The burden of choice

ICON Oncology's opinion of how we can reach for the stars with a moonshot

Dr Martin Lachs, Dr Reinhard Eisebitt and Dr Valerii Fedorov at ICON

Pharma companies continue to turn to biologics to drive success in the market. The team at ICON discuss how the oncology field has been at the forefront of this pursuit, with new challenges and risks arising from this venture.

The drive to precision medicine, whereby we hypothesise that each patient's disease is unique requiring the person to be treated as an individual, places a heavy burden of choice and complex thinking about how we run clinical trials and critically, which clinical trials to run. This is no less impacted by the array of possible combinations of immuno-oncology drugs. With more and more immuno-oncology drugs being approved in increasing numbers of cancer indications, pharma companies may be anxious as to which combinations and indications to pursue. Consequently we are increasingly observing development programs having to change course, sometimes radically, with great speed in response to the plethora of emerging data.

Approximately one third of the work in which ICON engages is in oncology and our specialized global oncology group is ICON's largest therapeutic team with over 260 project management professionals and medical consultants (board certified oncologists and haematologists). So the challenges and conundrums of oncology drug development are something we live and breathe at ICON every day.

Considering precision medicine, there can be said to be two paradigms. The most well worked model is the traditional biomarker paradigm. In short, we look for a gene mutation that can be correlated with a phenotype. Breast cancer patients who express higher levels of the HER2 gene will respond to particular EGF-R antibodies, such as trastuzumab. Lung cancer (NSCLC) patients who express higher levels of the PDL-1 will respond best to pembrolizumab. However, in both examples, we also need to consider that in fact there is greater complexity. Not all high level expressers of HER2 or PDL-1 will respond to a particular drug. Clinical judgement is also a key factor and empirical evidence points to clinical matching algorithms combined with biomarker driven selection as being a more sensitive and specific approach to precision medicine than relying upon biomarkers alone. From a clinical trial perspective this is challenging, but the ability to mine data from electronic health records provides a platform from which we can better glean key clinical data. ICON's work with EHR4CR, TriNetX, Explorys and IBM Watson are potentially critically impactful platforms from which to facilitate access to key genomic and clinical information. However we recognize that 1) data is increasingly heterogeneous; 2) we need to further increase the sophistication of data entry terms and search/recognition functions and 3) there has to be greater data sharing across networks to achieve state of optimal utility.

As a larger component of precision medicine is a genomics-driven oncology paradigm, the disease is no longer defined by the organ in which the primary tumour develops, but by its genomics profile. Therefore we have moved toward study designs that look at multiple drug combinations across multiple anatomical cancer indications. ICON is leading the way in applying adaptive design techniques to clinical studies that require multiple drug combinations and cancer indications. The number of permutations of drugs, dosing levels, subject expression of particular biomarkers etc. can be mind-boggling. Although the adaptive approach allows us to drop and add arms according to read outs along the way, which allows for more rapid go/no go decisions on research continuation with a given combination, we still have to decide upfront which trials to start with.

To address the burden of "backing the right horse", ICON is participating in a Cancer Moonshot project exploiting the computational power and algorithmic power of quantum computing.

There is an abundance of data, including genomic data, clinical trial data and data from various healthcare records, available to pharma companies to assist them in the design and execution of their oncology development programmes. Search engines, machine learning and predictive analytics are currently the main tools that allow the exploration and discovery of non-

"There is an abundance of data, including genomic data, clinical trial data and data from various healthcare records, available to pharma companies to assist them in the design and execution of their oncology development programmes"

trivial patterns within these massive, and most often, poorly structured data sets. The respective results are crucial for the design of targeted, ethically sound and economically optimal trials. The approach is based on mathematical models and techniques that aim to solve computationally "hard" problems, i.e. they require computational power that is close to or beyond the current limits of classical computing.

ICON and Lockheed Martin have teamed up to combine modern trial designs with the power of quantum computing to enable more advanced analysis of massive data sets in clinical trials. The current progress in quantum computing gives ICON's trial design experts a chance to combine advanced statistical methods and accumulated scientific information and unify the concepts of umbrella, basket, and platform trials into a cluster clinical trial concept. Cluster trials are made up of sub-trials involving common features such as cancer type, phenotype or genetic signature, to assure the homogeneity of respective sup-populations and at the same time to gain inferential strength by sharing information between them. The careful interplay between homogeneity of each sub-trial and diversity of the whole cluster trial may lead to huge time and budget savings. Note that in this approach quantum computing is mainly needed to train various machine learning models to predict clinical trial outcomes from genomic and phenotypic information.

While neither advanced statistical methods, nor advanced computing techniques can on their own address the research problem in oncology, their combination creates scientific machinery that speeds the development of more effective, individualised cancer therapies.

- *Dr. Martin Lachs – VP Project Management, Oncology & Haematology, ICON*
- *Dr. Reinhard Eisebitt – SVP, Innovation Centre, ICON*
- *Dr. Valerii Fedorov – VP, Innovation Centre, ICON*

Experts in Oncology Clinical Studies

Over the past five years, ICON has successfully completed almost 350 oncology studies worldwide. Our oncology services expedite every aspect of a cancer drug trial.

- Early Phase & Consulting
- Adaptive Trial Design
- Site Performance Management – FIRECREST ®
- Patient Recruitment Solutions
- Medical Imaging
- Extensive Laboratory Testing Capabilities
- Resourcing & FSP
- Commercialisation & Outcomes

Download ICON's whitepaper:
Identifying and Reducing Barriers to Oncology Clinical Research at the Site Level.

ICONplc.com/oncology