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Clinical Trials in which main indication is Achondroplasia

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Abstract

Achondroplasia is a rare disease which is caused as a result of mutation in the FGFR3 gene. That mutation leads to impaired growth of the bones. This disease is the most common form of dwarfism known by now. There have been organized and conducted clinical trials focused on target therapies, such as Vosoritide and other FGFR3 Inhibitors, the aim of the organized clinical trials is to address and find the genetic defect that is causing the defect.
By this time only 41 Clinical trials are reported in which the main disease under study is Achondroplasia, the earliest is organized in the 1996 and the latest which is ongoing at this period of time is organized in December 2024.

In this article there will be a review of the findings, methodology and implications of clinical trials that are organized in which the disease under study is Achondroplasia, also the safety, efficacy, and the potential for improvement of the quality of life of the individuals with this disease will be implicated.

Key Words: Achondroplasia, Clinical Trials, Rare Disease FGFR3 gene, Gene Mutation

Introduction

Achondroplasia is one of the most common causes of dwarfism and affects about 1 in 27500 people [1]. The cause of the disease is a genetic mutation in the fibroblast growth factor receptor 3 gene, which leads to overreaction of the protein. The overreactive protein leads to impaired endochondral bone growth. The disease is inherited autosomal dominant, which means that only one mutated gene copy is required for occurrence of the disease. Circa 80% of cases occur in children of parents who are not affected by the disease, and result from a new mutation, most commonly originating as a spontaneous change during spermatogenesis [2].

There are studies that are showing that

The gene mutation leads to higher production of collagen and other components in the bones and tissues.

In situations in which both the parents are affected of this disease, in most of the cases the children who are inheriting the mutated gene, die prior do their birth or during their early infancy, most of the deaths are related to problems with breathing.

Clinical signs and symptoms of this disease are the most known, dwarfism, short proximal limbs, large head, spinal kyphosis, frequent ear infections and varus and valgus deformities of the legs.

The children that are affected of this disease in most of the cases have less muscle tone, due to the delay in walking and the lack of physical activities.

The adults that have this disease have problems like obesity and sleep apnea.

Pregnancy for woman with achondroplasia is with higher risk compared to the woman who are not affected of this disease.

There has been couple of promising undergoing clinical trials, in which treatment of achondroplasia is being investigated, in this article only the medication Vosoritide will be mentioned:

Vosoritide - a synthetic peptide analog of C-type natriuretic peptide. It is a medication that is regulating the growth of the bones. The medication is attacking the signals that are produced by the FGFR3 mutation. The medication affects the ossification, and the produced cartilage is turned into bones. So far, the medication is approved to improve growth velocity in children with achondroplasia based on results in Phase 3 human trials, although its long-term effects are unknown [3]. The collected data so far is giving hope that the end result will be positive.

The safety and efficacy of vosoritide in improving growth were evaluated in a year-long, double-blind, placebo-controlled, phase III study in participants five years and older with achondroplasia who have open epiphyses. [4]

Regarding the number of patients with achondroplasia, a 2020 review and meta-analysis estimated a worldwide prevalence of 4.6 per 100,000 [5].

Materials and Methods

The number of all the organized clinical trials involving Achondroplasia is collected from https://clinicaltrials.gov/ it is the biggest and the most reliable source for information for clinical trials. On this web page, publicly and privately funded clinical studies conducted all around the world are reported.

The only one filter that was used during the review of the material was related to condition, as condition/disease, Achondroplasia was chosen. Since there are not a lot of organized Clinical Trials for this disease, other filters were not relevant.

After getting the results it can be noted the number of organized clinical trials from the first trial organized for indication Achondroplasia. Also, there is information regarding the age of target population in these clinical trials, the gender of the population in the organized clinical trials, the study types of the organized clinical trials, the phases of the organized clinical trials and also the location of organized clinical trials.

Some of the available data will be sorted in diagrams for better visualization.

Result & discussion

From the available information can be noted that overall, there are 41 clinical trials in which the main indication is Achondroplasia.

From the available information can be noted that the first clinical trial was organized in United States of America in 1996, and the last organized clinical trial is in December 2024 in Denmark.

