Trial Transcending Themes in DORP

DORP is structured around four pillars, Project Management (PM), Monitoring (M), Statistics (S) and Patient Participation (PP). DORP activities are structured, formalized and executed in a project-based approach based on these angles.
Investigators can request support from DORP. The issues or requests are generally trial related. Actual support from DORP is rewarded when outcome of the support contributes to the overall mission of DORP. This is the so-called trial transcending element to be addressed, and which generates a concept, knowledge or product that will be of use (and available) for all investigators.
These trial transcending elements can be structured by defining specific topics / themes. The following five topics / themes have been identified as to cover the greatest common denominators of transcending issues.

Overall Themes:

1. Trial design
2. Trial timelines
3. Financials
4. Quality aspects
5. Professionalization of research groups

The above topics will host the smaller (trial specific) projects as awarded for DORP support based on its trial transcending element. In addition we formalize identified overall trial transcending activities that are not yet covered in a trial specific support request. Therewith, this thematic approach facilitates activities in and across the pillars.

1 Trial design

Oncology research is organized in divisions around tumor types. The observational cohort study is the basis in which all patients with a specific cancer tumor type (based on location) can be enrolled. It enables the prospective and central collection of clinical data, biomaterial and patient reported outcomes. Such a database is valuable to research in overall disease progression, effectiveness of specific treatments pathways and enables to host (non) interventional trials so called Trials within Cohorts (TwiCs) as alternative to conventional randomized controlled trials (RCTs).

New techniques and innovative approached in oncology research are emerging. Biomarkers as ctDNA and DNA profiling ((Whole) Genome Sequencing) are starting points for personalized (tumor transcending) treatments. This will lead to new study designs, and therewith generate new challenges for investigators and research groups in trial preparation and performance. DORP supports through directions to expertise in the field and process support.

Projects:

- ‘toolkit’ for cohort studies: how to start-up a cohort study. What to think of, what to cover, contracts, PIF/PIC, blue print, governance, DPIA, operational challenges, available tools for data and sample collection, templates, etc.
- Monitoring of cohort and related sub studies: combining (onsite and remote) monitoring efforts, introduce collaborative, site based and risk based approaches, thus covering multiple studies (cohort and/or sub studies) in one monitoring visit.

- New statistical modelling approach for new trial designs, such as TwiCs: (cohort related matters: bias, patient reported data), compiling expertise, development and implementation of new approaches (in relation to new study design).

2 Trial timelines

Patients are central in (investigator initiated) trials. It starts with obtaining reliable patient numbers during the feasibility and a realistic planning of any new trial in preparation and execution. After formal approval for the trial execution the next challenges are timely opening of involved sites, and matching patient and trial, at the right moment, and retaining the patient to study completion. Therefore, we focus on having the right information (in layman's language) available at the right place, at the right time.

Projects:

- Netherlands Cancer Register (NCR) for trial feasibility: how to use the NCR data for feasibility of new trials, realistic timelines for patient recruitment (per site), route-mapping.
- Patient referral: implications of patient referral; strategies to prevent 'losing' patients for trials due to insufficient / inadequate referral procedures.
- Patient inclusion: strategies, best practices.
- Functional illiteracy and trial participation.
- Patient involvement: when, how to involve patients in various steps of investigator initiated trials (IIT's).

3 Financials in investigator initiated trials

Independent Review Board (IRB; METC in Dutch) request all financials for the trial to be covered (at submission). In order to get sites involved, costs need to be determined and negotiated, i.e. who covers what: sponsor, hospital (standard care based on DBC), or external partners. Investigators often rely on the usual sources/funds for financial support of their investigator initiated trial (KWF, ZonMw). When a subsidiary application is rejected or does not cover for all costs involved, alternative or additional resources need to be explored.
How to deal with costs related to trial activities that are not covered (anymore) through the health insurance as part of the standard care. How to prevent that patients are not charged and withdraw or drop-out in trials.

Projects:

- Subsidiary options: alternatives for 'usual suspects'.
- Cost effectiveness monitoring strategies: monitoring on site level, risk based monitoring.
- Cost effectiveness, referential cost rating, centralizing or decentralizing services, cost items for e.g. patient participation.

4 Quality aspects

Monitoring is an essential instrument to ensure the quality of WMO-required research. It serves to confirm that the rights and well-being of patients are protected, that the data collected are correct and consistent with source documents and that the execution of the research is done in accordance with the approved protocol/amendment(s), ICH-GCP and relevant regulations.
Monitoring is a time and cost intensive activity. It is important to make use of monitors time in the most optimal way that ensures quality and avoids duplication or overlap, and to design towards more risked based monitoring.
The overall quality of trial execution needs to be covered at all times. Therefore, it is preferred to strive for standardization and to create consensus on overall procedures and standards. A lot is covered through national research initiatives and policy making organizations to compile and disseminate, in which DORP in linking and / or actively involved.

Projects:

- Define monitoring standards: template for monitoring plan, monitoring instructions, monitoring visit reports, etc.
- Facilitate EDP access for monitors in collaboration with DCRF; motivate use of CCMO CTA template with Annex 4 letter for monitor, etc.
- Participation into relevant working groups at national initiatives (such as DCRF).

5 Professionalization of research groups

Investigators in oncology have organized themselves around tumor types. Depending on the size of the patient population / tumor type, the specific need to be organized, availability of people and resources, and support by stakeholders, they have established a certain organizational maturity. DORP would like to support research groups in their ambition to further professionalize towards the next level (short term and long term ambitions).

Projects:

- Organizational structures: type of organization, governance, contracts, bylaws (incl templates), routing, process coaching.
- Clinical trial roadmap – 'timetable' for preparation and execution of IIT.
- Local feasibility (European Clinical Trial regulation) – implementation into roadmap.
- Effective and efficient monitoring; risk based approach, site related versus trial related monitoring, template(s), facilitate access to EDP (ACRON-Nefarma procedure).
- Educational services: oversight on courses in Good Clinical Practice (GCP), clinical trial management, clinical trial statistics, (risk based) monitoring, patient participation (PGO-support).