STATISTICAL ANALYSIS UDC: 616-082:303.42(497.2)

Clinical Trials in Republic of Bulgaria in the period of 2020-2023

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DOI: https://www.doi.org/10.59710/oaijoaru2421026s

Abstract

Clinical trials are a research method that studies the health and the diseases of the people. In clinical trials an answer to the questions like, how the human body works, how the disease is starting, developing and progressing, how the body can handle a treatment, what can people change in their way of life, so a disease won't occur is given.

The clinical trials can also be called interventional studies because the aim is to learn more about intervention that can be new medication, new medical device, or a new procedure.

In these studies, the researchers assigned an eligible participant to test the new product and to get more evidences that it will be safe to use in future. The new product that is tested in the clinical trial can not be used by the doctors as regular treatment of a disease prior to the received approval of it.

In the clinical trials the researchers are trying to find people that can met all the eligibility criteria that is required for someone to be part of it, patients of certain age and gender, patients who have a certain disease or a health condition, patients with or without some medical history condition, patients with or without some prior treatment of the targeted disease, patients who are or who are not exposed to something that can affect the condition that is treated.

The eligible participants in the clinical trials may or may not get any benefit from being part of the study. During the trial the researches do not have the information if the new treatment can be beneficial, harmful or same as the standard of care for that disease.

Key words: Clinical Trials, clinical studies, new treatments, new medications, medical devices

Introduction

The clinical trials as a method for research depending on the type of the study and the primary end point can be organized in different ways. The clinical trials can take places in research organizations, hospitals, universities, at the home of the participants, over the

phone or internet. The length of the study can be from few days up to few years, again depending on the type of the study and the primary end point of the study.

As it is well known there are 4 phases of one clinical trial:

- Phase I – is the first test in small group of healthy volunteers, in this phase, safe dose range and some side effects are evaluated. 15-50 volunteers are needed for this phase. In this phase the focus is on questions such as bioavailability and body compartment distribution of the drug and metabolites. It also provides preliminary assessment of drug activity. [1]
- Phase II – This phase is conducted once it is determined that phase one went well. This phase is designed to determine if the new treatment has promising efficacy so a further investigation can be made. In this phase up to 100 volunteers are part of the trial. The participants in this phase are often carefully selected, with narrow inclusion criteria. [1]
- Phase III – In this phase a comparation between a new treatment and a standard treatment is made. There is one control group in this phase that gets the standard treatment and there is one study group that gets the new treatment. A computer program randomly decides who will be part of the two groups. In these phases 300-3000 volunteers are part of the trial. Phase III trials of chronic diseases or conditions usually have a short follow-up evaluation period, relative to the period of time when the intervention is used in practice. In addition, they focus on efficacy or effectiveness, but knowledge of safety is also necessary to evaluate fully the proper role of an intervention in clinical practice. For instance, the FDA warned that morcellation to treat uterine fibroids by laparoscopic means, a procedure that had been used for years, could lead to spreading of unsuspected uterine sarcoma [2]
- Phase IV – This phase is conducted after the product receives approval from the authorities. A further testing is done in a wide population over a longer timeframe.

The 2 primary types of studies that are used to test new drugs or procedures or compare competing drugs or types of procedures are interventional and observational clinical trials.

In the observational clinical trials there is not any randomized patient or subject that is receiving the treatment under investigation, the patient is only observed. [3]

The researches from the study may assigned different patients in different groups of the study depending of the previous mentioned reasons, type of the study, primary and point of the study and the organizational structure of it. In the studies there are more possibilities for the different group of patients: some of the patients randomly can be assigned for comparation of two drugs, which will work better, which of them will have less adverse events reactions. Others can be assigned in a group to compare the medication with a placebo which is a substance or treatment that looks like the drug, but it does not have any active substances of a medical product in it. There also may be a third group, a group that can compare the result of getting the treatment and not getting the treatment.

The patients in the groups in the clinical trials are randomly assigned, they do not have information in which group of the study are participating.

During the clinical trials the researchers are collecting data from the patients, the data can be some answers on questionaries or surveys, collecting information from imaging methods like MRIs or x-rays, taking samples of the participants, like blood, tissue that can be checked in a laboratory. Also the researchers can do measurement of the patients, like weight, height or blood pressure, like a typical physical examination.

