

Best Process, Best Outcome

Faced with a string of critical decisions during oncology clinical research, Thomas Ng and Patrick Melvin at Premier Research Group Ltd explain how meticulous planning for the feasibility assessment may pose short term challenges but offers long term benefits

The key to success in conducting an oncology clinical trial is recognising the practical concerns and limitations of the trial. A good quality feasibility assessment provides vital information and suitable solutions if implemented effectively. Understanding the associated challenges pertinent to an oncology trial and optimising the feasibility information are important and can lead to proactive strategies for efficient study execution, thus maximising the study outcome.

Given the devastating effect of cancer and the urgent need to find more effective therapies, oncology research has remained one of the greatest challenges faced by pharmaceutical and biotechnology companies. Under the current, highly competitive environment of clinical research in this therapeutic area, knowledge is the key to success for a clinical study. In order to obtain the information needed, a good quality feasibility assessment is a prerequisite. The findings from the feasibility assessment should provide guidance on how best to design and execute the studies, including to facilitating subject enrolment. Therefore, understanding how to effectively perform such assessments for oncology trials is of paramount importance.

THE ROLE OF FEASIBILITY ASSESSMENTS

Feasibility assessments provide vital information that can have a significant impact on the operational and financial considerations of a clinical study. Besides evaluating enrolment potential and an investigator's interest in a study, feasibility assessments can assess whether the study is 'do-able', 'achievable', and 'manageable' based on study-specific variables such as timelines, study design, inclusion/exclusion criteria, prerequisite treatment and so on.

- A top-level assessment of 'do-ability' provides preliminary information on subject recruitment potential based on

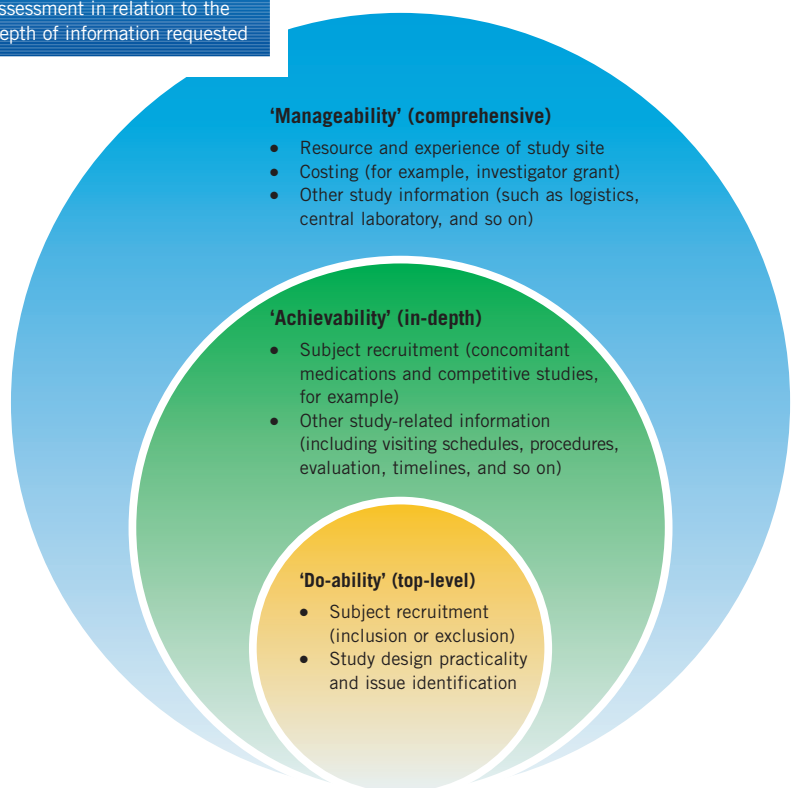
key inclusion/exclusion criteria, as well as the practicality of the study design

- A more in-depth assessment of 'achievable' evaluates subject recruitment potential (for example, the use of concomitant medications and the presence of competitive studies) and other study-related information such as visits schedules, procedures, evaluations, timelines, and so on
- A comprehensive assessment of 'manageability' examines the

resources and experience of potential study sites, study-related costing (the investigator grant for example) and additional study related information including, but not limited to, logistics and the use of central laboratories

In the preliminary planning stages, it is critical to determine the desired information output in order to ensure that the right questions are asked, and that the assessment is structured properly depending on the level of information required.

