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Patient Retention Stewardship in Real world Evidence Studies: the Pentad of P's Model

Amit Kumar[1]*, Sanjay Kalra[2] and Vandna Rana[3]

[1]*AstraZeneca Pharma India Ltd, India*

[2]*Bharti Hospital, Karnal, India*

[3]*Indegene Lifesystems Pvt Ltd, India*

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***Corresponding author:** Amit Kumar, Astra Zeneca Pharma India Ltd, India, Email: Amit.KumarAK@astrazeneca.com

Abstract

Real World Evidence (RWE) studies generate data that helps fill the knowledge gap between clinical trials and actual clinical practice setting. RWE studies generate data across different age groups, races, ethnicities, varying severities, unstudied co-morbid conditions, differing concomitant drugs (including OTC medications), lifestyle variations and differing adherence/compliance patterns. RWE studies are across very large number of patients and therefore may help unearth rarer ADRs which are not evident in relatively smaller populations in clinical trials.

By definition the RWE studies are across larger and more diverse populations than the more controlled setting of Clinical trials which are conducted across a relatively smaller number of subjects. Given that controls are lesser in real world setting of actual practice, it is difficult to enrol and more importantly retain patients in these real world studies. The very basis of these real world studies is to generate rich data from a larger population and patient retention being a challenge, the results RWE study would lose significance if the challenges of retention are not addressed at the very beginning. This article is an endeavour to discuss various risk factors affecting patient retention and suggests a practical approach by the entire study team to effectively address and mitigate these risks.

Introduction

The main purpose of drug development is to bring drugs and devices to market faster and improve patient's health outcomes. But what happens once those drugs and devices are in the market? Real World Evidence (RWE) provides deep insight into how a drug is actually used and how it performs in the "real world" with all its variety of settings and circumstances. RWE is obtained from real world evidence studies, which may be of various types (Table 1)

Table 1: Real-world studies.

Late Phase Research
Observational Studies
Non-Interventional studies
Postmarketing surveillance (PMS)
Registries
Epidemiological studies

Factors Affecting Study Success

There Are Many Factors, Which Can Affect Study Success (Table 2)

Table 2: Factors affecting study success.

Patient Recruitments
Patient Retention
Study Design
Interest of participating sites and patients

Importance of retention

While patient recruitment is often highlighted as the key aspect in ensuring study success, the area of patient retention in RWE studies is often overlooked. Retention of patients throughout the life of study is however critical from scientific as well as economic point of view. Retaining as many patients as possible should be a priority since it directly affects the statistical power of the study. Some reasons for subject dropout are within

the control of study or can be addressed through careful study design and during conduct of the study.

Factor Affecting Retention

Retention Stewardship

A good retention plan needs stewardship by Sponsor, CRO & Sites. This is done through a good patient retention plan, which can be developed at the initiation of the study and that can be implemented throughout the life of the study to mitigate patient retention risks. There paper emphasizes on 5 key elements Table 3 which can lead to good retention stewardship.

Table 3: Factors influence patient retention.

The Pentad
There are many elements which can influence the patient retention and can be listed as a pentad (the five 'Ps')
Protocol
Patient consent & participation
Patient population & education:
Physical attributes of site
Personnel at site

Protocol

A study protocol is a document that describes, in detail, the plan for conducting the study. The study protocol explains the purpose and function of the study as well as how to carry it out. During protocol development, sponsors should consider how the study design will translate into patient burden for study participants. The number of study visits, complexity of the tasks the patient must perform, and the convenience of the site location can all build into unrealistic patient burden that leads to early discontinuation from the study.

A proactive approach to integrate into the study design phase is to conduct a feasibility or Panel discussion with NCI/ study chair person & SC members (National Co-ordinating Investigator & Steering Committee Members), which comprises of experience Investigators of the country. This group can offer the sponsor insights into patient perceptions & practical challenges of the study. A Sponsor can pen down common questions and seek clarity during the discussion. There are few questions mentioned in Table 4.

Table 4: Sample of Questions.

Sample of Questions
What should be study duration?
What should be the follow up number and timing of study visits?
Is it feasible for patient to visit the clinic every weeks or months, as required?
Which study procedures are you most concerned about?

The investigator meeting can also provide an interactive forum for all PIs & site staff to exchange successful strategies for addressing patient concerns.

Patient consent & participation

At the time a patient consents to participate in a study, the consent process should be a detailed discussion or explanation of what will occur during the conduct of the study, risks and benefits, study duration, Number of follow-ups and timing of study visits and potential side effects. The principal investigator is key to setting the right tone at this first visit. Recognizing and addressing a patient's concern during consent process and throughout the study is important to retain the patient till study completion. During the consent process if a patient has a fear, it has to be addressed by the principal investigator who listens to and answers their questions.

