How breast cancer patients value taking part in clinical trials: pointers for improved practice

Under embargo
Chapter 6 – How breast cancer patients value taking part in clinical trials: pointers for improved practice

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Abstract

Clinical trials (CTs) face unprecedented challenges because of rising costs and increasing complexity in conduct. To achieve the full potential of CTs, more attention should be paid to the patients participating in the CTs. Therefore, this research aims to gain insights into personal experiences of patients partaking in breast cancer CTs in the Netherlands. In total, 19 semi-structured interviews and one focus group (eight patients) with breast cancer patients were conducted. The findings were validated by an expert meeting of seven patients. The results revealed that overall patients were positive about CTs. Experiences were mostly related to recruitment and information supply, focusing on motivation to take part, decision-making, and random assignment. Support and communication skills of clinicians were essential. Written information was considered too scientific, general and juridical, and random assignment caused insecurity in some patients. Although the decision to take part was dependent on many factors, it appeared to be largely an intuitive decision. In conclusion, although experiences were generally positive, there is room for improvement. Proposed improvements include a more individual approach, providing feedback of results, and reminding patients about their participation in the CT.

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6.1 Introduction

Clinical trials (CTs) are considered to be the most reliable basis for evaluation of innovative diagnostics and new cutting-edge treatments (Baum and Houghton 1999; Dellson et al. 2010). However, CTs face unprecedented challenges (Rosenberg 2003; Roundtable 2003; Sung et al. 2003) with widespread concerns regarding increased costs and complexity in conduct. In addition, CTs are not always considered patient-friendly and few eligible patients consent to participate (Hill et al. 1994; Ellis and Butow 1998; Ellis et al. 2001; Wright et al. 2002; Sung et al. 2003; Marsden et al. 2004; McDonald et al. 2006; Dellson et al. 2010; Brintnall-Karavelas et al. 2011). As a result, CTs face difficulties in achieving their recruitment target. Many initiatives have been undertaken to address these issues, such as increasing the numbers of researchers, implementation of bioinformatics, and improving communication skills of researchers (Avins and Goldberg 2007; Hietanen et al. 2007; Dellson et al. 2010). While these initiatives are important, they are primarily focused on researchers and CT organizations. However, to achieve the full potential of CTs, it is essential to look further, and to pay more attention to the participants in the CTs, namely the patients (Avins and Goldberg 2007).

Over the past years, there has been increased attention for the perspectives of patients in CTs (Boote et al. 2002; Telford et al. 2002; Hanley et al. 2003; Caron-Flinterman 2005; Serrano-Aguilar et al. 2009; Elberse 2012). Insights into the personal trial experiences of patients could benefit CTs, since they could identify the strong and weak parts of CTs (Morris and Balmer 2006; Avins and Goldberg 2007; Kerrison et al. 2008). Their perspectives have been instrumental in improving many aspects of CTs: study design (Kerrison et al. 2008), Patient Information Sheets (PIS) (Ferguson 2002; Tosounidis and Kontakis 2008; Knapp et al. 2009; Dellson et al. 2010), communication between clinicians and patients (Cox and McGarry 2003; Tosounidis and Kontakis 2008; Dellson et al. 2010; Chu et al. 2012), feedback of results (Madsen et al. 1999; Cox and McGarry 2003; Kerrison et al. 2008; Tosounidis and Kontakis 2008; Chu et al. 2012) and inclusion rates and compliance (Brintnall-Karavelas et al. 2011). The perspectives of patients could also play a role in improving the image of CTs among the general public and among specific target groups if patients report to others that they have had a positive CT experience (Bevan et al. 1993; Chu et al. 2012).

The aim of the study presented in this article was to gain insights into the personal experiences of patients taking part in CTs for breast cancer in the Netherlands. These insights could contribute to improvement of CTs and address the recent problem of reduced inclusion and accrual.

6.2 Methodology

Qualitative research activities took place between February 2011 and June 2012. A project team was established, composing the authors and three researchers of the Athena Institute (VU University Amsterdam) who executed the research, the director of the Dutch Breast Cancer Trialists Group (Borstkanker Onderzoeksgroep, BOOG), a policymaker and a patient representative of the Dutch Breast Cancer Patient Organization (BorstkankerVereniging Nederland, BVN), and a policymaker of the Cancer Society (KWK Kankerbestrijding). The project team was responsible for reflection on the findings and identifying ways of recruiting participants.