From this it can be noted that the scientists and the researchers are interested in finding a new medication that will make the life of the patients with Achondroplasia better.

Regarding the Gender of the patients, from all the 41 reported organized clinical trials, only on one of them only male patients are the targeted population. In the rest 40 clinical trials both male and female patients are eligible to be part of the studies.

Regarding the age of the participants in the organized clinical trials, from the first clinical trial up until the last one, in 4 of them only adult population is the target population, in 22 of the clinical trials only young population under age of 18 years is the target population, and in the rest of 15 clinical trials both adult and young population is eligible to be part of the trials.

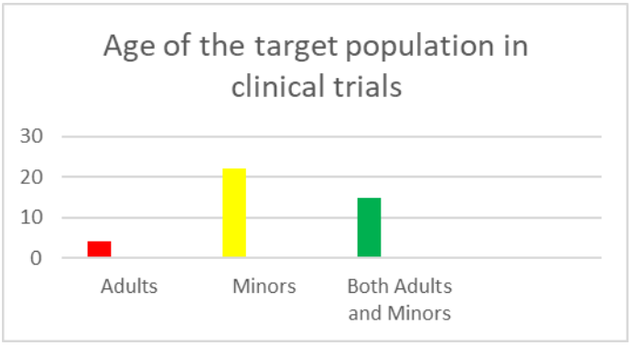

Chart 1. Age of the eligible population in clinical trials

The number of clinical trials divided by the age of the target population is expected, the highest number of clinical trials in which the minors are target population is expected since this disease is from the beginning of life of the patients, the clinical trials in which target population are the adults patients are clinical trials in which it is investigated if the new medication will cause some changes in the life of patients, and overall the number is low, only 4 clinical trials.

From the available information on https://clinicaltrials.gov/ can be seen that there are clinical trials of investigational type and clinical trials of observational type.

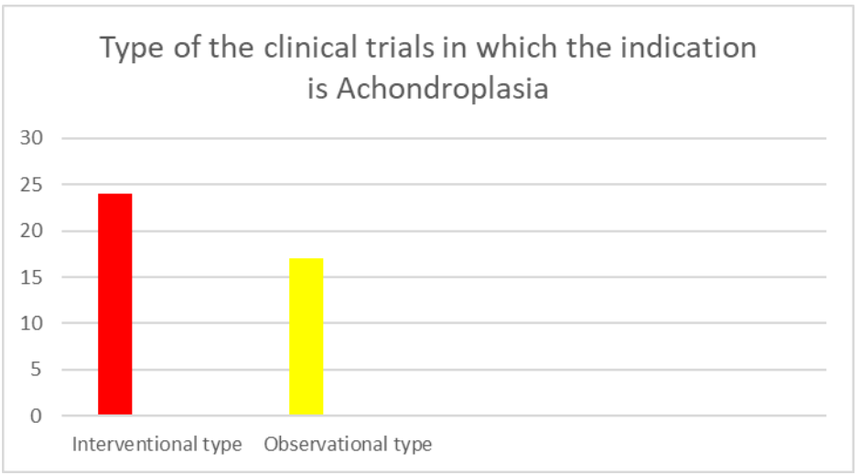

Chart 2. Type of clinical trials in which the indication is Achondroplasia.

The results of 24 clinical trials of interventional type, and 17 clinical trials of observational type are expected. The number of clinical trials of interventional type is higher which is expected because the patients are receiving some type of intervention related to the disease, however the number of observational clinical trials is not that low, which is showing that new information regarding the disease is collected. That can lead to more and more interventional studies in close future.

From the available information on https://clinicaltrials.gov/ can be seen that there are clinical trials in Phase 1, Phase 2, Phase 3 and Phase 4.

In Phase 1 there are 2 clinical trials, in phase 2 there are 18 clinical trials, in phase 3 there are 3 clinical trials, and in phase 4 there is only 1 clinical trial. For 17 of the clinical trials information regarding phase was not available during the research.