After the data is collected the researchers are analyzing it according to the study protocol of the clinical trial. The protocol is used as a document to assist the communication among the working participants in the trial. It should also be available to other audience upon request. [4]

After everything is collected the researchers are sharing all the data with the organization that is responsible for the clinical trial.

All the data is shared with FDA in USA or EMA in Europe and their experts will look in it and decide whether this new medication, device or treatment should be given approval to be used as a treatment for a certain condition.

Materials and methods

The research of this study includes review of reported and published information 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.

ClinicalTrials.gov is a repository of information for clinical studies and the summing results and together with special research tools, provides a unique window into the clinical research world, which includes all ongoing, initiated, completed or terminated clinical studies. Researchers usually use the information available from the database to assess the reported research practices, or to characterize the clinical research enterprise. [5]

The filters that were used to get the results are:
1. Country in which the clinical trials take place, as a country is chosen Republic of Bulgaria,

2. Period in which the clinical trials take place. The start date is chosen to be 01/01/2020, the end date is 31/12/2023.

3. The study phase of the clinical trial in the reported period in Republic of Bulgaria.
4. The age of the participants in the clinical trials, younger than 18 years and older than 18 years.

5. The study type of the clinical trial reported in this period.

After getting the results, they are sorted into diagrams for better visual display.

In the results available is information for the number of clinical trials in this period, cities in which the clinical trials are taking places and the type of clinical trials in this period.

Result & discussion

In this study we will present the statistical analysis of the clinical trials conducted in Republic of Bulgaria in the period of 2020 to 2023.

The major purpose of this study is to get a conclusion how many clinical trials are conducted in Republic of Bulgaria. To get a conclusion in which phase of clinical trials are most of the conducted clinical trials in Republic of Bulgaria. To compare the number of the trails in which the target population of patients are adults and the number of clinical trials in which the target population of patients are kids in Republic of Bulgaria, and what type of clinical tries are taking place in Republic of Bulgaria.

The figures that are shown in this study are publicly available at ClinicalTrials.gov.

According to the statistical information available on ClinicalTrials.gov we can see that in Republic of Bulgaria in the period of 2020 to 2023, 590 clinical trials were conducted.

According to the statiscial analysis available on ClinicalTrials.gov we can see that from the reported 590 clinical trials in this period, 42 were in phase 1 of the study, 172 were in phase 2 of the study, 323 were in phase 3 of the study and 16 were in phase 4 of the study.

For 37 of the conducted studies in this period information for the phase of the study is not available at the momment.

