Progeria is the fact that this is a rare disease, and that worldwide there are not a lot of known cases of this disease. According to the web page of Progeria Research foundation, overall there are 261 known cases of Progeria, located in 52 different countries. Another challenging part is that the disease is progressing relatively fast, and the long-term efficacy of the treatments can hardly be tracked. Also, the ethical considerations in these clinical trials are critical, since the patients treated in these clinical trials are children.

Materials and Methods

The materials used for this article were from https://clinicaltrials.gov/.
It is the most used and known data source for clinical trials organized worldwide.
For completion of this article only one filter was used on the web page, since Progeria is a rare disease and there are not a lot of clinical trials organized.
After getting the results it can be seen the total number of organized and reported clinical trials. The phase of the organized clinical trials and the study type of organized clinical trials.
The results will not be entered in charts or tables, since the number of organized clinical trials is low.

Result & discussion

From the available data it can be seen that overall, there are only 11 clinical trials organized. The first one was organized in 2004 and the last one was organized in January 2025.
As expected in 10 of 11 clinical trials with indication Progeria, target population are children, only in one target population are adults, this is due to the fact that the most

patients with this disease are children. In the one clinical trial in which target population are adults, the main goal is to evaluate the safety, tolerability, Pharmacokinetics and Pharmacodynamic of healthy volunteers. This is a clinical trial in phase 1.
As expected, 11 of 11 clinical trials are enrolling both male and female patients. This was also expected, since Progeria is a rare disease, and as mentioned before only 261 patients are known worldwide and every patient from both the genres is important.
From the reported 11 clinical trials, there are 3 clinical trials, which are in phase 1, and there are 5 clinical trials in phase 2 of the phases of clinical trials. This is relatively good information, since 5 clinical trials have passed phase. For 2 of the clinical trials information about the phase is not available. This is due to the fact that these are clinical trials from observational type, information regarding the disease is required for further purposes, that is why this type of clinical trials are organized.
One of the reported clinical trials was related to the medication that is already approved Lonafarnib.
8 of the clinical trials are with interventional type, which means that the treatment is investigated.
Regarding the location of organization of the clinical trials, 8 of all the 11 clinical trials are organized in the United States of America, 2 are organized in France, and there is one clinical trial organized in Republic of Korea.
Interesting fact about these clinical trials is that one of the observational clinical trials which are organized is planned to be ongoing for 25 years. This again is expected because new information regarding the disease and regarding possible treatment in future is needed. The clinical trial was organized in 2023 and is expected to be ongoing by 2048.

Conclusion

The study is based on a data available at https://clinicaltrials.gov/.
From this data it can be noted that the number of organized clinical trials in which the main indication is Progeria is low. However, the low number of organized clinical trials is expected because the indication is a rare disease, and there are not a lot of patients that have this disease. Overall, worldwide there are only 261 known patients with this disease in 52 countries, compared to the number of patients with this disease the number is not that low.
Regarding the phase of the reported organized clinical trials, the number of phase 1 and phase 2 studies is also expected, there are 5 clinical trials in phase 2, which means that they have successfully passed phase 1.
Interesting is the fact about the length of one of the observational clinical trials of 25 years. However, this is also expected because this is a rare disease, and there are not a lot of known information about it. So, every information regarding the disease is important.
Also, the fact that one of the clinical trials have received approval is a really good information, even though future information is needed, however as time is passing by and as new information is collected it can be beneficial for the disease.
Regarding the location of the organized clinical trials, as expected the highest number of organized clinical trials are in United States of America, according to the web page of the Progeria Research Foundation, the number of cases with Progeria is highest in USA, and also the health care system in United Stats of America is organized, and organized healthcare system is needed for organization of clinical trials which have indication rare disease as this one.
Most of the clinical trials have in common that the organizer or the one who is leading the reported clinical trials is an organization called Progeria Research Organization. This is giving hope that there are groups that care about these patients and there are possibilities of finding the right treatment for the disease.

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