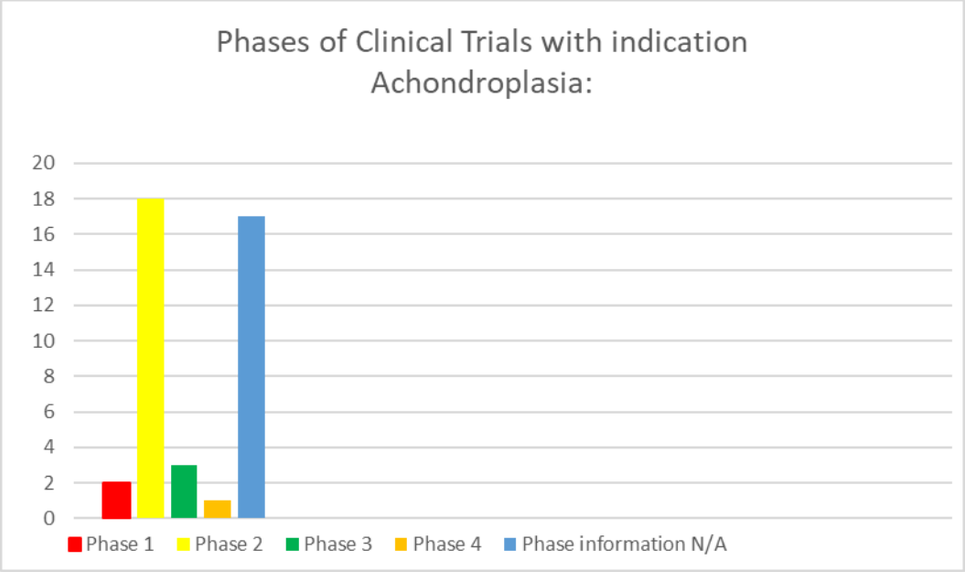

Chart 3. Phases of Clinical Trials with indication Achondroplasia

These results were expected, most of the clinical trials are in phase 2, in which the effectiveness of the medication is investigated. Currently the number of phase 2 clinical trials is highest which is showing that the medications have passed the phase 1. This is showing promising possibilities for potential new medications. Also, the number of clinical trials for which the phase is not known, is high, this is showing the information that the researchers should do better job in reporting the clinical trials.

Regarding the location of the reported organized clinical trials, 26 of all the 41 clinical trials are organized in USA, 2 of the clinical trials are with location Denmark, 2 of the clinical trials are with location Australia, 2 of the clinical trials are with location People's Republic of China, 2 of the clinical trials are with location Japan, and in Germany, Italy, France, Argentina, Norway and Austria there is 1 organized clinical trial each. For one of the reported clinical trials pieces of information for the location is not available.

Conclusion

The study is based on a data about the Clinical Trials available on https://clinicaltrials.gov/ which is the biggest and the most reliable source for information of this kind. It is a database web page of privately and publicly funded clinical studies conducted all around the world.

From the reported and reviewed data, it can be noted that the number of clinical trials in which indication is Achondroplasia is low. This low result is due to the fact that achondroplasia is a rare disease and, still there are a lot of information that needs to be collected, prior to organizing a relevant clinical trial.

From the available data it can be noted that in almost all the biggest part of the clinical trials both young and adults are eligible to be part of the trials, and also both male and female patients can be part of a relevant clinical trial.

Regarding the type of clinical trials it can be seen that the number of both Interventional and observational types is close one to another, this is due to the fact that new information should be collected prior to organizing relevant investigational clinical trial.

Regarding the Phase of clinical trial, in the reported clinical trials there are from all the 4 phases, phase 1, phase 2, phase 3 and phase 4. There is one clinical trial in phase 4, which is showing that phase 3 of one of the clinical trials have passed successfully. There are 3 clinical trials in phase 3, which is showing that 3 clinical trials have successfully passed phase 2 of the clinical trials. The number of clinical trials in phase 2 is highest, which is showing that the trials have successfully passed phase 1, and there are 2 clinical trials in phase 1.

Overall, this information is promising and is showing that there is possibility for positive results of the medications that are part of the clinical trials.

Regarding the location of the organized clinical trials, most of the clinical trials are organized in USA, and there is up to 2 clinical trials reported in other developed countries. This is as a result of the organized health care system in those countries. This type of clinical trials are complex to organize, and in countries in which the healthcare system is not on high level it is very difficult to organize this type of clinical trial.

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