Patient Response to Proposal for new DCIS Clinical Trial
Independent Cancer Patients' Voice Study Day 4th March 2011

Background

For many years there has been considerable controversy about the diagnosis and treatment of DCIS – not just in the UK but across the world. There have been headlines about over diagnosis leading to overtreatment leaving some women feeling angry and distressed following major surgery. However, others are grateful as they consider that they have been given surgery which prevented their condition becoming malignant.

There is opposing expert opinion:

- The Nordic Cochrane group –and others in UK including Prof. Michael Baum – are heavily critical of the UK Screening Programme's information and service and of "overtreatment" of DCIS diagnosed on mammography. They go as far as to doubt the value of the money spent on screening.
- The UK Breast Screening Programme and Prof Jack Cusick are clearly in favour of continuing regular mammography with surgery for those diagnosed.

Both groups produce very compelling statistics which are available to interested women and which we all find very confusing.

Breast Cancer Care held a debate in London on this issue with input from Prof Baum and others. This was notable for the level of anger and distress shown by some of the audience who considered that they had received "mutilating" surgery which they now felt had been unnecessary. However, others felt relieved that a potentially life-threatening problem had been removed by their surgery.

At our study day held at Bart's (November 2009) we heard from Prof Cusick about the lives saved by screening and his statistics were convincing to the delegates but are challenged by the Nordic Group – leaving some lay people very confused!

The Patient Information Leaflet produced by the UK Breast Screening Programme was acknowledged to need updating and adapting and Joan Austoker at Oxford University was appointed to produce a new leaflet. An ICPV member made repeated enquiries and requests to the BSP for consultation on both the screening programme and the leaflet and eventually was given access to Joan Austoker. Consequently, ICPV had a very constructive meeting with Joan who welcomed our input and said she would suggest adding a link to ICPV to the leaflet. She would keep us updated and thought we would be happy with the new leaflet. It was tragic that Joan died after presenting, but before acceptance of, her adaptation. (ICPV would be interested in comments on the new leaflet!)

ICPV members feel that women should be given factual information which includes acknowledgement of lack of evidence regarding DCIS and the pros & cons of treatment. They can then make a more informed choice regarding screening and treatment. There continue to be differing opinions amongst our members on these issues but a clear consensus emerged for the need for access to all known facts and for further research.

Presentation at ICPV study day 4th March 2011 Adele Francis Surgeon

Adele gave an excellent and honest presentation of the current diagnosis and treatment of DCIS. After showing some slides of headlines from tabloid press illustrating the extremes of both sides of the debate, she gave definitions of "overdiagnosis" and some statistics regarding probable overtreatment of DCIS

21,683 women diagnosed with breast cancer in 2006 = 7,000 unnecessary diagnoses per yr in UK
2,000 women screened 3yrly over 20 yrs = 17.6-11.4 lives saved, 8.6-2.3 over diagnosed
Annual DCIS in UK:- Low grade -500, Intermediate grade -3,000, High grade - 7,000

There has been a dramatic increase in the number of cases of DCIS diagnosed since mammographic screening but if DCIS lead to invasive cancer you would expect to see a drop in the invasive cancer rate over the last 30 years. Instead it has risen.

Hippocratic oath

Adele gave us both the original and modern version of the relevant part of the Hippocratic oath taken by doctors – the latter is *"I will apply, for the benefit of the sick, all measures that are required, avoiding those twin traps of overtreatment and therapeutic nihilism"*

DCIS Biology

Adele explained the biology of DCIS and the difference with invasive cancer – although there were abnormal cells they remained within the basement membrane and did not spread. Once they spread beyond the membrane it became invasive and, at present, there was no effective predictor of which DCIS would progress to invasive cancer. Should this actually be labelled as cancer before it became invasive?

She explained that a trial is needed to address the following issues:-

- Is surgery necessary for all DCIS? Which DCIS diagnoses do not require surgery?
- Can we predict by biopsy which DCIS requires surgery –ie. is it life threatening?
- Can we quantify these risks better to give patients an informed choice?

The proposed trial would only recruit those patients diagnosed with low grade DCIS which has been confirmed by central pathology review

Patients would be randomised into

1) standard treatment ie surgery +/- radiotherapy plus standard F/U or
2) active monitoring with annual mammography for 5-10yrs.

The trial endpoints would be diagnosis of invasive breast cancer in same breast and patient reported outcomes: Overall survival, Translational predictors of progression to invasive disease, Time to surgery/mastectomy/mastectomy rate and Health economics.

