Research Article

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Recent Advances in Clinical Trials

# Additional Strategic Empirical Tools for Recruitment and Retention of Patients to the Randomized Clinical Trials

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## ABSTRACT

***Annotation:*** *The process of enrollment to the clinical trials and then keeping the patients active in treatment being called recruitment and retention respectively. This process is both an area in clinical trial, which must be performed only according to protocol and therefore successfully. If there is a deviation in performance so it heading to fail of trial partly or fully. There is many strategies in keep performance these process ongoing but anyway the number of clinical trial fail is still very high: up to 86% percent if fail on the enrollment phase and then up to 15% of involved patient drop –out the study. We investigated the rate of recruitment in the light of our authentic strategist.*

***Materials and Methods:*** *Retrospective analysis of data of three clinical trials II-III phases in oncology conducted since 2013 to 2022 years.*

***Study Objectives:*** *To investigate the study recruitment rate during the enrollment period using the authentic strategy a for recruitment and retention.*

***Statistical Analysis:*** *Data had been analyzed by the descriptive statistic.*

***Results:*** *It was determined that using the proposed strategy is improve the enrollment and retention.*

***Discussion:*** *Recruitment is active process and additional tools for improving these processes need to be flexible and developing according to the current situation and that why there is so many such tools. We proposed the additional one.*

## Keywords

Clinical trial

## Introduction

Clinical trial is the important part of evidence-based medicine [1] Enrollment of patients to clinical trial is important part of any clinical trial [2]. Due to fail in enrollment up to 86% of clinical trial unsuccessful [3,4], and more over after the patient randomized to the trial the following keeping them active in study and then follow-up period also the challenge and being called retention of the patients and fail in this period [5] also will lead to fail of the trail and the fail in retention period consist up to 15% of trails. Factors influencing to recruitment and retention is diverse and difficult to estimate due to highly variable [6,7]. D. Fogel [8] found more than 30 factors influencing to recruitment and much of them can ruin the trials due to fail of recruitment. M. Rutger at al., (2017) and found more than 30 factors acting differently to recruitment. Authors seeks the way to facilitate the enrollment [9,10]. In order to facilitate the enrollment and retention based on studied factors and barriers G. Huang Et al., (2018) had grouped these factors to three ones to develop the strategy - (1) trial design

and protocol development, (2) trial feasibility and site selection, and (3) communication.

## Methods and Materials

We developed the strategy to enroll and to save the patients in study and investigated data of enrollment and retention period in three successful on enrollment studies participating in phase 2-3 trials in oncology for the period from Jan 01, 2013 to December 31, 2021 and approaches to improve enrollment and retention applied in these trials.

We used next tools for boost recruitment based on the principle of permanent presence with study team.

1. Building the network of local site managers out of site's staff - all of the site's team has an appointed study coordinator who was responsible for the enrollment and retention;
2. Trainings visits separately or combined with monitors – all sites were visits at least once for initial training either on initiation visit or separately before the start of enrollment on the particular site;
3. Motivational visits – all sites were visited once right after the start of enrollment on order to address issues and question raised during the:
4. Physician support on some medical aspects of study-specific procedures and some management of this based on the experience from other sites - by the sponsor it was assigned separately employed physician and each site were visited by this doctor in order to address medical aspects of the protocol;
5. Building the referral network of physician who will send the patients to the site – each site's principal investigators were provided to the sponsor the local doctors well known to the PI who has the patients with the protocol nosology;
6. Direct searching of pts on the database of site – each coordinator locally were obliged to make a search of the eligible patients per local database;
7. Contacts with the societies of pts – each local principal investigators have a communication with the local society of protocol nosology patients;
8. Others contact with doctors from other regions - each local principal investigators have a communication with the out of local physician who has protocol nosology patients:
9. Motivation through the fee – each site was proposed to have a few gradual payments per determined period;
10. Motivation through the publication or article – high enroller was proposed to be an author of upcoming article;
11. Motivation through the conferences - high enroller were proposed to be a visitor of conference per protocol nosology.

In order to evaluate the efficacy of applied strategy it was investigated figure of final enrollment, screen failure rate and dropout rate of the patients per each site.

The number of involved cities, involved sites and protocol-required patients are presented in Table 1.

**Table 1:** Etymology of studies, number of cities where centers opened, amount of centers opened, number of patients to be involved according to protocol.

| № | Nosology | The number of cities in which centers were opened | Number of clinical centers | Study power - required number of patients (n) |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |
| 1 | Endometrial cancer | 19 | 23 | 500 |
| 2 | Ovarian cancer | 9 | 10 | 333 |
| 3 | Head and neck cancer | 2 | 2 | 136 |
| Total | | 30 | 35 | 969 |

## Statistical Analysis

Following done:

- Calcuation of enrollment per each site
- Calcuation of screening failure (including drop-out)
- Calculation of mean and error where applicable

## Results

Following enrollment figures presented in table 2.

