Designing and conducting clinical trials in rare diseases - what industries expect for partnering with clinical sites"

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This webinar focuses mostly on the industry perspective of what is needed to adequately conduct a clinical trial, what are the main issues that are usually encountered in clinical trials, how to overcome those, and how to prepare your center as an investigator for an industry sponsored clinical trial.

Why drug development for the rare diseases is so difficult?

-Rarity: only a tiny minority of rare disease have in general enough patients in development to have a full understanding of the benefit/risk compared to the standard that are used for more common diseases

-Highly heterogeneous: significant clinical differences and evolution amongst patients, often not completely understood given the limited knowledge available on the disease

-Little know of these diseases: limited literature or natural history data available make drug development and trial design particularly challenging

-Complex therapies: most of the therapeutic targets for these diseases are undruggable with traditional chemically-defined small molecules and with traditional biologics, so this is why in rare diseases there has also been a significant number of clinical trials and new products in development with innovative, and thus less understood, therapeutic modalities (gene therapies, cell therapies, RNA-based therapies)

What are the elements that are impacted by rarity in a clinical trial?

Design

- In most of the cases, trials do not have a formal sample size estimation and are often underpowered or based on less solid assumptions.

- There is very limited possibility to identify a specific study population, especially if the study population is a subpopulation of the overall patient group with the disease.

- It's very difficult and very challenging to collect and adequately understand the impact of concomitant medications.

Execution

- Sites are often identified and selected because there are patients, with a different logistic approach than large indication's trials.

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- The logistics is more complex because there are multiple destinations for the products and sometimes the center is far away from patients' home.

Results

The representativeness, the meaningfulness, the size of the confidence interval, and the reproducibility of the data all depend on the design and execution of the study.

Termination of clinical trials

The main reason for early termination of clinical trials is basically failure in recruitment of patients.

The second consequence of a clinical trial's operational failure (including drop-outs and poor quality) are violations:

- Failure to ensure adequate consent of participants

- Failure to comply with protocol's instructions leading to multiple data corrections, and enrollment or protocol deviations

- Failure to handle the medicinal product properly (and document it)

- Failure to keep the appropriate study records and consistency with health records

- Failure to communicate from the patients to investigators and viceversa or between the investigators and collaborators or between the investigators and sponsors or CROs.

How to avoid violations?

- Ensuring knowledge of the protocol by all the people involved in clinical trials through training and re-training

- Design a recruitment strategy

- Use forms, checklists and process flow that are part of the study documentations

- Document what are you doing

- Participate in the life of clinical trials (e.g. investigator's meetings and calls, monitoring visits, etc.)

What are industrial sponsors doing to improve the critical issues of the clinical trials for rare diseases?

- Better materials, investigator's meetings/trainings, feasibility, consent forms

- Improving monitoring technologies

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