

No trials about us without us!

Patient advocates demand a seat at the table

→ Peter McIntyre

Patients are not scientists. But given the chance, they can help clinical researchers design trials that patients want to join and stay with, and that answer questions they care about. They want the culture of the consent form to be replaced by a genuine partnership between researchers and patients.

Researchers design clinical trials to answer scientific questions. But patients who have a life-threatening disease join those trials in the human hope of a cure, better treatment or better quality of life. Patient groups are now asserting their right to be consulted at an early stage so their perspectives can help inform the aims, design, practice and reporting of clinical trials. They also want better access to information about trials that they might want to join.

At ECCO 14 in Barcelona, Lex Eggermont, incoming president of the rebranded European CanCER Organisation (ECCO), spoke out in favour of patient involvement, telling the Patient Forum that patients who are well informed and well prepared will be more likely to want to take part, and can make research more relevant.

However, many cancer researchers continue to treat patients as little more than an input into a scientific exercise.

A PLACE AT THE TABLE

Lia Van Ginneken-Noordman, from the European Myeloma Platform and an advocate for patients with multiple myeloma and Waldenström's macroglobulinaemia in the Netherlands, says, "Patients have a right to be more involved, because it is their disease. Patients should know the aims of the clinical trial, the expected outcome, and for whose benefit the trial is being done. Is it for the benefit of the patient or the researchers or the pharmaceutical company?"

On the other side of the Atlantic, her point is echoed by Norman Scherzer, chief executive of Life Raft, a patient group for people with gastrointestinal stromal tumours (GIST). "Cancer patients enter clinical trials because there are usually no alternatives in terms of effective treatment. The other players in the clinical trial process, although they are looking to be helpful and none means the patients harm, have a different agenda.

"The pharmaceutical people want to see if they can bring this drug to market. The focus of the researcher is to conclude the research in a successful way, even if to do so might not be best for certain patients. It is my belief that only a patient group can bring to the table the objectivity needed to put the interests of the patient first.

"The question for those of us representing the patient is, can we even get into the room where decisions are made? The answer is no. Yet it is we and the people we represent who will be subject to whatever risks are involved in this trial."

CAN YOU JOIN A TRIAL?

The first, and possibly biggest, risk is that patients do not find out which trials they might join, and what the benefits might be. Without better information, patients can never be equal partners in research.

The European Cancer Patients Coalition (ECPC), which represents

250 patient organisations across the European Union, has been campaigning since 2003 for better access to information under its slogan, “nothing about us, without us!”

Jan Geissler, vice-president of ECPC, points out that participating in trials can bring significant benefits to patients. For example, phase I trials, which are only open to cancer patients who have failed previous therapies, benefit just over 10% of the patients who take part. Phase IV trials, looking at long-term risks and optimisation of effective therapies, make it more likely that resistance to treatment or progression of the disease will be detected earlier.

But, speaking at the ECCO conference in Barcelona, Geissler said that

some doctors are ill-informed or unwilling to enrol patients, while a culture of secrecy is enforced by pharma companies. The results of 6 out of 10 clinical trials are never published, while only half report their methodological details adequately. Registration of trials is still poor, especially phase I and II cancer trials, leading to duplication of research and a lack of transparency.

The WHO launched its International Clinical Trials Registry Platform in May 2007, to give clinicians and patients better access to information. This is a search portal – not a separate register – but has the potential to become a ‘one-stop shop’ for information about trials. However, six months after the launch only four primary registers (plus

data from the US-based ClinicalTrials.gov) have been included and four more have become collaborating registers, of which only one, Eli Lilly, is a drug company register. The number will increase – another 11 registers are in the process of becoming contributors – but there are still some big gaps.

The European Medicines Agency EMEA has its own database, EudraCT, with more than 13,000 clinical trials recorded by Member States. But it is only accessible by ‘competent authorities’, not by doctors or the public. Information on paediatric trials will, however, be made

ILLUSTRATION: FRED VAN DEELEN



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generally available under a revised EU regulation on paediatric medicines. ECPC has been talking to EMEA about greater openness, but recognises that it would require a change in European law to open up EudraCT. However, Geissler sees the exception made for paediatric trials as a positive sign. “This might help to call for greater transparency for adult trials later... little steps will make a large change.”

EMEA hosted a meeting with the European Commission in London last October to discuss the operation of the much-criticised Clinical Trials Directive. ECPC used the conference to argue for greater transparency, and for patients to be given a seat on all medical ethics boards.

ECPC is not convinced that patients’ rights protection in non-commercial clinical trials or clinical trials sponsored by pharmaceutical companies have improved significantly. “Patient groups were not sufficiently consulted and involved when the Clinical Trials Directive was drawn up and adopted. Even now patients are rarely consulted when new cancer trials are being set up.

