ATAC: A Novel International Model for Clinical Trial Accrual

25TH ANNUAL SAN ANTONIO BREAST CANCER SYMPOSIUM 6

Recruitment of patients to randomized trials is a major challenge in clinical research. It is not uncommon for actual recruitment rates to fall short of projected accrual, threatening the success of a study. The ATAC trial was a unique global collaboration between industry and academia, and the rapid recruitment of over 9,000 patients internationally to this study was a major achievement, particularly if one considers that the 1995 International Overview included only 3,077 postmenopausal women with ER-positive tumors who received five years of tamoxifen. A recent survey of ATAC trialists reported that key elements leading to participation were the trial's scientific rationale and practical design.

ATAC TRIAL TIMELINE

July 12, 1996	Enrollment opened
May 1998	Target recruitment increased to 7,500
September 1998	Target recruitment increased to >8,500
March 24, 2000	Enrollment closed
June 29, 2001	Cutoff date for follow-up
December 2001	First presentation of data
May 2002	Presentation of ASCO technology assessment
June 2002	Lancet publication of first results
December 2002	Update presented

PHYSICIAN INCENTIVES TO ENTER PATIENTS ON THE ATAC TRIAL*

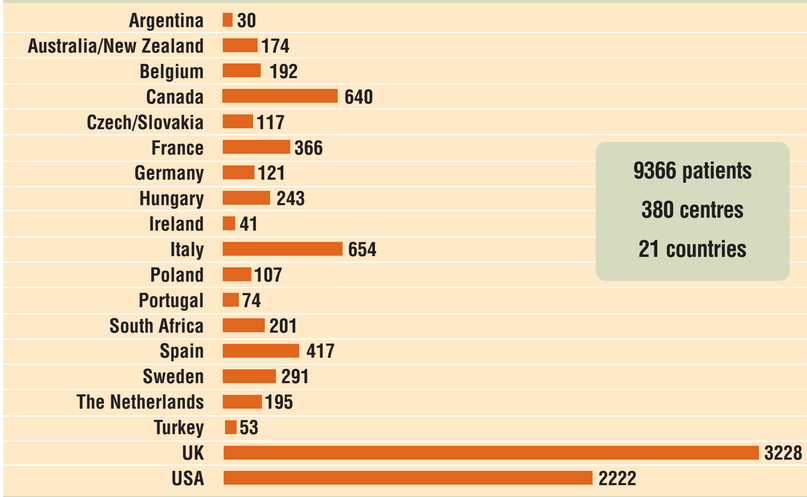
Incentive	% rating "very important"
Attractive scientific rationale	84%
Design easy to explain to patients	79%
Pragmatic design in line with standard practice	76%
Infrastructure well-organized	70%
Endocrine treatments oral and relatively non-toxic	69%
Logical extension of earlier endocrine trials	67%
Free trial medication	47%
No other open adjuvant endocrine trial	36%
International nature	30%
Level of financial support provided	29%
Endorsement by Consumers Advisory Group (UK only)	6%

***238/381 trialists responded to the survey**

DERIVED FROM: Baum M. *Eur J Cancer* 2002;38:1984-1986.

ATAC PARTICIPATING COUNTRIES

RECRUITMENT PER COUNTRY — PATIENTS ENTERED



ATAC TRIAL ORGANIZATION

Steering committee (SC): Executive responsibility for conduct of trial

International coordinating committee (ICC): International breast cancer experts, resolved local issues and made recommendations to SC regarding trial conduct

International project team (IPT): Operational management of trial

Independent data monitoring committee (IDMC): Reviewed safety and efficacy data provided by independent statistician

DERIVED FROM: Forbes JF. Poster presented at Aromatase 2000, Australia.