Patient population and education

Patient population for a study depends on the disease prevalence in the surrounding areas of the site. For example, there are good transport facilities in plain areas versus hilly areas, so studies which require frequent follow up will have better retention in the plains. At present almost all the studies require educated patients. For example, diabetes studies design includes patient's diary or questionnaires for collection of information regarding blood glucose values and other patient reported outcomes such as quality of life. This means that site with lot of illiterate patients will not be able to retain patients because they need support to fill the details and in long term they can feel it's a burden or pressure

Physical attributes of site

Recruiting a large number of participants and retaining them in the study usually requires involvement of a considerable number of centres. However, all centres need to have a patient pool of adequate size and the infrastructure and resources to recruit and manage the projected numbers of patients efficiently

Site resources: One should assess personnel resources including the number and type of personnel available, their functional responsibilities, and their relationships to other institutional departments, referring physicians and community organizations. Participating research clinics need to be centrally located, easily accessible, well organised and efficient in scheduling tests, collecting information and so on. They should offer flexible appointment times and sufficient time with the clinical trial staff for participants to adequately understand the study's rationale, its requirements and risks and have all their questions answered.

Site facilities and procedures: Site facilities & procedures can also affect patient's retention like

- Availability and responsiveness of site staff; Patients will feel more secure having 24/7 access to trained study staff.
- Convenient timing of appointments: Will facilitate patient's compliance with the study schedule and prevent missed visits.

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• Logistic issues can also lead to study procedure's fatigue and patients may lose their interest in participation further.

Personnel at site

Though the PI is responsible for the conduct of the study however the Study Co-ordinator (SC) is the heart and soul of the study and that, ultimately, it is the SC who carries forward the research goals and play a significant role in the success of the study. Employing an experienced and dedicated SC at each participating centre is key to successful recruitment, retention, and reduces the time demanded of investigators. Same site personnel/SC throughout the study duration helps to facilitate trusting relationship with the patient. SC should be skilled at verbal communication (in languages) and responding to subjects' questions and concerns.

Site experience: Past experience in conducting studies in a similar patient population and assessment of past enrolment & retention performance metrics is important in deciding whether a site can fulfil the need.

Communications: Strategy of maintaining a strong communication with the patient over extended periods of time during the study is essential. Patient retention involves great customer relationships therefore SC should focus on creating a pleasant "Soft Skills" experience for the subject. Patients are people too and treating them in the same way as you would want to be treated will build trust and confidence required to retain a patient in the study.

Use of Technology in Retention Plan

Technology solutions can provide a supportive role in retention during the patient participation phase, ensuring the patient has a positive experience at the clinical study site and this remains critical for ongoing patient participation.

1. Telephone/mobile based: One of the traditional techniques, telephonic contacts to engage with patients between clinic visits can be utilized. Calls to patients between visits help to address patients concerns, remind for upcoming visits etc. And it can be done from both the methods:

A. Voice

a. Automated

b. individualized

B. Text

a. Automated

b. Individualized

2. Internet based: Study-specific websites provide a way to offer ongoing support and information about the study.

3. Smart solutions: convenient timing of appointments facilitates patient's compliance with the study schedule.

Some key points to keep patient engaged and motivated are listed in Table A.

1. Respond in positive manner :

a) For example if patient has a concern for frequent visit required for the study then it can be responded in positive manner like frequent visit can translate into close medical attention.

b) Some RWE studies do not offer immediate benefits to individual patient and patient always think about "WHAT'S IN IT FOR ME". Investigator or SC can convey like this: There is no immediate clinical benefit to you. However, the information gained from this study will benefit the doctors which will lead to better management of patients in future.

2. Same site personnel/SC throughout the study helps to facilitate trusting relationship with the patient.

3. Calls to patients between visits help to address patients concerns, remind for upcoming visits.

4. Convenient timing of appointments facilitates patient's compliance with the study schedule.

5. Study-specific websites provide a way to offer ongoing support and information about the study.

Conclusion

Patient motivation for participation in the study is multi-factorial and is a continuous process. Part of this process includes reinforcing the study purpose and the value of their participation at each study visit. The practices described above, may be quite effective in identification and fixing the problem of patient dropouts at the right time. The ''Pentad of P's model'' is a simple method that Study Team (sponsors, CRO and sites) can use to prepare a good retention plan, minimise the retention risks and ensure effective retention stewardship.

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