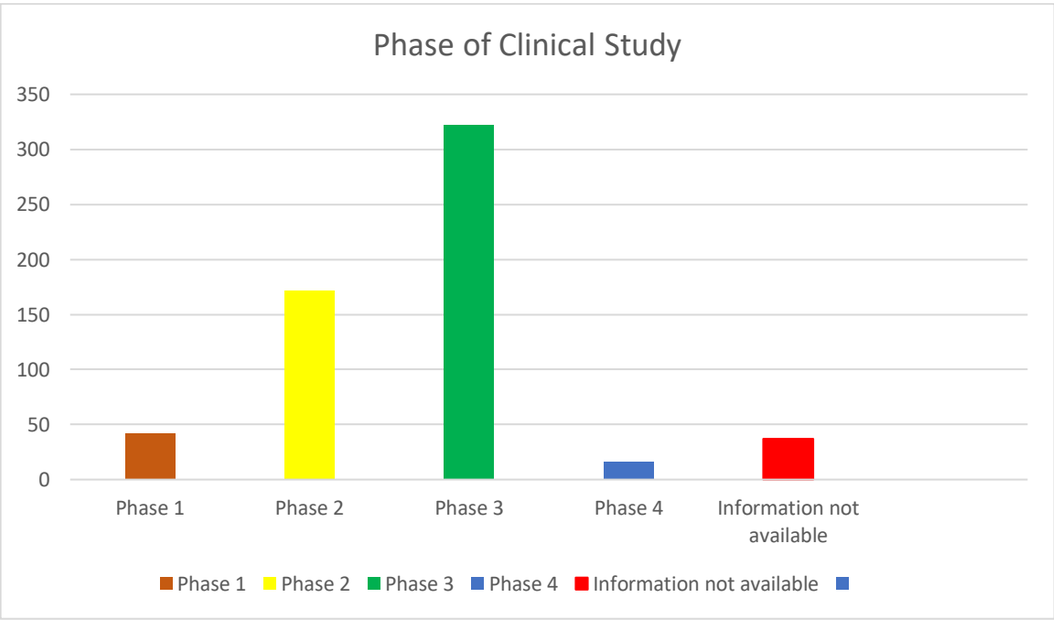

Chart.1 Phase of Clinical Study

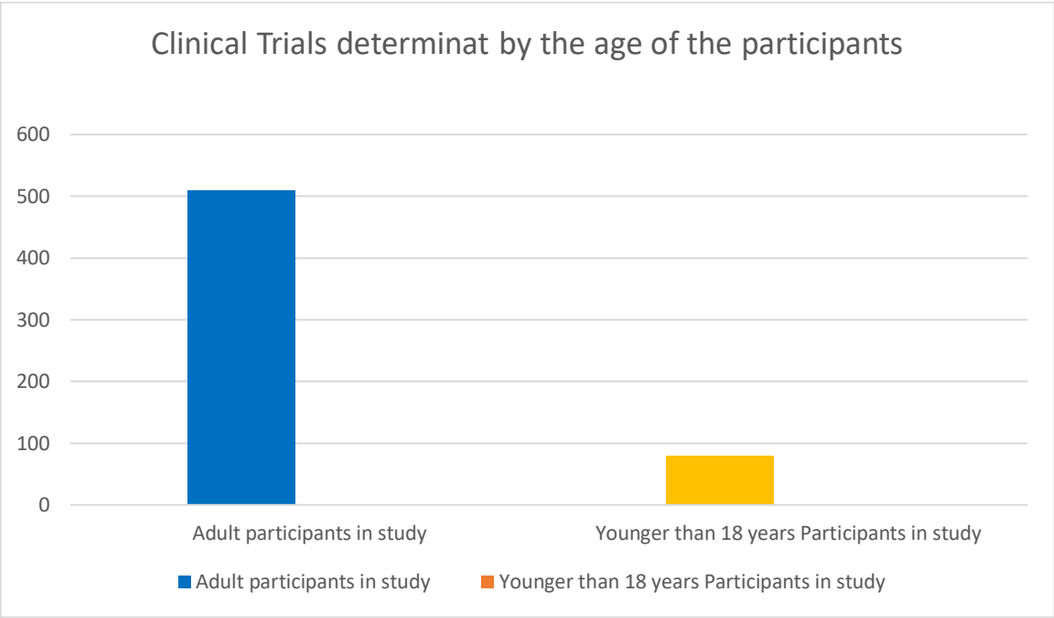

Chart.2 Clinical Trials determinate by the age of the participants

According to the statystical analaysis available on ClinicalTrials.gov we can see that in Republic of Bulgaria in the period of 2020 to 2023 from the 590 clinical trials organized, in 80 of them target population were kids, in the rest of the 510 clinical trials only adult participants were the target population.