FACTORS IN RECRUITMENT SUCCESS OF ATAC

"Contributing reasons for their participation in the trial and subsequent rapid recruitment were the scientific rationale of the trial, pragmatism of the study design (reflecting standard clinical practice as closely as possible), and the relative safety of the treatments involved…The investigators were impressed by this trial as it was considered to be scientifically robust, well organised, and the design made the trial easy to implement in busy clinics. These reasons are very likely to have influenced the rapid recruitment into the ATAC trial, and they are in contrast to the Cancer Research Campaign breast conservation trial, which was designed to compare mastectomy with wide local excision, with the sample target of 1200 patients. This trial was aborted after recruiting only 150 patients over 3 years. In the future, studies (either in the field of oncology or in other therapeutic areas) that consider the factors outlined in this paper in the trial design may maximise the potential recruitment rate.

…Finally it could be argued that the respondents were less than honest in their replies in the name of 'social desirability' or 'faking good', by minimising the importance of the cash incentive for recruitment. This is of course a possibility, but has been minimised by the anonymous nature of the questionnaire and lack of face-to-face contact between the researcher and investigator which are proven techniques in improving the validity of responses in these kinds of studies."

—Michael Baum, ChM, FRCS
Eur J Cancer 2002;38:1984-1986.

EVOLUTION OF THE ATAC TRIAL

I chaired the steering committee and have seen this trial through from back-of-an-envelope discussions in a pub to completing accrual of over 9,300 patients in record time. It's an amazing international collaboration — particularly an Anglo-American collaboration. There was a statistically predetermined number of events we were looking for, which triggered the first formal analysis.

—Michael Baum, ChM, FRCS

UNBLINDING THE ATAC TRIAL DATA

As the independent statistician, I was the only person able to link the data from the trial with the treatment code and to provide the coded results to the data monitoring committee. As a result, I was the only person who saw the unblinded data as it evolved, and it was very, very exciting. It was very difficult to keep quiet as the results began to appear. Tamoxifen has been the standard endocrine treatment for breast cancer for 30 or 40 years. Now a new treatment looks better, not only in terms of efficacy, but also safety.

—Jack Cuzick, PhD

INTERNATIONAL RESEARCH COLLABORATION

The ATAC trial group came together extremely successfully. I believe that doctors and patients prefer very simple trial concepts with biological and clinical plausibility. The ATAC trial had these features. We had reason to believe that the aromatase inhibitors were going to be better than tamoxifen. We knew something about these agents. And the ATAC trial had a very simple randomization. I think simplicity and appeal were the key elements.

We are utilizing this international model for several U.S. cooperative group trials. We realized that we had parallel trial development efforts going on in Europe and the rest of the world. It makes sense for women internationally to come together to answer important questions in an efficient and accelerated fashion.

—Nancy Davidson, MD

SELECT PUBLICATIONS

The ATAC Trialists' Group. **Anastrozole alone or in combination with tamoxifen versus tamoxifen alone for adjuvant treatment of postmenopausal women with early breast cancer: First results of the ATAC randomised trial**. *Lancet* 2002;359:2131-2139.

Early Breast Cancer Trialists' Collaborative Group. **Tamoxifen for early breast cancer: An overview of the randomised trials.** *Lancet* 1998;351:1451-1467.

Baum M. **The ATAC (Arimidex, Tamoxifen, Alone or in Combination) adjuvant breast cancer trial in post-menopausal women.** *Breast Cancer Res Treat* 2001;69(3): Abstract 8.

Baum, M. **The ATAC (Arimidex, Tamoxifen, Alone or in Combination) adjuvant breast cancer trial in postmenopausal patients: Factors influencing the success of patient recruitment.** *Eur J Cancer* 2002;38:1984–1986.

Forbes JF on behalf of the ATAC Trialists' Group. **The ATAC breast cancer adjuvant trial in post-menopausal women: A model for adjuvant trials.** Poster presented at Aromatase 2000, Australia.

Lara PN et al. **Prospective evaluation of cancer clinical trial accrual patterns: Identifying potential barriers to enrollment.** *J Clin Oncol.* 2001;19(6):1728-1733.

Winer EP et al. **American Society of Clinical Oncology Technology Assessment on the use of aromatase inhibitors as adjuvant therapy for women with hormone receptor positive breast cancer: Status report 2002.** *J Clin Oncol* 2002;20(15):3317-3327.