

NCRI Breast Clinical Studies Group

The Group has welcomed five new scientific members this year and would like to thank the five committee members who stepped down for their most valuable contributions over several years. In total there are 27 scientific members and nine observers/funding body representatives.

Subgroups

Two Subgroups Translational and Imaging have been established, chaired by Professor R. Leonard and Professor L. Turnbull respectively. The Translational Subgroup has provided advice and contributed to successful TRICC applications and is leading on the possible involvement of the BCSG in the international study evaluating treatment decision making based on gene profiling, the MINDACT study run by the Breast International Group. The Imaging Subgroup has formulated some preliminary options for study which are being developed into formal study proposals. Professor M. Dowsett, who is also a member of our Group, continues as chairman of the NCRI Translational Clinical Studies Group. Professor Leonard or Dr R Stein represents the BCSG at the CR-UK phase I/II committee.

Portfolio and accrual

There are currently 37 breast cancer trials open to accrual across the entire spectrum of the disease including screening, prevention, lifestyle, survivorship and psychosocial studies as well as the more traditional treatment studies. The total number of breast cancer patients entered into NCRN trials during the period April 2005 to March 2006 was 17,492, up by 62% from 2004/05 largely due to increased recruitment into genetic epidemiology studies.

Accrual of breast cancer patients into trials in the year 2005/6 was 36.1% of the estimated annual incidence of breast cancer, and 42% of all patients entered into NCRN studies from all the site-specific groups. 5,443 patients were entered into NCRN treatment trials (27% of total from all disease groups). However the number of patients entered into nationally funded treatment trials (3371) is the lowest annual figure since the NCRN was initiated. This largely reflects the very long set-up time for the high recruiting, large adjuvant studies and requirement to negotiate additional funding from industry over and above the funds available from CTAAC. Large adjuvant trials simply cannot be funded through the current CTAAC system alone. Over the past year the only adjuvant trial recruiting significant numbers of patients has been AZURE, an academic study but funded by industry. The current adjuvant trial TACT 2 is now open (and recruiting well) but required extensive negotiations to secure industry support and experienced delays in initiation due to sponsorship and governance issues.

3163 women were entered into screening/prevention trials (39% of total from all disease groups) and 8,886 patients were accrued into genetic epidemiology studies (68% of total from all disease groups). 798 were recruited into adopted local trials on the NCRN portfolio.

There are 36 trials closed to recruitment and in follow-up with results or publications anticipated over the next few years. In addition to open and completed trials, there are currently seven funded initiatives in start-up. Additionally there are a number of potentially very large studies in development addressing issues in the preoperative setting, care of elderly women with breast cancer, use of trastuzumab in the adjuvant setting and treatment of metastatic disease.

Achievements

Among the notable events in 2005/6 was publication of the HERA trial in the New England Journal of Medicine which reported a highly significant reduction in the risk of recurrence in women with tumours over-expressing the HER2neu growth factor surface receptor. The results from this study were probably unprecedented in their

importance and have changed both the pathological assessment of patients with the routine introduction of HER2 testing and the rapid introduction of adjuvant treatment with trastuzumab for appropriate patients in many parts of the country. Updated results (Ian Smith - ASCO 2006) confirmed that the large improvement in disease free survival has translated into a significant overall survival advantage.

Updated results of the IES study run by Charles Coombes and Judith Bliss from the UK comparing five years of adjuvant tamoxifen to two to three years tamoxifen followed by the aromatase inhibitor exemestane to complete five years' therapy were also presented at ASCO 2006. This trial has now shown that there is a significant 15% reduction in the risk of dying from breast cancer in addition to the known benefits in terms of recurrence.

The ALMANAC trial evaluating sentinel lymph node biopsy has been published in Journal of the National Cancer Institute and the technology is being rolled out across the country under the supervision of Professor Mansel.

