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Editorial

The Value of Patient and Public Involvement in Trial Design and Development

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The Independent Cancer Patients' Voice (ICPV; www.independentcancerpatientsvoice.org.uk) is a patient advocate group bringing the views and experience of those affected by cancer to the cancer research community. The ICPV believes that clinical research is improved by patients being partners with healthcare professionals, rather than passive recipients of healthcare.

Patient and public involvement (PPI) once seemed to be imposed on researchers, a box that needed ticking in order for a funding bid to be successful or for a trial to get the approval of an ethics committee. One or two patients might have been asked to give their approval for a study proposal, enabling researchers to say that patients had been involved in the research process.

Over time, the ICPV found that some researchers began to recognise the value of quality PPI in the development of their research and started to involve patient groups at all stages of their research.

The ICPV was founded in 2009 as an independent patient advocate group. Through education, mentoring and support, the ICPV has expanded and nurtured its membership and gained the respect and trust of many researchers. Having been involved in the development of over 100 trials, ICPV members now represent lay people/patients on many trial management and steering groups.

The ICPV has collaborated with researchers to deliver presentations at UK and international conferences. Workshops, trials focus groups and educational events have been hosted by academic centres across the UK.

Trial proposals, protocols and other documents are reviewed by ICPV members at the invitation of researchers via a closed google group.

Here four researchers who have involved the ICPV from early stages of their research write about the value of PPI in their work:

Dr Mariam Jamal-Hanjani and Professor Charles Swanton

TRACERx (TRACKing Cancer Evolution through therapy (Rx)) is a multicentre lung study, which is currently recruiting patients, and involves the collection of early stage non-small cell lung cancer (NSCLC) tumours [1].

Having shown significant intratumour heterogeneity in NSCLC [2], the primary objectives of the TRACERx study are to determine the relationship between intratumour heterogeneity and clinical outcome, in terms of disease-free survival and overall survival, and to determine the effect of adjuvant platinum-containing chemotherapy on intratumour heterogeneity.

TRACERx is the first study of its kind in NSCLC, whereby tissue and blood sampling is collected longitudinally from diagnosis to relapse to death, with the intention of tracking the clonal evolution of NSCLC, to not only understand its pathogenesis, but to assess the effect of intratumour heterogeneity on the clinical course of the disease, including therapeutic response and survival outcomes.

Patient advocate groups, clinicians, scientists and healthcare professionals must work alongside each other as multidisciplinary teams in order to establish good clinical and research practice. TRACERx and PEACE were developed and set-up in close collaboration with the ICPV. Their

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collaboration has been so crucial and valuable in the development of both.

Studies involving longitudinal tissue sampling, extended periods of follow-up and study procedures after death, require thoughtful and sensitive approaches, in terms of study documentation and patient approach. The ICPV has been of particular value in addressing these components in both TRACERx and PEACE. Their experience and knowledge of clinical trial set-up, the ethical implications of trial procedures and interventions, tissue biobanking, patient recruitment and patient interaction have been invaluable. ICPV has been involved in the development of the study documents, such as patient information sheets and informed consent forms, and the set-up of the studies, including gaining study ethical approval and the initiation of study sites. They have been an essential part of the study consortia and their participation in study meetings has often led to improvements in patient pathways.

Professor Judith Bliss

Hormone sensitive breast cancer is a common disease in postmenopausal women. Generally seen as less aggressive than other breast cancer subtypes, patients have a continued risk of relapse for 15+ years [3], thus the cumulative risk is not insubstantial. Efforts continue to identify patients who are at continued residual risk of relapse in order to develop new treatment strategies. Previous trials [4] suggested that aromatase inhibitor treatment for 2 weeks in the peri-surgical 'window-of-opportunity' results in detectable biomarker changes (Ki67) and predicts long-term outcome. Gene expression profiling offers opportunities to identify patients showing early resistance to endocrine therapy.

POETIC (Trial of Perioperative Endocrine Therapy – Individualizing Care) is a UK-wide randomised controlled trial devised to provide definitive results on the role of perioperative aromatase inhibitor treatment. Biopsies were taken at diagnosis and 2 weeks later at surgery, thus allowing an *in vivo* assessment of aromatase inhibitor sensitivity. To succeed, POETIC needed to overcome substantial barriers in relation to compliance with cancer wait times, recruitment of women at diagnosis, varied clinical practice and to ensure receipt of sufficient quality tissue samples for analysis of biomarker end points. Patient advocates were involved from inception and proved invaluable in overcoming many of these early challenges.

Specifically, the patient advocates gave reassurance to the Ethics Committee and research staff that requesting additional tissue samples at pre-treatment and surgery was acceptable, as long as this was conducted by a competent team and all donated tissue could be utilised via a tissue bank. In addition, the patient advocates were supportive of approaching patients about the trial at the time of diagnosis, gave reassurance that patients would be open to consider consent within 24 h and that there should be open discussion of the effect of trial participation on the scheduling of surgery.

POETIC succeeded in recruiting 4486 women from 130 UK centres and paired tissue samples (i.e. at diagnosis and

surgery) were received for 96% of patients. The success of the trial is a testament to the involvement of patient advocates within the set-up and recruitment phases. Patient advocate involvement is continuing in the trial follow-up phase through membership of the Trial Management Group, with continued valued support, particularly in relation to the use of tissue and data to maximise scientific output.

Dr Matthew Krebs

As clinical and translational researchers we aim to do the best science with the best possible clinical trial design, but it is sometimes hard to know how things look from the eyes of our patients who lie at the heart of everything we do. We have recently developed the Manchester Cancer Research Centre TARGET trial (Tumour chARacterisation to Guide Experimental Targeted Therapy) to profile patients' tumours for a range of genetic faults to help select a relevant experimental cancer medicine trial. We raised the possibility of detecting germline abnormalities with significance for patients or their family members as a by-product of our analyses. Although this risk is very small based on the scientific approach, we wanted to tackle the issue 'head on' and consent patients for this possibility. Addressing these issues in the patient information sheet and informed consent form proved challenging and opened a host of potential ethical issues.

I was honoured when the ICPV agreed to review our documents and trial proposal. Within less than 2 weeks a team of professional and courteous ICPV members had read and reviewed our documents with insightful feedback on several issues we had not considered. Crucially they provided strong positive feedback on the trial overall and recommended tackling those genomic issues that sometimes, as investigators, we feel it may be better to avoid. Not only did this provide us with peace of mind as a group of clinicians and researchers but also for our patients. To see that fellow patients or their advocates have been involved in the development of the project provides a sense of reassurance and approval. This goes a long way to putting our patients' minds at rest in difficult and vulnerable situations and provides transparency to our scientific research.

I have approached the ICPV on several matters both before and since this protocol and always truly value their input and guidance, both of which are full of insight. Ethics boards and funding panels are increasingly requiring PPI input and in my mind it should be considered a core element of any clinical project application. TARGET was approved by our local Research Ethics Committee (REC) within less than 5 min!

In Conclusion: Maggie Wilcox, President and Founder Member of the ICPV

The ICPV welcomes the symbiotic relationship with our professional partners in cancer research, which has developed as the result of hard work, enthusiasm and

commitment on both sides. There is mutual respect, trust and willingness to learn – and to teach – which has enabled ICPV members to be confident providers of an educated and realistic model of patient involvement in cancer research.

Our independence has been key to successful development as effective lay advocates in cancer research because it ensures a direct patient and carer perspective, unfiltered by political, financial or academic strategic requirements.

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