Medical Xpress

Throwing light on how to conduct a personalized pancreas cancer clinical trial

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Dr Lorraine Chantrill

After performing thousands of unsuccessful experiments in his attempt to perfect the light bulb, Thomas Edison famously remarked: "I have not failed, not once. I've discovered ten thousand ways that don't work."

Australian leaders of an ongoing pancreatic cancer clinical trial known as the Individualised Molecular Pancreatic Cancer Therapy or 'IMPaCT' trial, could say exactly the same thing as Edison.

In conventional terms, the trial could be viewed as a failure, as it has been unable to recruit eligible patients to-date. In reality, ways have been identified in which it can bring about a new paradigm of personalised cancer care for pancreatic cancer and other aggressive cancer types.

The American Association for Cancer Research (AACR) is throwing a spotlight on the experience of IMPaCT, details of which will be presented at its annual meeting in Philadelphia this week.

Professor Andrew Biankin and Dr Lorraine Chantrill, clinical researchers from Sydney's Garvan Institute of Medical Research, are in Philadelphia to discuss their observations with colleagues. They are also the lead authors on a manuscript about the IMPaCT trial that is published online today in the prestigious AACR journal *Clinical Cancer Research*. AACR is issuing its own media release to highlight the issues encountered and lessons learned by the trial investigators.

IMPaCT arose to exploit results from genome sequencing of pancreatic cancer under the auspices of the Australian Pancreatic Cancer Genome Initiative, a member of the International Cancer Genome Consortium (ICGC) in Australia. Sequencing revealed that small subsets of patients with changes in their tumour genome could benefit from existing therapies.

The pilot stage of the IMPaCT trial assessed the feasibility of acquiring

suitable tumour specimens for molecular analysis and returning high quality actionable genomic data within a clinically acceptable timeframe. It screened for three molecular targets.

Out of 93 patients whose tumours were examined, 76 samples were of sufficient quality to be screened using next-generation genomic sequencing. Only 22 patients were deemed eligible to participate in the trial because their cancer cells contained one of the three molecules that could be treated with existing therapies.

Unfortunately, none of the eligible patients went on to receive targeted treatment. The researchers encountered many hurdles. The technology was very new; there was much skepticism about 'genomic medicine' to overcome; many complex administrative processes and protocols demanded by current clinical trial frameworks had to be observed in setting up the trial at three hospital sites; and they were dealing with a cancer that killed swiftly once diagnosed, so sequencing of the tumour had to be fast.

"It became very clear to us that patients with advanced pancreas cancer can't afford to wait protracted periods of time for sequencing results before they start treatment, and they also don't want to be 'randomised' and risk being given 'standard-of-care' therapy - which isn't very effective in the case of pancreas cancer - rather than targeted therapy," said Dr Lorraine Chantrill.

"We are now particularly aware of the need to have efficient multi-disciplinary teams that can work quickly to obtain patient consents, collect high quality tumour samples, analyse them, and return the results within a month or less."

Two amendments have been made to the trial to make it more appealing to patients and their doctors. Patients will now receive the best-known

treatment available while they wait for sequencing results - which will then guide further treatment in all cases. No-one will be randomised from now on.

Professor Andrew Biankin observed that while the sequencing could be performed rapidly, simple logistics such as specimen access from hospital pathology departments resulted in the greatest time delays. "We can do the scientific part, but the societal and systemic parts pose the greatest hurdles," he said.

"A disruptive approach, such as our ability to sequence cancer genomes, poses substantial problems for traditional healthcare systems, which have grown organically to accommodate other technologies and other practices.

"We now need to modify and align conventional health and research systems with new technologies and practices, interact more closely with regulators and payers and work with government and industry partners to circumvent hurdles for the benefit of our patients.

"We have made a good start in mapping out what is necessary, the challenges that we need to overcome. Only by actually doing it, will we work out the right way forward," says Biankin.

Like Thomas Edison, the trial leaders are working out the "ways that don't work" to find the way that does.

Professor Biankin, who is now based at the Wolfson Wohl Cancer Research Centre at the University of Glasgow in Scotland, will be undertaking parallel trials in the UK, implementing all the lessons learned through the IMPaCT trial.