Successful trials that closed in the past year include the AZURE Trial, which accrued 3,360 patients in 28 months, testing the potential benefits of the potent bisphosphonate, zoledronic acid on prevention of metastases in women at increased risk of relapse (N+ or T3/T4) from early breast cancer and TEAM, a trial evaluating the role of adjuvant exemestane in early breast cancer. Among other initiatives accruing particularly well, POSH continues to recruit women with invasive breast cancer diagnosed at the age of 40 years or younger, with the aim of comparing the long-term outcomes of treatment in women with hereditary versus sporadic disease. This study has recently been extended from its original target of 2000 women to 3000.

For the first time an industry sponsored study (ClIMB) was included on the portfolio. Only relapsed HER2+ patients were eligible for this study and it was hoped that incorporation onto the portfolio would encourage referral to participating centres. As it happens the study was closed prematurely due to an unexpectedly large benefit from the addition of the new agent, lapatanib, no capecitabine chemotherapy.

Meetings

A very successful Annual Trials Day was held at Church House, Westminster in January and as in previous years was oversubscribed. An excellent programme was well received by delegates and good interface with most of the relevant pharmaceutical companies who generously supported the meeting was possible.

Following the trials day an open-membership Working Party Meeting was run to primarily facilitate protocol development of preoperative and adjuvant therapy studies. Out of this has come several concrete proposals, two of which have already been submitted as outlines to CTAAC.

A further open forum is planned for September to address lifestyle interventions in breast cancer including diet and exercise with a view to trying to develop this aspect of the portfolio.

Other activities

Over the past year there have been multiple NICE appraisals of relevance to breast cancer management requesting input from the BCSG. These have included adjuvant use of trastuzumab, taxanes and aromatase inhibitors. The Group has been particularly involved in the aromatase inhibitor and trastuzumab reviews. A consensus document on the use of aromatase inhibitors was produced and forwarded to NICE as part of a joint submission from the NCRI, the Joint Council of Clinical Oncology and the Royal Colleges of Physicians and Radiology. For trastuzumab, practice guidelines were produced and again forwarded as a joint submission. Certainly the latter has had a significant effect on the draft guidance issued by NICE.

Priorities for 2006/07:

1. Increased accrual to treatment trials
2. Development of studies with biological and clinical endpoints in the preoperative window
3. Development of studies addressing lifestyle issues in breast cancer
4. Increased partnership with industry especially for phase III and adjuvant evaluation of new targeted therapies

Breast Cancer Group Portfolio

Acronym	Title	PI(s)	Status
ACTION	Adjuvant chemotherapy in older women	Professor Robert Leonard	Set-up
ALMANAC	A randomised trial of sentinel node guided axillary therapy compared with standard axillary therapy in early breast cancer	Professor Robert Mansel	Closed
AMAROS	After mapping of the axilla: Radiotherapy or Surgery: EORTC 10981-22023	Professor R Mansel	Open but In set-up in UK
Annual zoledronate	Effect of an annual infusion of zoledronate on bone mineral density in patients with treatment induced bone loss	Professor R Coleman	Closed
aTTom	A large, uniquely simple, randomised study to assess much more reliably the balance of benefits and risks of prolonging adjuvant tamoxifen treatment in early breast cancer	Professor Richard Gray, Mr Martin JR Lee, Dr Daniel Rea	Closed
AZURE	Does adjuvant zoledronic acid reduce recurrence in patients with high risk localised breast cancer	Professor Robert Coleman	Closed
BBC Study	A national population-based study of treatment effect and endocrine, genetic and cellular risk factors for contralateral primary breast cancer in women in Britain	Professor Julian Peto	Open
BBC-NCRN cohort study	British Breast Cancer Study - NCRN cohort	Professor Julian Peto	Open
BETTER-CARE Study	Breast cancer, early disease: toxicity from therapy with adjuvant epirubicin regimens: cardiac assessment and risk evaluation study	Dr Hugh Montgomery	Open
BISMARK	Cost-effective use of BIS phosphonates in metastatic bone disease - a comparison of bone MARK er directed zoledronic acid therapy to a standard schedule	Professor Robert Coleman	Open
BRCA Trial	Breakthrough Breast Cancer & Cancer Research UK Genetic Breast Cancer Trial: A randomised phase II pilot trial of docetaxel compared to carboplatin for	Dr James Mackay	Open