Figure 1: The levels of feasibility assessment in relation to the depth of information requested



CONSIDERATIONS SPECIFIC TO ONCOLOGY TRIALS

In order to best prepare for conducting a feasibility assessment, one must evaluate all influences that may impact the proposed clinical trial and review these in the context of geographical, socio-economical, clinical and epidemiological considerations given the particular indication under investigation. Such evaluations may include:

- As research has progressed, better treatment options have become available: such as Trastuzumab in the treatment of patients with HER-2 positive early breast cancer, and Bevacizumab with platinum-based chemotherapy in the treatment of advanced, metastatic or recurrent non-small cell lung cancer of non-squamous origin. Nevertheless, these treatments may not be approved, widely available or reimbursable by the health authority in every country. This may complicate the selection of the comparative treatment when the trial's nature is global.
- In order to minimise the clinical development timeline, study design in oncology studies has become increasingly complex. With the advancement of imaging techniques (such as the PET-CT scan) in tumour assessment and more laborious evaluation of disease activity using biomarkers, the conduct of oncology studies becomes more intensive and increasingly expensive (1). The availability of protocol-required high-tech equipment and sufficient

research and support staff at the investigative sites has to be considered.

- Patient enrolment is known to be the foremost challenge in oncology clinical research. According to a survey that included more than 500 study centres across Europe, the US, Latin America and Asia-Pacific, only 15 per cent of clinical trials were able to enrol on time, and patient enrolment was delayed by more than one month in more than 40 per cent of trials (2). Despite the benefits of potential new treatments to improve survival and quality of life, only five to 10 per cent of adults with cancer participate in oncology clinical trials (3). With an increase in complexity of study design including more frequent study visits and arduous study evaluations, patient enrolment may further be affected as well as the patient's adherence to the study schedule. If the latter is in question, it will undoubtedly affect the analysis of both efficacy (survival) and safety endpoints.
- The incidence and prevalence rates for the target cancer in a particular country or region, together with the number of competing trials in that region, should be reviewed prior to launching the feasibility assessment in order to ensure that the most appropriate countries or regions are being selected.

Understanding the impact from these challenges will provide useful guidance for developing the feasibility questionnaire.

OPTIMISING FEASIBILITY INFORMATION

The quality of information obtained from a feasibility assessment is highly dependent on its approach. The process requires meticulous planning, from proper preparation of the feasibility questionnaire through thorough analysis of the data collected. During the feasibility assessment process, the information requested and received needs to be properly evaluated and optimised so that important decisions can be made regarding the effective execution of the trial (see Figure 2).

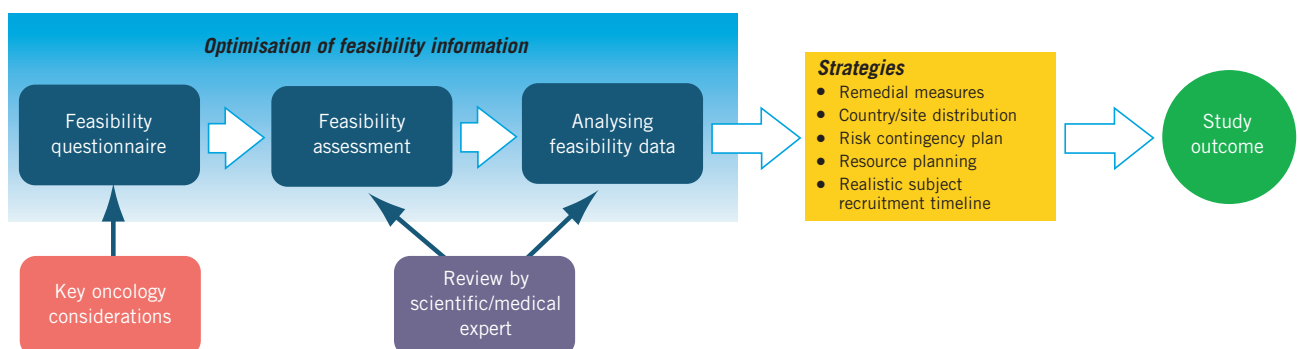
In order to optimise the feasibility information, there are a number of practical tips to bear in mind:

Feasibility Questionnaire

For global trials, it is strongly recommended that if English is the language of choice, the vocabulary and sentence structures are kept simple and specific. This is particularly important when English is not the investigator's native language, because it will help to avoid misunderstandings and minimise time delays for clarifications.

