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Evaluation of eligibility and recruitment in breast cancer clinical trials

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ABSTRACT

Objectives of the study were to measure recruitment rates in clinical trials and to identify patients, physicians or trials characteristics associated with higher recruitment rates. Among patients who had a clinical trial available for their cancer, 83.5% (345/413) met the eligibility criteria to at least one clinical trial. At least one trial was proposed to 33.1% (113/341) of the eligible patients and 19.7% (68/345) were recruited. Overall recruitment was 16.5% (68/413). In multivariate analyses, trial proposal and enrollment were lower for elderly patients and higher in high cancer stages. Trials from pharmaceutical industry had higher recruitment rates and trials testing hormonal therapy enrolled more patients. Breast cancer patients' accrual to a clinical trial could be improved by trying to systematically identify all eligible patients and propose a trial to those eligible and to whom the treatment is planned to be equivalent to the standard arm of the trial.

Introduction

Literature on recruitment in clinical trials is fairly consistent in reporting low recruitment rate in clinical trials [1]. A report of the Cancer Therapy Evaluation Program (CTEP) of the National Cancer Institute (NCI) found that 22% of randomized phase III trials are closed due to poor accrual rate [2]. In a study on recruitment in breast cancer clinical trials in Ontario conducted by J.L [3]. recruitment rates varied from 5.4 to 8.5% between 1997 and 2002. More than 30% of breast cancer patients were diagnosed in hospitals where no clinical trial was available. Since this study was population-based, we have decided to study in more details patients' characteristics, physicians and trials characteristics in a specialized breast cancer centre.

The objectives of the present study were to measure recruitment in clinical trials and to identify patients, physicians or trials characteristics associated with higher recruitment rate.

The ultimate goal was to find the area where gain can be made to improve recruitment rates while respecting the autonomy of the patient to consent or not to a trial.

Patients and method

This study was a retrospective cohort study conducted at the Centre des Maladies du Sein Deschênes-Fabia (CMS), which is a specialized breast cancer clinic in Canada, where there is a public health care system. This clinic deserves more than 90% of women with breast cancer in Quebec City and surroundings. This study was approved by the Institutional Review Board. Clinical trials for non-metastatic breast cancer opened to accrual between June 2004 and March 2008 were selected. For each clinical trial, the trial's main criteria were used to define the target population (e.g. triple negative breast cancer). Using the CMS database, patients corresponding to the target population (defined in the statistical section as patients fitting main criteria) of the trial and diagnosed during the time period the trial was opened to accrual were identified. Patients' charts were then reviewed to collect the data (not all charts were reviewed and a sample was selected using the increasing chart number).

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Table 1
Characteristics of the trials.

Clinical trials	Study ID[a]	Number of days the trial was opened	Menopausal status	Hormone receptors status	HER2 status	Phase	Setting	Intervention studied[b]	Sponsor	Number of eligibility criteria[c]	Number of patient-trials reviewed ($n = 985$)
BACH	NCT00550771	320	DNM	DNM	Positive	II	Adjuvant	Chemotherapy	Industry	26	34
BEATRICE	NCT00528567	77	DNM	Negative	Negative	III	Adjuvant	Targeted therapy	Industry	37	3
FACE	NCT00248170	466	Menopause	Positive	DNM	III	Adjuvant	Hormone therapy	Industry	28	137
NCIC CTG MA.27	NCT00354302	965	Menopause	Positive	DNM	III	Adjuvant	Hormone therapy	Cooperative group	29	245
NEOCAN	NCT00247650	594	Menopause	Positive	DNM	II	Neoadjuvant	Hormone therapy	Industry	24	33
NEOSPHERE	NCT00545688	168	DNM	DNM	Positive	II	Neoadjuvant	Targeted therapy	Industry	25	5
NSABP B-36	NCT00087178	1506	DNM	DNM	DNM	III	Adjuvant	Chemotherapy	Cooperative group	39	173
NSABP B-38	NCT00093795	799	DNM	DNM	Negative	III	Adjuvant	Chemotherapy	Cooperative group	40	133
NSABP B-39	NCT00103181	1059	DNM	DNM	DNM	III	Adjuvant	Radiation therapy	Cooperative group	35	222

DNM = did not matter.
NSABP = National Surgical Adjuvant Breast and Bowel Project.
NCIC CTG = NCIC Clinical Trials Group.
All trials were multi-centered, randomized and open-label; none with placebo.
[a] According to clinicaltrials.gov.
[b] For studies that were still recruiting at the time of data collection, closing date was censored at May 31st 2008.
[c] Includes both inclusion and exclusion criteria.

All eligibility criteria (inclusion and exclusion) were assessed to confirm if the patient did or did not respect the criteria and to classify the patient as eligible or not for the trial. Some of the criteria were considered "not assessable" (e.g. willingness to use contraception) or "not evaluated" (e.g. if a left ventricular ejection fraction value was needed and no value was available in the chart). For these criteria, we considered them met since most of the time, should the eligibility criteria had been assessed, it would have been met (e.g. most patient have a normal left ventricular ejection fraction but this test is not routinely performed in patients not receiving chemotherapy). The only exception was for the NCIC Clinical Trial Group (NCIC CTG) MA.27, comparing exemestane to anastrozole as adjuvant therapy in postmenopausal women with hormone receptor positive breast cancer. During the study period, participation in a specific arm of one of the two substudies became mandatory and only patient with low bone mineral density could participate. In that case, if no bone mineral density was available, it was assumed that the patient had a normal density and therefore, deemed not eligible for the NCIC CTG MA.27 bone substudy.

It was considered that a patient was offered participation in a trial (or that physician considered it) when the trial was mentioned in the physician's note or the research nurse had screened or met a patient. When available, reasons for refusal were collected.

Patient was considered "recruited" when a signed informed consent was in the chart.

Characteristics associated with recruitment

The following patients, physicians and trials characteristics were collected. For patients' characteristics, age, tumor stage (TNM 5th edition), hormone receptors status, HER2 status and menopausal status were collected. For physicians' characteristics, the following variables were collected: sex, age and speciality (medical vs. surgical oncologist). Lastly, trials' characteristics were: phase, neoadjuvant or adjuvant trial, number of eligibility criteria, sponsor (cooperative group vs. pharmaceutical industry) and category of intervention tested.

Statistical analyses

Descriptive statistics were used to depict eligibility, proposition of trial and recruitment. Since one patient could have been eligible to more than one trial during the time period, two methods were used to calculate proportions in order to better appreciate the data. First, calculations were conducted at the patient level (which is means that if a patient was eligible to more than one trials, it was counted as one), using the following equations [4]:

$$\text{Eligibility fraction (4)} = \frac{\text{Number of patients eligible for at least one trial (E)}}{\text{Total number of patients fitting main criteria of at least one trial (F)}}$$

$$\text{Enrollment fraction (4)} = \frac{\text{Number of patients recruited into at least one trial (R)}}{\text{Total umber of patients eligible for at least one trial (E)}}$$

$$\text{Recruitment fraction (4)} = \frac{\text{Number of patients recruited into at least one trial (R)}}{\text{Total number of patients fitting main criteria for at least one trial (F)}}$$