	patients with metastatic genetic breast cancer		
CAPP-IT	A randomised placebo controlled trial of pyridixine in controlling capecitabine induced hand-foot syndrome	Dr Pippa Corrie	Open
Childhood Trauma	Towards the prediction and management of long-term distress after treatment for breast cancer: the role of childhood trauma	Professor P Salmon	Closed
CliMB/EGF100151	Capecitabine +/- lapatinib in metastatic breast cancer – a randomised phase III study	Professor Robert Coleman	Closed
Cognitive Effects of Chemotherapy	Observational longitudinal study of the effects of adjuvant chemotherapy on cognition on women with breast cancer	Dr David Bloomfield, Dr George Deutsch, Dr Val Jenkins, Dr Val Shilling	Closed
COMICE - 99/27/05	Multi-centre randomised controlled trial examining the cost-effectiveness of contrast-enhanced high field magnetic resonance imaging in women scheduled for wide local excision	Professor Lindsay Turnbull	Open
Coombes Study 77	A randomised, double-blind, multicentre phase ii trial to evaluate the biological effects, safety and pharmacokinetics of single agent zd1839 (iressatm) and zd1839 in combination with anastrozole (arimidex®) in patients with primary breast cancer	Mr Hemant Singhal, Mr Dimitri Hadjiminas, Dr Janine Mansi, Professor Charles Coombes	Closed
COS	Case-Only Study on the interaction of diet and genetic predisposition in the occurrence of breast cancer in young women.	Ms L Sharp	Closed
DCIS II Trial	Randomised trial testing observation (no radiotherapy) against radiotherapy in women with low-risk completely excised ER positive ductal carcinoma in situ (DCIS) of the breast on adjuvant endocrine therapy.	Professor Nigel Bundred	Open
DEVA	A multicentre randomised trial of sequential epirubicin and docetaxel vs epirubicin in node +ve postmenopausal breast cancer	Professor Charles Coombes	Closed
DietCompLyf	The role of diet, complementary treatment and lifestyle in breast cancer survival	Dr Tony Leathem	Open
EATIMS	A pilot study to evaluate the effectiveness and acceptability of using auriculotherapy in a small group setting to manage the menopausal-type symptoms (specifically hot flushes and night sweats) in women	Dr Jane Maher, Teresa Young, Beverley de Valois	Closed

	taking Tamoxifen, Anastrozole (Arimidex) or Letrozole (Femara) as an adjuvant treatment for early breast cancer.		
EORTC 22922	Phase III randomized trial investigating the role of internal mammary and medial supraclavicular (IM-MS) lymph node chain irradiation in stage I-III breast cancer (Joint study of the EORTC Radiotherapy Cooperative Group and the EORTC Breast Cancer Cooperative	Walter Van Den Bogaert	Closed
EMBRACE	Epidemiological study of BRCA1 and BRCA2 mutation carriers	Professor Doug Easton	Open
ERISAC	Effects of Exemestane and COX-2 inhibition on oestrogen receptor positive ductal carcinoma in situ.	Professor Nigel Bundred	Open
ESTEEM	Endocrine therapy or surgery for elderly patients with early breast cancer	Miss Lynda Wyld	In set-up
Exercise Study	The effects of exercise therapy upon quality of life in women who have had breast cancer	Dr Amanda Daley	Closed
FABCC	Familial Association in Breast Cancer Collaboration	Professor Julian Peto	Open
FAST	Prospective randomised clinical trial testing 5.7Gy and 6.0Gy fractions of whole breast radiotherapy in terms of late normal tissue responses and tumour control	Professor John Yarnold	Open
FEMALE	A randomised, multicentre study of first-line treatment of postmenopausal metastatic breast cancer, comparing concurrent vs sequential chemoendocrine therapy with Letrozole vs Letrozole single agent.	Dr Andreas Makris	Abandoned
FH01 - HTA Mammography Trial	Evaluation of mammographic surveillance services in women under 50 with a family history of breast cancer	Dr James Mackay	Open
GBG 26/ TBP	A multicenter randomized phase III study to compare capecitabine alone or in combination with trastuzumab in patients with HER2 positive metastatic breast cancer and progression after previous treatment with trastuzumab	Dr Rob Stein	In Set-up
GENFABARCA	Genetic factors affecting breast cancer progression	Angela Cox	Open
HERA - recommended	Trial of 1 vs 2 years of Herceptin vs no Herceptin in Women with HER2-positive primary breast cancer who have completed adjuvant chemotherapy	Professor Ian Smith	Closed
HOT	Randomised phase II trial of hyperbaric oxygen therapy in patients with chronic arm lymphoedema after radiotherapy for early breast cancer	Professor John Yarnold, Professor Peter Mortimer	Open
HRT	UK Randomised Trial of Hormone	Miss Jo	Closed