“In ECPC’s view, participation of patient groups in the design process of clinical trials can improve consent, recruitment and outcome of clinical trials. Involvement of patient groups at the beginning of the trial design would allow patients to contribute their ideas and requirements, and would avoid unneces-

sary or misleading research work.”

Geissler says patient groups need to adopt a carrot-and-stick approach, encouraging patients to join good trials and discouraging participation in those that do not meet the standards. “Patient groups are in the driving seat to enforce change.”

Europa Donna, the breast cancer coalition, also believes there is a need for better public information. Executive director Susan Knox says, “Very often a woman hears about a clinical trial when she is being treated and that is already a very traumatic time. To make a decision about a clinical trial without knowing anything about the way that research is conducted is extremely difficult for a patient.”

Van Ginneken-Noordman notes that relatively few cancer patients in the Netherlands volunteer for clinical trials because they are not well informed and they can usually obtain the latest therapies from their physicians. However, in eastern Europe joining a clinical trial may be the only way to access the most up-to-date drugs. Clearly, this puts heavy pressure on the patient.

Scherzer warns that it makes informed consent very difficult. “Researchers say we are going to protect the patient by getting them to sign a consent form. Well, the consent form is a sham because this patient is so desperate that they will sign anything including the mortgage to their own home.”

QUALITY OF LIFE

Deborah Collyar, president of Patient Advocates in Research (PAIR), has been involved in patient advocacy in the US for 15 years. Ten years ago she chaired an NCI committee whose report led to the creation of the cancer.gov website. However, she does not think that things have changed fast enough in relation to patient involvement in decision making.

“The clinicians and scientists I have worked with through the years are all really dedicated people. At least 99% really want to improve things for their patients. But they are so influenced by the scientific side and their training as medical doctors that often what gets left out is the experiential side of the clinical trial. They want clear scientific objectives. They forget how difficult it may be to participate.”

A typical proposal from a researcher might be that each patient gives multiple biopsies during the trial. “We say, ‘OK, sanity check!’ How difficult is this going to be for someone? Do they really need it or is it just cool science? We explain that eliminating patient barriers may mean better enrolment and adherence to their clinical trials.”

Van Ginneken-Noordman agrees that the patient experience is neglected. “The quality of life is very important in cancer treatment and research – the level of illness, tiredness and pain and the level at

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which it interferes with daily life. You can go through a very difficult trial with a lot of burden and side-effects and uncertain outcomes. Perhaps it only lengthens your life by one month but makes your life much more miserable. These are issues that patients should decide, not researchers.”

In June 2007, the James Lind Alliance and the *Lancet* held a seminar in London to ask how clinical trialists could serve the needs of clinicians and patients more effectively. Hilda Bastien, head of Patient Information and Research at the German Institute for Quality and Efficiency in Healthcare (IQWiG), said patients had a love–hate relationship with research and often felt they were in a maze.

“It is very hard to come up with any direct way to answer the specific questions that people have, like, ‘When will I get back to work?’ What you have is something that tells you that the average patient feels a 3 on a scale of 5 on something or another. That is quite frustrating.”

She says that researchers need better links with patients, clinicians and across disciplines to address relevant questions. “Trialists should each have qualitative researchers they would not dream of taking a step without, and should have relationships with patient advocates and be trying to cooperate with other disciplines.”

PATIENTS DON’T LIKE PLACEBOS

One particular issue for people with cancer is the (admittedly small) number of trials that allocate some patients to a placebo.

Collyar recalls that researchers wanted to test a new agent on asymptomatic patients who were at high risk of metastasis. “They were talking about a

two-armed study with a placebo and I kept pushing for multiple arms. I told them, ‘People gravitate towards hope. Would you like a 50–50 shot of having nothing, or a 25% chance of getting the placebo and a 75% chance of getting something?’ It was like light bulbs going on in their heads. They did not understand until then.”

The Life Raft group had a dispute with Pfizer Oncology when they were trialling sunitinib (now marketed as Sutent) against a placebo for GIST patients who were showing signs that Glivec (imatinib) was no longer working.

Life Raft argued that the control group should continue to be offered Glivec, since it does not stop working completely. They felt justified when in January 2005, the trial was stopped seven months early, and everyone on a placebo was immediately offered the new drug. In

effect, for the duration of the trial, those on the placebo had been at extra risk.

Scherzer said, “If someone proposes a clinical trial where a placebo will be given to a randomised group of people, the burden of proof must be on those who are proposing it that there is no alternative.”

FINDING OUT RESULTS

Patients not only want to know about trials they might join – they also need to know the results. But trials which show disappointing results are often not reported, while patients in other trials may hear the results first in the media.

