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Research Article

Principal Investigators and Site in the Challenges of Clinical Trials Recruitment and Contemporary Tendencies

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Abstract:

Annotation:

Clinical trial is cutting edge of science to bring the so needed medicines to the suffering patients over the whole world. Cutting edge always the challenge and modern challenges now substantially increased and consist of digitalisation, decentralization, personalization and many others new tendencies and the meantime the old challenges like recruitment of patients keeps saved. From the one side challenges is facilitating the trial but from others it requires much more education, trainings and a time. It could seem that role of investigators and site can be reduced by these tendencies and to reveal it we will highlite the tendencies by the perspectives of site and site. The role of principal investigator anyway still continues to be the important for all of this challenges.

Materials and Methods: Review of the publicaitons randomly found on the topic of challenges and Principal investigators and site in the challenges of clinical trials - recruitment and contemporary tendencies.

Study objectives: to highlight Principal investigators and site in the challenges of clinical trials - recruitment and contemporary tendencies

Statistical analysis: there were no statistics and only the observation of journal open sources.

Results: It was reviewed the modern and old tendencies in clinical trials Principal investigators and site in the challenges of clinical trials - recruitment and contemporary tendencies.

Discussion: Recruitment as an old challenge to continue to be important part of clinical trials and this challenges and role of site and principal investigators continue to be important. Modern tendencies as new challenges require the site and principal investigator even be a more involvoing to the clinical trial compare to conventional centralyzed trials.

Keywords: zinner syndrome; seminal vesicle carcinoma

Introduction:

Clinical trials as of today is the way to provide the society with the effective and safe treatment and diagnostic approaches to the patients (Friedman, L, 2010, Toerien M. Et al., 2009).

Over 34000 clinical trials are conducting annually in the world. Data of clinicaltrial.gov for 2021 year consist of 34,528 studies including all phases.

The number of patients who is participating in clinical trials annually is dozens of millions. But anyway, this not more than 2-5% out of patients could be participating (Mona N. Fouad at all, 2013)

Cost to reach the approval is so high that it could seems that the more cost done the more success is expecting. For example, now to reach the succes in clinical trial it could be spent more than 10+ years and more than 2+ bln USD, but only 1% bring the approaches to the patient or reach the market or, by other words, having overcome all approvals and studies to be safe and effective in order to give favor to the patients (Woodin K. at al., 2003).

The reasons of this result are due to challenges rasing during the development of the Investigational Medicinal Product.

Methods and Materials:

It was done the review of the randomly found publications the topic of challenges and Principal investigators and site in the challenges of clinical trials - recruitment and contemporary tendencies. It was grouped found challenges and tendencies in a few gropus and discussed it.

Statistical Analysis:

No statistical analysys done.

Results:

Clinical trials traditionally are conducting in hospitals or medical centers and being called CENTRALYZED or conventional trials and this is set up in ICH GCP any revisions (ICH GCP).

Based on the literature (Herzhoff Y., 2022, Bonner K., 2022) we grouped following challenges:

Challenges:

1. Related with the study itself (protocol, site, recruitment)

2. non-related with site – pandemic, politicial reasons.

Challenges related with the study could be shown like below:

1. **To proof that the new approach effective and safe**.

EfficacySafety and efficasy is the first aims of any clinical trial and this is indeed the challenge to proof that the new IMP more effective and safer than the previous IMP.

2. To finance the study Fundraising the study.

Definitely when study started sometime company who run the study could not find the resources to finish the study.

3. To involve and keep patients in study.

Recruitment of the patients. Retention of the patients.

Recruitment and retention are pertaining to the patients and boths is the big challenge

4. To be always motivated to perform a study.

Motivation to do the study is one of the key drivers inside the site's team, follow the P.G de Jong (2015) and O. Rengering (2014) the approach when the more dedicated and motivated investigator locally the more recruitment rate will appear. Motivations has to have a leader and it must be a principal investigator.

5. Others challenges related with the study:

Many others (regulatory, eligibility criteria, education of staff, diversity)

The most important challenge is the recruitment of patients and retention them in study. The studies which are failed in recruitment of patients is reaching up to 80% (Kelsey M. 2011). Additionally, 85% trial fail to retain a patients and drop-out rate reached up to 15-30% (Brooks' S. Et al., 2015)

CHALLENGES NON-RELATED with study

- Pandemic (COVID-19)
- Disasters
- political reasons (conflicts)

The challenges in clinical trials partly calls a tendency of clinical trials. Of course, the tendencies are the evolution of clinical trials.

Not all the tendencies have a clear determination and description (Lazarus A, 2004, DeSantis, S, 2005, Munroe J., 2004, Ruano G., 2004, FDA, 2006,).