	Replacement Therapy (HRT) in Women with a History of Early Stage Breast Cancer	Marsden, Mr Nigel Sacks	
IBIS-II	An international multicentre study of Anastrozole vs Placebo in Postmenopausal Women at Increased Risk of Breast Cancer, and also An international multicentre study of Anastrozole vs Tamoxifen in Postmenopausal Women with Ductal carcinoma in Situ (DCIS)	Professor Jack Cuzick	Open
IMRT trial	Radiotherapy in early breast cancer: cosmetic outcome	Dr Margaret Moody	Open
Living with Secondary Breast Cancer	A study of the experience of living with secondary breast cancer	Professor Jessica Corner	Open
Long term effects of chemo on bone	An investigation of the long term effect of chemotherapy on bone, particularly focusing on the incidence of osteoporosis	Professor Robert Coleman	Closed
MATCH	Attitudes of Men with Breast Cancer in the United Kingdom	Dr Jonathon Gray	Closed
MARIBS	UK Study of MRI for Breast Screening	Professor Martin Leach	Closed
NEAT	Nationwide Breast Cancer Study of Epirubicin plus CMF versus Classical CMF Adjuvant Therapy (NEAT)	Professor Lawrence Young	Closed
NEAT-A	A Multicentre Phase II Feasibility Study of Accelerated Chemotherapy - Sequential Epirubicin Followed by IV CMF - Using Pegfilgrastim for Women with Early Stage Breast Cancer	Dr Daniel Rea	Open
Neoadjuvant	The Role of Magnetic Resonance Imaging and Spectroscopy in Predicting Early Response of Breast Cancer to Chemotherapy	Professor Lindsay Turnbull	Open
Neo-Excel	Neoadjuvant trial of pre-operative exemestane or letrozole +/-celecoxib in the treatment of ER-positive postmenopausal early breast cancer	Miss Adele Francis	In Set-up
Neo-tAnGo	A neoadjuvant study of sequential epirubicin + cyclophosphamide and paclitaxel ± gemcitabine in the treatment of high risk early breast cancer with molecular profiling, proteomics and candidate gene analysis.	Dr Helena Earl	Open
OPTION	Ovarian Protection Trial In Oestrogen Non-responsive Premenopausal Breast Cancer Patients Receiving Adjuvant or Neo-adjuvant Chemotherapy	Professor Robert Leonard	Open
p53 Study	First prospective Intergroup Translational Research Trial assessing the potential predictive value of p53 using a functional assay in yeast in patients with locally advanced/inflammatory or large operable	Dr Herve Bonnefoi, Dr David Cameron	Open