**Table 2:** Enrollment.

| № | Study | Enrollment | Screening Failure | Drop-out |
|---|---|---|---|---|
| 1 | Endometrial cancer | 54 | 2 | 0 |
| 2 | Ovarian cancer | 29 | 1 | 1 |
| 3 | Head and neck cancer | 25 | 0 | 0 |
| 4 | **TOTAL** | 111 | 3 | 1 |

We see that rate of screen failure consist of 2,7% and drop out rate less than 1% which means that strategy is works.

The breakdown of the patients per sites presented in table 3.

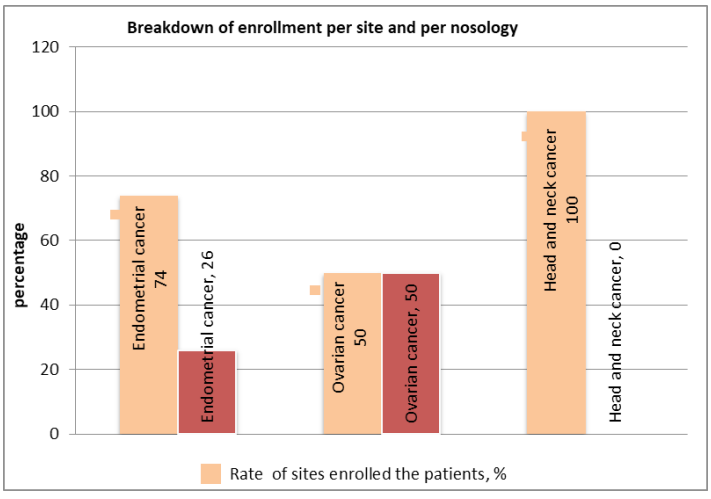


**Figure 1:** Rate of enrollment.

**Table 3:** Etymology of studies, number of cities where centers opened, amount of centers opened, number of patients to be involved according to protocol.

| № | Nosology | The number of cities in which centers were opened | Number of clinical centers | Number of sites did not enroll any patients (%) |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |
| 1 | Endometrial cancer | 19 | 23 | 6 (26%) |
| 2 | Ovarian cancer | 9 | 10 | 5 (50%) |
| 3 | Head and neck cancer | 2 | 2 | 0 (0%) |
| Total | | 30 | 35 | 11 (37%) |

We see that percentage of sites did not enroll any patient is in average - 37%. (26 – 50%).
Cumulative figure presented on figure 1.

## Short Discussion

One of the crucial factors on the first stages of the clinical trial is the permanent stream of the pts into the study independetly on the circumstances [8]. This drive the sponsor, CRO and investigator and all of the parts which is participating in the study. In the meantime authors (Bachenheimer J. F., Bonnie A. Brescia [11] mentioning that out of 80% of patients have a good will to particiapte in study but only 10% of them is actually participated and from other side 33% of sites and principal investigators can not enroll even a single patients to the study [12] and only these two factors is heading to fail up to 76% of clinical trials of II and III phases. R. Blenkowski at al. [4] is saying on 80% of screen failure rate for mostly of the clinical studies. The patients is generating the so needed data for the reaching the final results [13,14] – either failure of the study or the overcome to the next phase and eventually to market phase to be helpful for the patients. To reach the patients recruitment in adequate pace or, at least, in adhere to timeline, each company is applying different approaches. Some authors [8] determines the necessity to see the diseases for each way of recruitment.

For this particular article, I can select some few approaches;

1. No approaches or minimum approach - without investing resources;
2. Extensive approach – with involving of peoples and sites into the study;
3. Intensive approach – with permanent management of this process during all of the duration of recruitment according to protocol with investing the time, finances and people resources.

Approaches could describe the type of growth of the contract research organization, namely the third approaches is more typical for just new players which is need to show a good results and result is means their growth. The first is typical for already grown companies, which is similar to brand of market.

Here we will touch third approach which is seems crucial for small companies.

Follow the P.G de Jong [15] and O. Rengering [16] the approach when the more dedicated and motivated investigator locally the more recruitment rate will appear we developed the strategy – PPS (**permanent presence on site**) and have shown the enrollment rate after applied this strategy. From our point of view this startegy quite effective. Such tools is requires when sites started to recruit the patients and can be applied separately. Before recruitment is very important to evaluate rightly the possible recruitment locally in site.

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