During the consultation phases, a focus group discussion and semi-structured interviews were conducted. New interviews were planned until saturation of data was reached. Patients were recruited via a patient organization
and several hospitals, and selection was based either on taking part in a CT in the last four years or the deliberate decision not to take part. Convenience sampling was used to capture the broadest set of information and to aim at maximum variation, involving patients with experiences of different types of breast cancer and different types of CTs, and treatment at both academic and regional hospitals. One focus group discussion (n=8, duration 120 minutes) and 19 interviews (ca. 90 minutes) were held with fourteen patients who participated in a CT, three patients who had decided not to take part in a CT, and two male patients who had suffered from breast cancer. The interviews had an average duration of 90 minutes, and were held in a location preferred by the respondents. Experiences with breast cancer, the decision to take part in a CT and experiences with CTs were discussed. With respondents who decided not to take part in a CT, only the first two elements were discussed.

The outcomes of the consultation were complemented and validated at an expert meeting with seven patients recruited for this purpose via a patient organization. These patients were selected based on the following criteria: (1) willingness to think beyond their own experiences, (2) higher education, and (3) participation in a CT or affinity with medical research/CTs. The expert meeting lasted four and a half hours, and the patients received a fee for their participation. The meeting was prepared and facilitated by two researchers. Beforehand, participants received a report with the findings of the consultation.

**Analysis**

All consultations and the expert meeting were audio-taped with consent, and verbatim transcribed. To check validity of our interpretations, a summary was sent out to respondents for member checks. The full transcripts were analyzed using an integrated approach. First, findings were analyzed according recruitment and information supply, treatment, and feedback. Second, themes within the three stages were identified through an inductive approach, comprising three steps: (1) open coding (identifying, categorizing and describing of concepts), (2) axial coding (creating subthemes by relating codes to each other) and (3) selective coding (developing storyline by relating subthemes to main themes). Two researchers coded the data separately, and developed a coding structure together. The project team reflected on and discussed the coding, and agreed upon the findings.

**Ethical considerations**

This study did not need approval of an accredited Medical Research Ethics committee because involvement was not related to treatment or gathering medical data and was non-invasive, was on a voluntary basis and the anonymity of respondents was guaranteed. Patients in the palliative phase were excluded because the project team decided this would be too burdensome for them.

**6.3 Results**

Taking part in a CT was overall positively experienced by respondents. This was often linked to good support during the CT because someone, often a research nurse, took time to listen, provide information and answer questions. The nature of the condition was thought to play a role in this positive experience: breast cancer is a potentially life-threatening disease, with an emotional and hectic treatment period. Most patients want to focus on the outcome of the treatment (being cured) and the experiences with the CT were secondary.
Recruitment and information supply

Most respondents were asked to participate in the CT by a research nurse. The nurse explained the CT in an understandable way, and provided ample opportunities to ask questions, as illustrated by several respondents:

“The communication with the patient is very important in how patients ultimately make their decision.”

“Yes, it was very pleasant. ... For me, she [research nurse] was able to create, every time, a balance between the serious, the sad, and [by telling me] you can also be a patient.”

The written information (PIS) was considered secondary, although a few respondents appreciated being able to read the information at a later time. All respondents agreed that the PISs were too complicated and that they could not fully understand them because of the scientific style of writing. Respondents also felt that there should be more emphasis on possible side-effects. However, these issues were not always considered problematic since the CT was explained well in conversation. None of the respondents got in touch with the contact person mentioned on the PIS for more information. Many respondents indicated that they discussed their decision with a third party (a relative or a general practitioner) which was considered to have been very useful. Members of the expert meeting added that PIS were not sufficiently tailored to the specific patient group and that they had not felt personally addressed. A respondent indicated:

“This [PIS] is not about me.”

They also stated that many patients feel insecure about the extensive insurance section because it gives the impression that there are major risks associated with taking part in the CT.

During the expert meeting, respondents mentioned that clinicians do not pay much attention to management of expectations, patient’s personal situation, and short and long-term implications. Many patients assume that taking part in a CT contributes to a higher survival rate, raising unrealistic expectations. In addition, taking part in a CT could be too burdensome for some patients because of their family situation (e.g. problems at home, small children) or work commitments:

“[The clinician] should have better insights into the personal situation of the patient ... and how that could combine with the research they are talking about. Because I think that they only talk about what is on the paper [PIS], and treat everyone equally.”

