Optimising Early Clinical Development Strategies in Oncology

According to the largest analysis of almost 7,500 clinical and regulatory phase transitions, the likelihood of an oncology drug progressing from Phase I clinical testing is 5%, the lowest of the 14 major disease areas analysed. Of the oncology drugs that do progress, twice as many are for haematological malignancies than for solid tumours.[1]

Despite this, drugs with cancer indications are approved at a faster rate than for any other major disease. A 2018 review of the 58 new cancer drugs approved by the FDA between 2012 and 2017 found that 95% of them qualified for an expedited development or approval pathway, including 79% for priority review, 45% for accelerated approval, 48% for fast-track approval, and 43% for breakthrough therapy status.[2]

While these new regulatory paradigms offer the potential to significantly reduce drug development time, this is only possible if a clear, highly effective, and regulatory acceptable strategic development programme is in place.

APTUS CLINICAL'S ONCOLOGY EXPERTISE

Aptus Clinical specialises in the early clinical development of oncology drugs and has been helping companies develop innovative programmes since 2014. Prior to that, the co-founding directors and the clinical development team spent most of their careers working for AstraZeneca and other pharma companies, designing, and overseeing global oncology trial programmes, including several leading brands.

This experience allows Aptus Clinical to expertly advise companies on innovative drug development approaches that help accelerate development timelines, reduce technical risk and utilise novel biomarker strategies, in a highly flexible and cost-effective manner. Aptus Clinical is also at the forefront of using digital technologies, biosensors and artificial intelligence to develop potential digital biomarkers to support regulatory submissions.

CHALLENGES IN ONCOLOGY DRUG DEVELOPMENT

The traditional regulatory development route for oncology drugs, where discreet testing phases culminate in a large, randomised superiority trial, has evolved into multiple development pathways. Advances in cancer biology understanding and molecular diagnostic technologies have led to ever-smaller patient subgroups being identified for molecularly targeted therapy. Many of these have shown unprecedented responses in early phase trials, leading regulators to approve them without the need for large scale studies.

FDA regulations enable the rapid review and accelerated approval of certain drugs in the absence of survival data. These regulatory approvals, and those based on large-cohort trials with surrogate or intermediate clinical end points or on non-inferiority trials, as well as new tumour-agnostic indications, set important precedents in the field.

High uncertainties in the transition from preclinical evaluations to human studies

Aptus Clinical has a thorough understanding of the preclinical programme requirements for new therapeutic treatments and approaches in oncology. The aim of the pre-clinical programme should be to support the decision for entering the clinical phase by providing a robust data package, which

includes tests in various different experimental settings and models that allow for an adequate initial benefit/risk assessment.

With respect to safety, it should be realised that toxicology study requirements for oncology products may differ considerably from other pharmaceuticals; they need to focus on schedule dependency where substantial savings could be obtained with the correct and optimal study design.

Aptus Clinical has broad experience in the design and implementation of translational science programmes, including due diligence for late stage preclinical and early clinical opportunities, assessment of preclinical results, and innovative trial design, to maximise the chance of success.

High failure rate after entering Phase III and missing regulatory requirements

Only a third of drugs completing Phase II development go on to Phase III trials and of these, many more will fail to reach approval. The challenges of drug development in oncology include complexity of the disease and underlying physiological processes, biomarker development and patient stratification, clinical methodology, defining dose and dosing schedules, selection of endpoint(s), and balancing regulatory and clinical requirements. Key to successful development is a flexible approach which allows integration of advances in the understanding of the specific type of cancer, evolving data of the investigational product and changes in regulatory environment.

Aptus Clinical's oncology experts have experience with integrated development planning and systematic approaches which maximise the efficiency of the development process, data quality and regulatory acceptability.

Targeted therapies – patient subpopulations

With more targeted treatments, both agencies and payers are increasingly demanding efficient patient selection and outcomes data in order to obtain regulatory approval and rapid reimbursement decisions.

Biomarkers are an important tool in the development of targeted therapies. The identification of predictive biomarkers helps to select patients who might benefit from the treatment or those who will not respond. It is essential to validate the biomarker thoroughly when developing as a companion diagnostic. Validated biomarkers can help to refine the development programme and the target product profile. Targeted therapies can provide added value to a specific subset of patients.

Aptus Clinical can help with biomarker selection to support key questions around pharmacodynamics and patient selection, and ultimately plan for success.

To find out more about Aptus Clinical, please visit aptusclinical.com or call +44(0) 1625 238662.

References: 1. Clinical development success rates 2006-2015. Available at: https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf. Accessed July 2020. 2. Hwang, T. J. et al. Efficacy, safety, and regulatory approval of Food and Drug Administration-designated breakthrough and non-breakthrough cancer medicines. *J. Clin. Oncol.* **36**, 1805–1812 (2018).