	breast cancer prospectively randomised to a taxane versus a non taxane regimen.		
PIMMS	A psycho-social evaluation of the impact of mammographic surveillance services on women under 50 at increased risk of inherited breast cancer	Ms Joan Austoker	Open
POSH	Prospective study of Outcomes of treatment in Hereditary versus Sporadic breast cancer	Dr Diana Eccles	Open
PRIME	The PRIME breast cancer trial (postoperative radiotherapy in minimum-risk elderly)	Dr Robin Prescott	Closed
PRIME II	Post-operative Radiotherapy In Minimum-risk Elderly Phase II	Dr Ian Kunkler	Open
RACE	Radiation Complications and Epidemiology – Inherited factors contributing to radiotherapy side effects	Professor John Yarnold	Open
REACT	Randomised EuropeAn Celecoxib Trial. A phase III multicentre double blind randomised trial of celecoxib versus placebo following chemotherapy in primary breast cancer patients.	Professor Charles Coombes, Dr Gunter von Minckwitz	Open
Reflexology Study	RCT of the effects of reflexology on QOL (including mood, adjustment, function coping & patient satisfaction) and host defences in early breast cancer	Professor Leslie Walker	Closed
RIB	A multicentre randomised trial of single dose radiotherapy compared to ibandronate for localised metastatic bone pain	Ms Orla Cummins, Dr Peter Hoskins	Open
SEARCH	A population based study of genetic predisposition and gene-environment interactions in breast cancer	Professor Doug Easton	Open
SECRAB	Sequencing of Chemotherapy and Radiotherapy in Adjuvant Breast Cancer	Dr I Fernando	Closed
Sentinel Node Biopsy - Breast	Sentinel node biopsy in primary breast cancer – a randomised controlled trial assessing morbidity, quality of life and cost effectiveness	Mr AD Purushotham	Closed
SoFEA	Study of Faslodex with or without concomitant Arimidex vs Exemestane following progression on non-steroidal Aromatase inhibitors	Dr Stephen Johnston	Open
SOFT	Suppression of Ovarian Function Trial	Professor Robert Coleman	Open
SPROG	Prospective randomised comparison of G-CSF (filgrastim) secondary prophylaxis versus conservative management of chemotherapy-induced neutropenia to maintain dose intensity in chemotherapy for breast cancer	Professor Robert Leonard	Open
START	Standardisation of Breast Radiotherapy (START) Trial	Professor John Yarnold	Closed

SUPREMO	Selective use of postmastectomy radiotherapy after mastectomy	Dr Ian Kunkler, Dr Peter Canney	In Set-up
Surgical management choices in breast cancer	Patient and professional factors influencing choice of surgery in the management of breast cancer: a qualitative and quantitative study	Professor MWR Reed, Miss Lisa Caldon	Closed
TAC	A randomised multicentre trial of neoadjuvant Taxotere and Adriamycin/Cytoxan (AC): a biologic correlative study	Dr Jenny Chang	Closed
TACT	A randomised trial of standard anthracycline-based chemotherapy with fluorouracil, epirubicin and cyclophosphamide (FEC) or Epirubicin and CMF (Epi-CMF) vs FEC followed by sequential docetaxel as adjuvant treatment for women with early breast cancer	Dr Paul Ellis, Dr Peter Barrett-Lee,	Closed
TACT2	Trial of Accelerated Adjuvant Chemotherapy With Capecitabine in Early Breast Cancer	Dr David Cameron	Open
tAnGo	A Phase III randomised trial of gemcitabine in paclitaxel-containing, epirubicin based adjuvant chemotherapy for higher risk early stage breast cancer	Dr Chris Poole	Closed
TEAM	An open label, randomised multicentre comparative trial of 5 years adjuvant Exemestane treatment versus 5 years adjuvant tamoxifen treatment in postmenopausal women with early breast cancer	Dr Daniel Rea	Closed
Telephone follow-up study	Comparing hospital and telephone follow-up for women with breast cancer: a randomised controlled trial	Dr Kinta Beaver	Closed
TEXT	Tamoxifen and Exemestane Trial	Dr Helena Earl	In set-up
TOPIC2	Randomised Phase III trial of navelbine/epirubicin vs adriamycin/cyclophosphamide as pre-operative chemotherapy in patients with greater than or equal to 3cm diameter early breast cancer	Professor Ian Smith	Closed
W.I.N.S. (UK) - Stage 1	Womens Intervention Nutrition Study (UK arm)	Mr Richard M Rainsbury	Closed
Will Weekly Win	A randomised 2-arm, prospective, multi-centre, open-label Phase III trial comparing the activity and safety of a weekly versus a 3 weekly Paclitaxel treatment schedule in patients with advanced or metastatic breast cancer	Dr Mark Verrill	Open
ZICE	Zoledronate versus ibandronate comparative evaluation trial.	Dr Nick Murray, Dr Peter Barrett-Lee	Open