The trial design is that of 'non inferiority' ie to show that active surveillance is just as safe in terms of developing breast cancer and 'quality of life'

The DCIS Trial Development Group included many eminent professionals from all relevant disciplines and collaborated with SLOANE and West Midlands Cancer Intelligence Unit

The group were very keen to access opinion from a wide range of patients and potential patients

Patient advocates had been involved in the discussions and Adele acknowledged that this would be a difficult trial regarding recruitment of both patients and professionals with a lot of debate about the different arms and the trial design. Lesley Fallowfield had held focus groups with good range of women - some of whom had had screening and some who hadn't. A Patient Information DVD will be produced about the trial to explain the logic and rationale. Quality of Life and psychosocial issues were extremely important considerations.

The Recruitment Strategy was outlined and, in addition to the focus groups, there will be a Scoping Day with Health Care Practitioners in Birmingham and some patient advocates are needed for this. It is essential that sites provided consistent information and used the patient information DVD. A Pilot Study with 200 patients will examine reasons for accepting/declining trial, reactions to diagnosis and patients' understanding of DCIS. It would also show if there was a need to adapt the recruitment approach. Posters and leaflets about the trial will be available at screening units.

Adele underlined why this trial is needed

- there is no randomised data demonstrating survival advantages after treating low/intermediate grade DCIS
- there are no systematically collected QOL data using validated patient reported outcome measures demonstrating harms/benefits of current practice.
- there is very little Health Economics evidence

AND, she felt that it was important to find evidence to ensure treatment was best practice for patient benefit as it is probably unacceptable to continue current practice.

Dan Rea then spoke to us as an oncologist with years of experience treating women with all types of breast cancer. Dan talked about the ethics involved in such a trial and the likely hurdles which would need to be considered in designing the trial and applying for approval and funding.

Discussion between researchers and ICPV members.

The discussion which followed was lively and covered a range of opinion
from – *"yes, this is needed - but, I would not agree to take part"*
to- *"I would be happy to take part – but only if confident in the monitoring"*

Most people were very aware of the controversy over diagnosis and treatment of DCIS and wanted more reliable information. The current differences in professional opinions are confusing but inevitable without a proper trial, including biomarker research, to provide real evidence of how individual DCIS should be treated. All agreed that such a study was urgently needed but that it would not be easy to recruit to such a trial. Some asked about a retrospective study or a non randomised study – however, the researchers explained why this would not provide the evidence needed.

Several people commented that it would depend on how the trial was "sold" to potential participants – which included a) how much they trusted the clinician b)how much they knew about trials/research beforehand c) how well the "pathway" was explained d) how they would be monitored if in non treatment arm – some felt that annual mammography was insufficient. (Adele did say that physical examination had proved to be of no value but I think we needed more explanation/reassurance on this point)

There was a demand for more information to be available to the public about the need for research Also that all screening & oncology units should be proactive in informing all new patients that these units are engaged in high quality cancer research and that patients should be informed about studies which may be suitable for them and which could be of benefit to them and to future patients. The information given to patients must be honest about the pros & cons of treatment and be clear and easy to comprehend by any patient. The person who approaches the patient must have time to explain clearly and to answer any queries – this also needed appropriate environment and an assurance that patients could change their minds.

Other comments.

- Patients in monitored arm will need reassurance re rapid access to treatment should this become necessary. Also to advice if worried between annual mammogram visits.
- How do you explain different treatment for similar condition in different patients by same surgeon?
- Is there any additional surveillance which could be added to give confidence?
- "If there is anything there with potential to become malignant/life threatening - I want it out!"
- If there is a way in which mastectomy can be avoided we need to know – it is such a big thing to come to terms with – body image etc.
- I would find it difficult to carry on with normal life from mammogram to mammogram, with the feeling that something could be brewing in my breast
- It would save a lot of NHS money/resources if surgery and radiotherapy could be avoided – also save time and money for patient and family.
- If evidence showed monitoring was safe this would also reduce stress but until the evidence is certain it will increase stress for patients and families.
- Women in monitored arm would need extra input from CNS re breast awareness and rapid access to investigation & treatment if needed.
  There was more discussion re low, medium and high grade and risk issues in selection of patients asked to participate - and their understanding of this.
- How many biopsies would/could be needed? Is there any risk of escaping cancer cells increasing risk? Would this be reduced by selecting more experienced surgeon?
- This is good opportunity to emphasise the impact of lifestyle on possible prevention or reduction of risk of both primary breast cancer and recurrence.
- Some breast cancer has spread between biopsy and surgery – if this occurred in monitored arm it may not be picked up until date of annual mammography – leading to increased risk.
- Is dense breast tissue or symptomatic diagnosis a reason for exclusion from trial?
- Grading is not a foolproof way of assessing risk – Is it ethical to design a trial whereby some patients will not be treated when we actually know so very little about the natural progression of DCIS and which types are likely to progress?
- If mammography is the reason for over diagnosis why is it the only tool used in monitoring arm
- Any link with research being carried out in USA by Thea Tisty into biomarkers as indicators of risk in DCIS? (NB increased problem there due to annual rather than 3yrly mammography)