Patients are also not always able to properly consider the implications of short or long-term side effects.

Decision-making

Three main reasons were given for participation in a CT: altruism, to receive better treatment and interest in scientific research. First, patients want to contribute to the advancement of science and medicine. Almost all respondents stated they are aware that current medical treatments are the result of patients having taken part in CTs in the past. They would like to contribute to the development of new and better treatments in a similar way for future generations. A patient mentioned about this:
“I really had the feeling that I profit so much from all those women who participated before me. With my treatment of Herceptin [a trade name of trastuzumab]. I was happy I could do something in return.”

Second, many indicated that taking part would provide them with better monitoring and extra check-ups which made them feel more secure about their treatment:

“A reason for me was also that I would have additional check-ups. That is a nice side effect.”

Third, a few respondents said they participated because of an interest in scientific research.

All respondents (regardless of whether they participated or not) had a positive feeling about CTs. They indicated that the actual decision was mainly based on intuitive consideration of many different factors, which is illustrated by the following quote:

“If they ask again, it may just be that I decide not to take part.”

First, patients are able to withdraw from the CT at any moment. Several respondents indicated that this had been vital in their decision-making:

“I think what ultimately was decisive was that I could say no at any moment.”

Second, most patients were asked to participate in the CT immediately after diagnosis and they had, on average, a week to consider whether to take part. Some patients criticized the timing and the short amount of time to consider their decision, which is illustrated by the following quotes:

“Your whole mood is different, of course, and you are confronted with something that is terrible. And then you have to decide [to partake in a CT]. And I found that very difficult in a short time frame.”

“I also had a week to consider [participation]. I do not know. A week was really enough for me.”

For one respondent, this resulted in the decision not to participate. However, most respondents also indicated treatment had to start on short notice so that they could understand the haste. Third, the type of CT plays a role in the decision. Participants are less likely to take part in a CT when the new treatment is less invasive than the treatment received by the control group because respondents became uncertain about making the ‘right decision’. For example, two respondents participated in a CT in which the new treatment involved the preservation of the lymph nodes in the armpit during surgery, while all lymph nodes in the armpit were removed in the standard procedure. Preservation would result in fewer side-effects (such as less moisture retention) which is positive, but the standard procedure gave more security because the cancer would be completely removed. Fourth, participation in a CT could represent more of a burden than standard treatment, for example extra travel time and more frequent clinical visits. For two respondents, this resulted in the decision not to take part, while a few other respondents indicated that this extra burden gave them the idea that they had done everything in their power to obtain a cure from breast cancer.

The random assignment caused uncertainty among several respondents. Some respondents were insecure about making the right choice. The expert meeting also considered that some patients have a preference for a certain treatment and only participate if they are assigned to this group. Given that patients could stop their participation
whenever they wished, they await the results of the random assignment (if the CT was not double-blinded) before deciding whether to continue.

_Treatment_

The majority of the respondents were not fully aware of their participation in a CT during treatment, since most patients did not distinguish between taking part in the CT and medical treatment. A patient indicated:

“No, I have been approached and I gave consent [to participate]. But further…”

In particular, patients who were assigned to the control group did not consider that they were taking part in the CT because they received standard treatment, which is illustrated by the following quote:

“No, I did not notice much about it [participation in a CT], I just received those treatments simultaneously.”

Some respondents emphasized that they also had other things on their mind. However, clinicians and research nurses did also not emphasize their participation during treatment. Members of the expert meeting furthermore suggested this confusion might be inherent in the Dutch language because the Dutch word for random assignment to the control group also means exclusion which could be taken to imply that patients are no longer participating in a CT.

Most respondents did not consider unawareness to be problematic:

“I think that you [as a patient] have something else on your mind.”

However, members of the expert meeting considered that, consequently, important side-effects or unexpected effects may not be monitored adequately. It should be noted that respondents who participated in a CT with a higher burden (as compared to the standard treatment) were more aware of their participation.

_Absence of feedback_

After participating, respondents did not receive any information on the results of the CT or any further response. A participant mentioned:

“No, you don’t know the follow-up. I would, I think, very much appreciate it if you [receive] something – not an entire report but just in a readable language, so that we all understand it, what the research has resulted in.”

