

ATLAS Steering Committee meets in Oxford, 9/2005
Final recruitment: ATLAS ~15 200 women

The ATLAS Steering Committee met in Oxford this September with representatives from almost all of the countries collaborating in ATLAS. The ATLAS Steering Committee meeting immediately followed the sixth meeting of the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) also held in Oxford.

The aims of the ATLAS meeting were

- to discuss progress in the study
- to focus on key objectives now that recruitment has been completed
- to listen to experiences from different countries about how the challenges associated with compliance and long-term follow-up might be managed.

Presentations from the ATLAS meeting can be found on the ATLAS website:- www.ctsu.ox.ac.uk/~atlas/



**ATLAS Steering Committee, Oxford
September 2005**



6th Main Meeting of the Early Breast Cancer Trialists' Collaborative Group

This was a preliminary meeting for the fifth cycle of the EBCTCG overview when EBCTCG trialists reviewed data from trials of local and systemic treatments of early, operable breast cancer. More information can be found at www.ctsu.ox.ac.uk/projects/ebctcg Data are still being collected from many trials in order to complete the overview analyses. When these data arrive, an extensive programme of data checking and analyses refinement will be needed. The EBCTCG will meet again in September 2006, and the latest findings from the overview will be published thereafter.

Recurrence risk: The importance of a long-term outlook

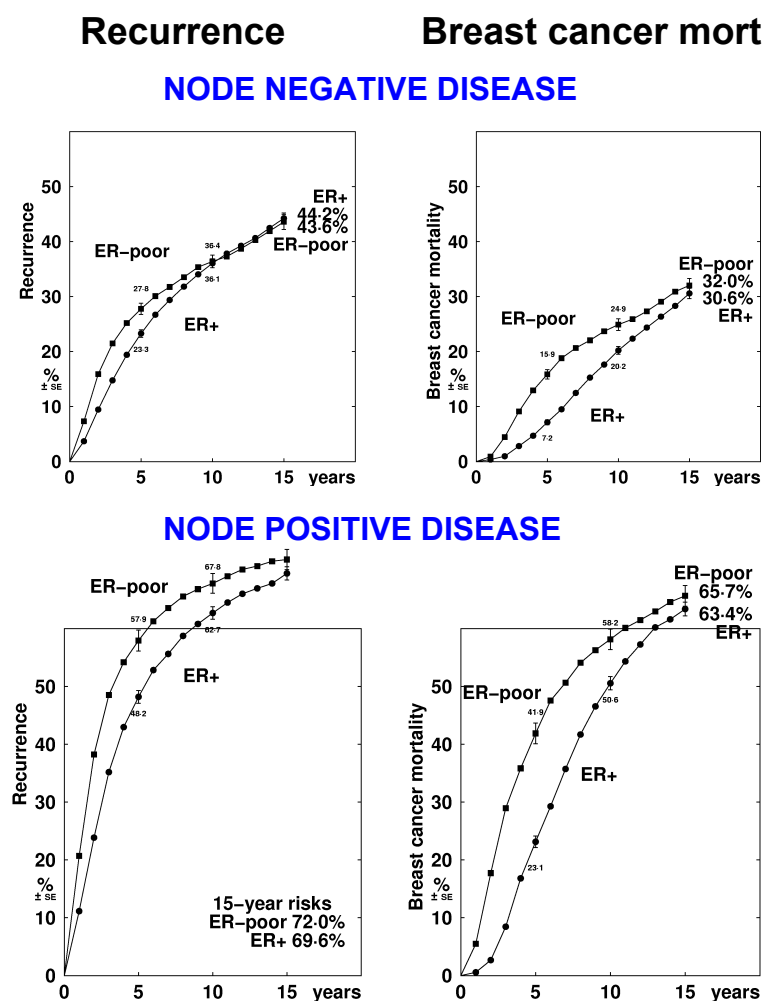
When assessing trials of long-term treatment, it is useful to review some of the published data concerning women who have NOT received adjuvant treatment either with hormonal treatment or chemotherapy – Table 1¹. These analyses give some idea of the risk of recurrence and death from breast cancer that women face after diagnosis.

Table 1: 15-year outcome for control women allocated no adjuvant chemotherapy or hormonal medication at all

Nodal & ER status	Recurrence	Breast cancer mortality
Node –ve ER poor	43.6%	32.0%
Node –ve ER +	44.2%	30.6%
Node +ve ER poor	72.0%	65.7%
Node +ve ER +	69.6%	63.4%

Among women in the control groups allocated no adjuvant medication in the early (1970s/80s) trials, long-term prognosis depends strongly on nodal status - not on ER status. Fig. 1 presents the same information in life-table format.