The tendecies now is:

1. Decentralization of the study
2. Implementing the patient-centric and personalised studies
3. Virtualization of the studies
4. Risk-management approach in conducting of clinical trial
5. Implementation of artificial intellect to the study
6. RWD/RWE approaches
7. Hybridisation of the studies
8. Clinical trials with using of bayesian statistics
9. others

All clinical trials are conducting by the principal investigators and his team even that for the 2021-year number of decentralyzed clinical trials is increased the "decentralyzed" does not mean excluding the site or clinical site from the particiation. Ed Miseta By Ed Miseta, (2021) Chief Editor, Clinical Leader is saying that centralyzed studies is dead. Centralyzed is alredy can be titled as traditional. Decentralised study is study which are conducting fully or partly out of clinical site.

When conducting the decentralyzed studies there is a necessity to conduct the protocol procedures out clinical site – in place of the patients and this cause a regulatory (like form 1572 for out of site nurse), ethical and some other considerations, but the recruitment and retetnion is vedry high compare with conventional studies (Adams, S. Et al., 2015

Patient-centric trials are defined as investigations that prioritize the needs of the patient at all stages, including design, activation, enrollment, data collection, completion and outcome reporting - (Bob T. Li B. et al, 2022) or by other words - Patient-centric studies is the study where the patient is determining the design of protocol in order to make it more comfortable to them

Virtualized studies

- Purely this means that studies are doing virtually. For example, some sponsor before the run of real studies doing the part of aspects virtually.

Risk-management approach in conducting of clinical trial

- This approach more spreaded and allow to protocol be very flexible and react to the rised risk in timely manner.
- **Implementation of artificial intellect to the study**

The evolution of precise tehcnology to nanotechnology is resulted to implementation of aritifical intellect (AI). AI as of now can track the very small and hardly revealed items related with safety for example. AI also a challenge (Bonner K, 2022

RWD/RWE approaches. Real world data and evidences now is more and more emerging tendencies and allow the patient and the investigator doing their job and simultaneolsy particpating in the study and nurse in these studies also doing their job in ordinary manner.

Hybridization of the studies

This is the mixture of any descibed above tendencise in the studies.

Discussion

Rapid changes in the outlines of the present and future future primarily concern global medicine and trends are associated with a shift in focus from illness to general health, patient-centricity, digitalization of medicine (Herzhoff Y., 2022) including artificial intelligence (Bonner K., 2022) and the global strategy until 2030 includes the following goals for improving health - to guarantee universal access, continuity, coverage and quality of care through adequate investments to strengthen health systems and implement effective policies at the national, regional and global levels.

Since the start of clinical research, the first mention of which dates back to the 18th century (Bull J, 1959, Lilienfeld A., 1982), clinical studies were conducted for a long time in the composition - a sponsor, a researcher, which was then joined by an ethical component, and until the end of the 20th century, the scheme included a clinical center where patients were concentrated and basic procedures were carried out.

Currently, the classical scheme has certain modifications associated with the introduction of new technologies and we can talk about the following types of clinical trials (Lazarus A, 2004, DeSantis, S, 2005, Munroe J., 2004, Ruano G., 2004, FDA, 2006, Hekmat R et al., 2021, Wilkinson M., 2018, Blake A. 2022, Li B. Et al.)

- Decentralyzed Clinical trial
- Personalyzed Clinical trial

- Hybrid Clinical trial
- Virtual CT
- Bayesian Clinical trial
- Real World Data
- Real Evidence Data
- Artifical Intellect

Also, from the trends in CI, a shift in localization from Western countries to Eastern countries is clearly visible. Miseta E. (2021) cites data that in 2016, 23.6% of all clinical trials were initiated in the USA, and 12.5% in China. In 2018, the ratio was already 21.6% in both countries, and in 2019, the number of initiated clinical trials in China was already 23.7%, while in the US it fell to 20%. In the countries of India, Iran, Japan, Germany, and the UK, the number of new trials increased from 4.4% in 2016 to 10.9% in 2019. The growth of CT in the East is affected by the cost per patient - the cost of a phase 3 study in immuno-oncology in The US is 60 thousand dollars, in China - 25,000.

The trend of the aging of the population as a whole is obvious and, for example, according to estimates in China alone, the number of visits per year of the aging population is 2.2 billion dollars and 50 million visits.

We must also take into account the current epidemiological (Ledford H., 2021, Unger J., et al., 2021, WHO report 2022, NIH report, 2021) and political situations (Dalio R., 2022, Alsumudaie M, 2022, Castaneda C. 2022)

Patient-centricity trends are typical not only for clinical trials, but also for preclinical trials (Taylor N., 2022). However, the patient-centricity of CI has also been criticized (Mermet-Bouvier, P., 2020).

The future lies in blending gaming technology with clinical research (Sinha A., 2022)

Global standardization of CI is also a trend (Koski G. Et al., 2018)

Nevertheless, despite the trends in the virtualization of clinical trials, enrollment of patients remains the prerogative of centralized trials (Miseta E., 2021).

At the end we did not find that role of investigators and site's team changed dramatically and reuires revised of the ICH GCP regulations which measn that principal investigator and hi team is still very important in the challenges of clinical trials - recruitment and contemporary tendencies.

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