Although they understand a CT has a long time span, they consider that such feedback would be desirable. Feedback would have been seen as a token of appreciation, especially since participating involved an extra investment during their treatment. A few respondents indicated that feedback could have confirmed that they had

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1 The Dutch word often used for random assignment to the control group (‘uitgeloot’) could imply patients are no longer participating, whilst the Dutch word for assignment to the new treatment (‘ingeloot’) clearly indicates patients are part of a CT.
made the right decision to participate because they would have contributed to improved treatments. During the expert meeting, it was suggested that patients should at least receive a thank you letter.

**Male patients**

The consulted male respondents indicated they would have participated in a CT if they had had the opportunity. However, until recently, there were no breast cancer CTs in which male breast cancer patients were able to participate in the Netherlands. The male respondents regretted this very much because they think it is very desirable to have more insights into the characteristics of breast cancer in men.

### 6.4 Discussion and conclusions

This article presents personal experiences of patients who have participated in CTs for breast cancer in the Netherlands. Overall, CTs were positively experienced by patients. Respondents’ experiences with CTs were largely related to recruitment and information supply, covering motivations, decision-making, random assignment, and PISs. For the subsequent stages of the CT, most patients did not have explicit experiences because they were not fully aware of participating in a CT.

Several issues that were identified in this study were already known from literature, such as motivational factors (Cox and McGarry 2003; Kemeny 2004; Cohen et al. 2007), randomization (Gross and Fogg 2001; Marsden et al. 2004; Avis et al. 2006), the complexity of PISs (Ferguson 2002; Tosounidis and Kontakis 2008), absence of feedback (Madsen et al. 1999; Kerrison et al. 2008; Tosounidis and Kontakis 2008). However, the findings also revealed new issues and experiences which contradict the existing international literature. For example, almost all participants in this study have positive experiences with participating in a CT and they were also relatively unaware of taking part in a CT (Kerrison et al. 2008; Dellson et al. 2010). In further contrast to the international literature, privacy, confidentiality (Tosounidis and Kontakis 2008) and investigators’ financial interests (Morris and Balmer 2006) are not mentioned at all in our study. This could be because of the relatively high trust of the general public in the Dutch health care system (Van der Schee et al. 2006) or because our study only focused on non-commercial CTs in which these issues might be of less importance. In addition, the decision to take part was mainly based on intuitive considerations. In an analysis of preferences in decision-making, Kahneman explains that decisions can be made in a fast or a slow mode (Kahneman 2011). The fast mode is primarily intuitive and emotional, while the slow mode is generally rational. Since respondents indicated that they had to make the decision to take part in a hectic and emotional period, it could be argued that their decision making was largely intuitive during the period in which they made their decision.

These experiences of patients offer pointers for the improvement of CTs. Some issues could be easily addressed by the CT organization, such as sending a thank you letter and a short summary with preliminary results after participation. Other points are more complicated to implement, such as providing information and attention which is more tailored to the individual. As also discussed by other scholars, higher inclusion rates could probably be achieved if more adequate information is provided (Dellson et al. 2010; Schipper and Abma 2011; Teunissen et al. 2011). Inclusion rates could probably also be improved by more attention for patient’s personal situation in the consultation with research nurses, encouraging the patient to discuss the decision to take part with a third party, removing insecurity towards less invasive new treatments and reducing the burden of taking part by, for example,
not making it necessary to have extra and longer visits. Improving PISs by making them more intelligible for a lay audience, tailoring them to specific patient groups and adjusting the sections on side-effects might also lead to higher inclusion rates. Adjustments to the section on insurance is more difficult to accomplish, since this section is legally required. The CT outcomes could probably also be improved if patients were more aware of their participation because this could facilitate more optimal monitoring of certain outcome measures and unexpected side effects. Patient awareness of their participation is also important from an ethical perspective (Nierse et al. 2012). This could be relatively easily achieved by making it clear that some questions during treatment about effects and indications are associated with the CT.

In this study, a variety of patients with different types of breast cancer, taking part in different types of CTs, and treated in both academic and regional hospitals were involved until saturation of data was reached. Given that patients in the palliative phase were expressly not included, their perspectives are not reflected in this article. The expert meeting was able to complement, reinforce and validate the experiences identified during consultation. A next step could be to realize active patient involvement in the design and execution of CTs because they would then be in the position to implement the necessary improvements of practice, and preserve the perspectives of patients during this implementation. These improvements could result in ‘earlier results and quicker application of new treatments in clinical practice’, beneficial for patients and society (Pittens et al. submitted-a). This step is currently being taken by BOOG and BVN.