Figure 1: 15-year outcome for control women allocated no adjuvant chemotherapy or hormonal medication at all



In **ER+** disease the annual breast cancer mortality rate is high not only in years 0-4, but also in years 5-9, 10-14 and beyond

ie the recurrence risk remains fairly constant throughout the first 15 or so years (while among women with ER– poor disease, the risk lessens after the first 5 years).

What does this all mean for ATLAS?

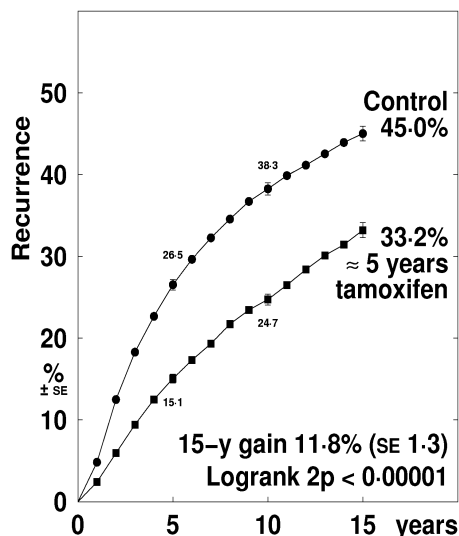


Figure 2: Recurrence in trials of 5 years tamoxifen vs not, women with ER+/ER unknown disease

The analyses on the previous page are of major relevance to ATLAS and to other studies of long-term hormonal treatment of hormone-sensitive disease. They demonstrate the fundamental need to look at treatments that could combat these later recurrences. Consider the recurrence rates among women who have received 5 years of tamoxifen already – **Figure 2**. recurrence rate is roughly constant during years 5-15.

What might be gained from even more prolonged therapy among these women who might have hormone-sensitive disease?

Available data from trials of “longer vs shorter” tamoxifen

As mentioned in the cover story, data from the current cycle of the EBCTCG overview are still being collected and analysed. Updated results are not yet available. However, with respect to the trials of longer versus shorter of tamoxifen, we can report that the amount of data now available has increased substantially, particularly from the trials of 10 vs 5 years of tamoxifen: three times as much data are now available, mainly from the contribution of ATLAS and its UK counterpart – aTTom. Among women with ER+/unknown disease, there are now more than 20 000 women randomised in trials of ~10 vs 5 years tamoxifen, providing 60 000 woman-years of information ie a mean of only 3 years of follow-up at the moment.

We are pleased to confirm that the conclusion about hormonal treatment duration as set out in the most recent EBCTCG publication still holds:

“Both for recurrence and, particularly, for mortality, much larger numbers of events will have to accrue in the trials of 10 versus 5 years of tamoxifen before statistically reliable evidence emerges.” This was also the conclusion of the ATLAS independent Data Monitoring Committee meeting, which meets regularly and most recently in June 2005.

Next steps in ATLAS: ER ascertainment, compliance & follow-up

•Wherever possible, confirm the ER of the original tumour

Trials like ATLAS may show that 10 years of tamoxifen produces better survival than just 5 years of adjuvant tamoxifen only in women whose original tumour was ER+. This underlines the importance of knowing the ER status of as many as possible of the women randomised in ATLAS. If the effects among women who are ER+ are not separated from those among women who are ER poor, then the size of effect in the ER+ women is likely to appear smaller than is actually the case. The worst case scenario would be that ATLAS has a false negative overall result, which could have been avoided by better knowledge of the ER status. This could adversely affect the treatment of several hundreds of thousands of women in the future.

Table 2: Percentage of patients with ER unknown at the time of randomisation

	“Older”* component (n=2354)	“Newer”* component (n=12898)
ER unknown	68%	37%

*Older: Women randomised with ~ 2 years of tamoxifen prior to randomisation

Newer: Women randomised with ~ 2 years of tamoxifen prior to randomisation

If the ER status of the original tumour can be ascertained retrospectively, then this will allow analyses of recurrence to be stratified by ER status and so significantly increase our chance of detecting any real benefit from longer tamoxifen treatment. It may not always be possible to ascertain the ER status of the original tumour on all women, but even if the original ER status could be ascertained for women who experience a recurrence of breast cancer, this would greatly increase the power of the study.

•Compliance and follow-up: Good, but must continue

Women should be encouraged to comply with their original random allocation, where clinically appropriate (see ATLAS newsletter 10, <http://www.ctsu.ox.ac.uk/~atlas/newsletters/jan05.pdf>).

We must have up to date information on all women **especially** with respect to

- **Contact details for the patient and the doctor**
- **Compliance with original random allocation**
- **Death (if died, date & cause of death)**
- **Recurrence (LOCAL or DISTANT, & date of first recurrence)**
- **Other (post-randomisation) primary cancers (site & date of diagnosis)**

Information on events resulting in hospitalization would be helpful.

HOW CAN WE HELP WITH THIS IN YOUR CENTRE?

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