The words 'recruitment' and 'enrolment' should be avoided when obtaining recruitment numbers as these terms are often used interchangeably and interpreted differently, limiting the usefulness of the assessment. Instead, using descriptions such as the 'number of patients available to be screened' or 'number of patients available to be randomised/dosed' should help to avoid any confusion.

Figure 2: A representation of the feasibility process



Feasibility Assessment

Individuals involved in conducting feasibility assessments need to have sufficient knowledge in the target oncology disease and understand the information requested in the questionnaire. Relevant training prior to the commencement of the assessment is recommended. Furthermore, these individuals should be supported by a scientific/medical expert that is available to discuss any queries and address any clarification from the oncology specialists.

In order to build a good rapport with the oncology specialist, it is advisable to have a one-to-one meeting or telephone conversation at the start of the feasibility assessment before relying on email for regular communication.

Oncology specialists have demanding schedules that include the daily clinical care of their patients despite their interest in conducting clinical research. As carrying out feasibility assessments requires an investment of time and resources, a reasonable duration to complete the assessment, proportionate to the depth of information required, will provide more useful data rather than a 'rushed through' assessment devoid of reliable information. A sufficient timeline needs to allow for the execution of a confidential disclosure agreement (CDA), if required, prior to discussing any study specific information.

Analysis of Feasibility Information

Analysing the data from the completed questionnaires is a pivotal part of the feasibility process, therefore devoting enough time for proper interpretation and evaluation of the information is essential. In order to maximise the usefulness of the data, input from a medical expert with previous clinical study experience in the target cancer is indispensable. The data should also be compared with information from previous studies of a similar nature (if available) and recent publications on the target cancer.

There are several potential pitfalls that may occur during the interpretation of the feasibility data. Simply referring to information from previous clinical studies and/or publications without

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receiving input from a scientific or medical expert could provide a false picture, exaggerating the reliability of the feasibility information. Clinical studies are rarely identical; the inclusion/exclusion criteria, together with other factors such as concomitant medications and the use of comparator drug, can significantly affect the subject recruitment of the study. Furthermore, potential investigators have a tendency to overestimate the recruitment information due to their eagerness to participate in a new study. It is also important to confirm that the evaluation of the investigator grant has included the services provided by the required specialists (for example the pathologists, radiologists and pharmacists), as well as other factors (for example, supportive treatment, patient allowances and site overheads) in order to avoid a significant underestimation of the grant.

By optimising the information from the feasibility assessment, proactive strategies can be developed, including proposed protocol changes, a cost-effective approach on country and site distribution, a realistic subject recruitment timeline, a risk contingency plan regarding subject recruitment, and resource planning. These strategies, if appropriately applied, should leverage operational expertise to provide the best scenario for successful trial management.

CONCLUSION

The advancement of oncology clinical research, while offering the greater promise of new cancer treatments, has created added complexity in the conduct of oncology studies. A good quality feasibility assessment provides useful information on the practicality and restrictions for an oncology trial. Understanding the specific challenges pertinent to the upcoming oncology trial and meticulous planning of the feasibility assessment further facilitates the process. Optimisation of the information allows informed critical decisions to be made to best support study execution, which ultimately maximises the study outcome.

References

1. DiMasi JA and Grabowski HG, Economics of new oncology drug development, *Journal of Clinical Oncology* 25 (20): pp209-216, 2007
2. Gambriell S, Changes in Asia-Pacific regulations-position region for more growth, *CenterWatch Monthly* 14 (11), November 2007
3. Tournoux C, Katsahian S, Chevret S and Levy V, Factors influencing inclusion of patients with malignancies in clinical trials [review], *Cancer* 106: pp258-270, 2006