Knox from Europa Donna says, “We believe very strongly that all trials should be part of a public registry and that when trial results come out they should be immediately posted for everyone to see. It should be a requirement that all trial results are

A FOOT IN THE DOOR

Patient groups are becoming more assertive about being given a place at the table. The European Myeloma Platform is in discussion with researchers in the European Myeloma Network about being included in their committee. Europa Donna is talking to EUROCAN Plus, the EU-backed initiative to coordinate cancer research in Europe, about a European database accessible to patients, detailing all current and recruiting clinical trials.

The UK Cancer Research Network was set up in the year 2000 and has at least two patient or carer representatives in every group. It has more than tripled the number of patients joining clinical trials. Other UK Networks are now following its lead and the overall UK Clinical Research Network appointed cancer survivor and patient advocate Roger Wilson to be associate director for patient and public involvement.

As Hilda Bastien of the German IQWiG told the James Lind Alliance/*Lancet* meeting: “There are going to be increasing numbers who would like to be in clinical trials, particularly when they have a life-threatening illness. They need to be able to join them and the results need to be fully accessible. It is a joint responsibility between the community and researchers and trialists to improve the image of clinical trials.”

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reported and available to the public. The participants should find out before it is in the media.”

Collyar has been involved in research with medical oncologist Ann Partridge, from the Dana Farber Cancer Institute in Boston, about informing patients of results. In 2004 they published a study suggesting that only 6 out of 10 oncology doctors and nurses routinely gave the results of research to patients, although 8 out of 10 were willing to do so.

Subsequent research on women with breast cancer who had taken part in a trial of Herceptin (trastuzumab), showed that more than a quarter first heard about the results from the media. After learning the results, one-third (mostly those who had received Herceptin) felt less anxious but one-quarter (mostly those who had not) became more anxious. However, only four per cent would not have wanted to know the results.

Collyar says that people can be traumatised by hearing results from the media, especially if the results are not good. “If you look at research about how to treat people better in trials, it is nearly all about how to recruit people. Where are all the trials and studies about how do you break bad news to people in your control group or your intervention group about what has happened?”

Collyar and Partridge are now co-chairs of a committee in one of the NCI-funded cooperative trial groups which is pushing to ensure that those who take part in research are properly informed about the outcomes.

POSITIVE BENEFITS

There are growing signs that when researchers do involve patients and give them a seat at the table, benefits flow. Europa Donna was involved in helping to plan the TRANSBIG MINDACT trial that focuses on the genetic signature of breast cancer and the risk of recurrence. They were able to influence the provision of patient information, which included a DVD in 13 languages to be used by a doctor or nurse with the patient and then taken home by the patient.

Fatima Cardoso, scientific director of the MINDACT trial, says in the Europa Donna newsletter, “The most difficult part of this trial is explaining it to the patient because it takes time, and time is not something conceded to physicians. When we developed the MINDACT consent forms we involved Europa Donna from the beginning and also we have asked individual patients to read and make sure that the forms were comprehensible.”

Life Raft too was able to identify clear benefits for patients and for researchers when they conducted their own quality-of-life survey for patients taking Glivec. There was concern about side-effects, particularly fatigue for people on the drug. Sure enough the survey showed high

levels of fatigue. But Scherzer says that they also found something surprising. “We discovered that the side-effects often got better over time, and the more severe the side-effects were, the more dramatically they got better. This discovery was important as it means, for many patients, that if they hold on, rather than abandon the drug, the side-effects get better.”

The result of such research has been to build a degree of understanding between the patient group and the drug companies. “Originally the pharmaceutical companies felt very threatened and suspicious, but when we sat down with the companies, Novartis being one of them, they have actually been quite responsive. What they saw was that we were not doing this in a provocative or confrontational way, but were actually adding to the information base.”

Deborah Collyar pioneered ‘clinical trials and people workshops’ between researchers and community groups to improve informed consent. These start by giving people information about clinical trials, but often lead to researchers learning from the public.

“Everybody thinks of informed consent as a way of communicating with the patient, but as you start the dialogue you also begin to identify design flaws or things that could change to make it more amenable to people. When you go into an informed consent discussion, people immediately ask questions about that trial. ‘Why was it set up that way? Why not do it this way?’ The dialogue can take them in a lot of different directions. If we have patient representatives involved in the development of the trial we will be much more successful because they help to eliminate barriers.”

For information on the launch of the World Health Organization Clinical Trial Search Portal see: <http://tinyurl.com/2ko7p7>. For the current list of participating registers see: <http://tinyurl.com/2tbnrp>. See also: A trial of strength: can industry resist the growing demands for greater transparency? *Cancer World* March–April 2006 (issue 11) www.cancerworld.org/magazine