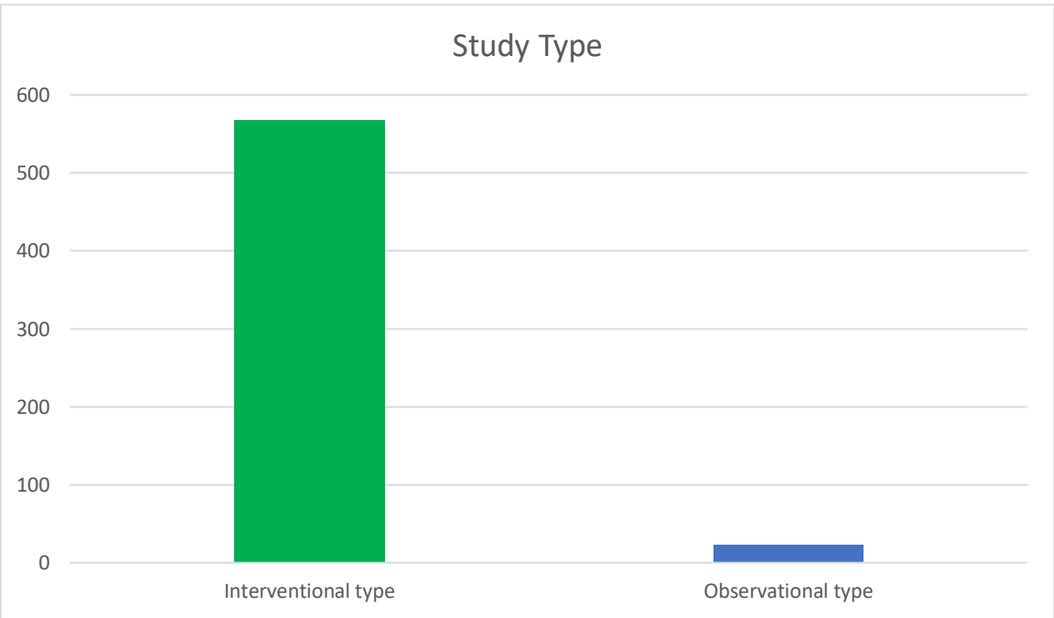

Chart.3 Study Type

Compared by the study type we can see that in the reported period there were 567 clinical trials in interventional study type and 23 of the whole studies were from the observational study type.

Conclusion

The study is based on statistical analysis reported and published on clinicaltrials.gov. From that results and statistical analysis we can conclude that the number of Clinical Trials in Republic of Bulgaria in the period of 2020 to 2023 is high. In this period there were 590 trials Organized.

From this number we can see that the number of clinical trials is high, and Bulgaria can become one of the leaders in the region for organized clinical trials. This can be due to the fact that Bulgaria is part of the European Union, there is good legislation in the laws compared to the other European Union members, and all the big pharma companies are considering Bulgaria as a serious region for conducting clinical trials.

With the organized health care system and with the high-quality staff that the Bulgarian hospitals and research centers have the number of the clinical trials can become even higher. Our expectations are that in future the number of clinical trials in Bulgaria will become even higher.

The highest number of the clinical trials organized in Republic of Bulgaria is in phase 3, which is expected because in this phase the safety and efficacy of a new medication or a new treatment is observed. Another known fact is that in this phase the biggest number of patients is required to the safety and efficacy of a new medication or treatment to a disease can be proven.

We can conclude that most of the clinical trials have target population of adults.

This result can be consiered as expected since the fact that the median age in Bulgaria is 44.8 years [6], which is higher compared to other countries. That is why more clinical trials in which target population are the adult patients are conducted compared to the clinical trials in which younger patients are required.

And from all the clinical trials organized in this period the comparation between Interventional type and observational type is also as expected higher number for the interventional type of clinical trials. This result is expected since in the interventional studies the new medication or treatmen is under survilence and it is used as an intervention for treatment of some disease, on the other hand the observational studies in most of the cases only are observing products that has received authorization prior to the study.

References

[1] International Harmonised Tripartite Guideline: General Considerations for Clinical Trials: E8. July

[2] Laparoscopic Uterine Power Morcellation in Hysterectomy and Myomectomy: FDA Safety Communication.

[3] Hannan, E. Randomized Clinical Trials and Observational Studies: Guidelines for Assessing Respective Strengths and Limitations. J Am Coll Cardiol Intv. 2008 Jun, 1 (3) 211–217. https://doi.org/10.1016/j.jcin.2008.01.008

[4] Beasley R. Worldwide variation in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema. Lancet (1998) 351: 1225–32

[5] Tse T, Fain KM, Zarin DA. How to avoid common problems when using ClinicalTrials.gov in research: 10 issues to consider. *BMJ*. 2018;361:k1452

[6] Worldometers; Bulgaria demographics; February 2024 [www.worldometers.info]

Charts and tables:

Chart 1. Phase of Clinical Study

Chart 2. Clinical Trials determinate by the age of the participants

Chart 3. Study Type