Are you organising an annual meeting or conference which you would like to tell our readers about?
Or would you like to write a report on a meeting or conference of particular interest?
If so, contact Patricia McDonnell at Oncology News on T/F: +44 (0)288 289 7023, E: patricia@oncologynews.biz

San Antonio Breast Cancer Symposium 2014

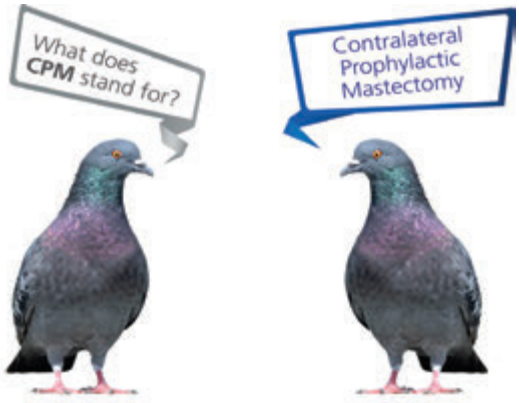
Date: 9-13 December 2014. **Venue:** San Antonio, USA

In the first plenary lecture of the 2014 San Antonio Breast Cancer Symposium, Matthew Ellis [Houston] explored the potential for driving genome-directed therapies in oestrogen receptor (ER) positive breast cancer. For patients receiving neoadjuvant endocrine therapy, whole genome analysis can inform response to aromatase inhibition. It is important to examine both common and low frequency mutations. Translocations of the ER can lead to resistance to hormonal therapy and drive hormone-independent growth. This type of resistance could be overcome with ER degrading agents such as pure anti-oestrogens and pre-clinical models show promise for this approach. Ultimately better neoadjuvant therapy for ER positive breast cancer will lead to better i.e. less chemotherapy. The POETIC Trial Management Group and Trialists reported changes in gene profiles in response to pre-operative aromatase inhibitor therapy. Mutational profiles and subclones are reproducible between core biopsy samples despite tumour heterogeneity with high concordance between sample/pairs taken at baseline and at surgery. Mutational counts were greater for poor responders compared with good responders and generally lower in surgical than baseline samples with most pairs of samples showing common clusters on exome-sequencing. Genomic analysis of ER positive breast cancers during development of endocrine resistance in post menopausal women revealed dramatic falls in mutation number amongst tumours responding to neoadjuvant letrozole compared to non-responders with progressive disease. J Michael Dixon [Edinburgh] emphasised how gene expression profiles change during therapy and baseline analysis alone will not suffice. Using integration of DNA and RNA sequencing in a group of patients enriched for non-response, a 4-gene model was developed which could successfully predict response to letrozole with an overall accuracy of 94%.

Immunotherapy approaches are progressing rapidly with improved understanding of immunogenic tumours and characterisation of triple negative breast cancer (TNBC). Teema Juntilla [Genentech] discussed the potential application of HER2 T cell-dependent bi-specific antibodies (HER2-TDB) for treatment of chemo-resistant HER2 positive breast cancer. HER2-TDB induces T-cell proliferation with anti-tumour effects conditional upon activation of T-cells. Moreover, the immune gene PD-L1 is found on tumour cells and a combination of HER2-TDB with anti-PD-L1 enhances growth inhibitory effects in genetically-engineered mouse models.

Controversies and trends in contralateral prophylactic mastectomy (CPM) were discussed in the first Clinic Science Forum moderated by Ismail Jatoi [San Antonio]. Increasing numbers of women are opting for 'maximal surgery' – removal of both the ipsilateral and contralateral breast. These trends are age dependent with dramatic increases in CPM amongst women <40 years of age. The annual hazard rate for death from contralateral breast cancer has been decreasing since 1985 due to widespread use of adjuvant systemic treatment. Contemporaneous rates for contralateral breast cancer are about 0.2% per year and

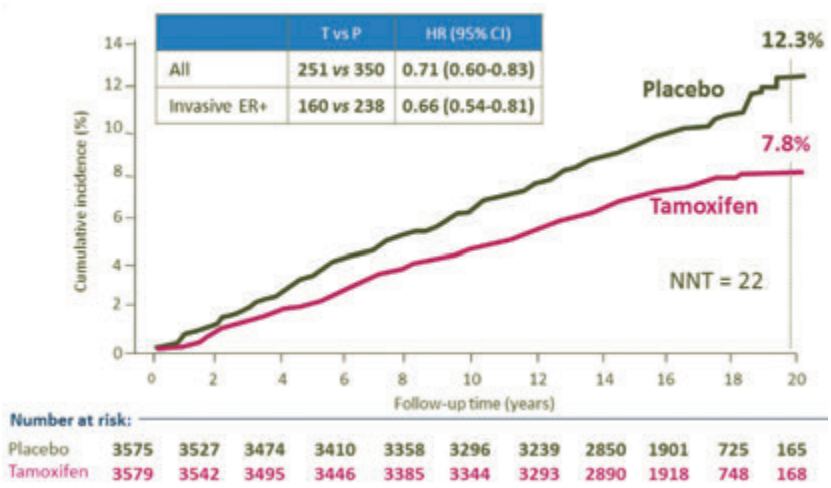
Clinical Science Forum - Controversies and trends in contralateral prophylactic mastectomy (CPM)



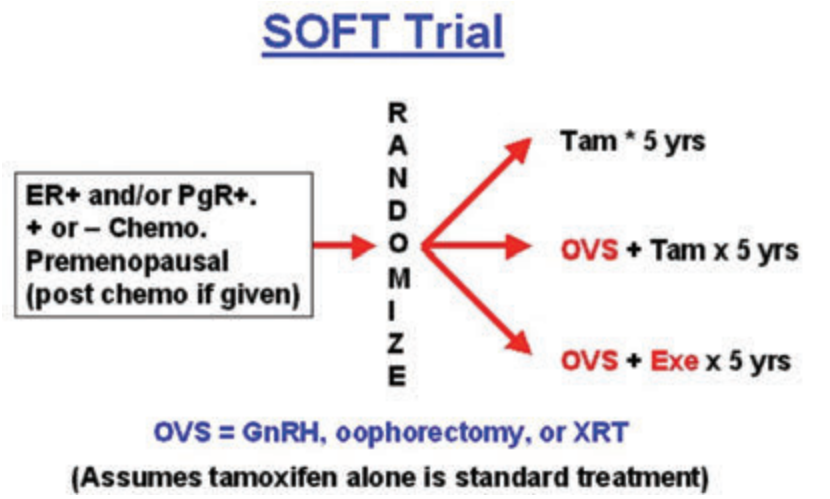
higher for those with BRCA mutations. Therefore rates of CPM are increasing, but paradoxically rates of contralateral breast cancer are decreasing. There is limited evidence that CPM may be associated with reductions of breast cancer specific and all-cause mortality. However, observational studies cannot establish a cause and effect relationship and are prone to confounding bias and type I error. A recent analysis found that CPM was associated with a lower breast cancer specific mortality (HR 0.84), lower all-cause mortality (HR 0.83) and lower rates of non-cancer deaths. This latter point confirms there is selection bias in these studies examining the impact of CPM on mortality and there is currently no robust evidence that CPM reduces mortality. Factors associated with decision-making in favour of CPM included genetic testing, family history of breast or ovarian cancer, MRI breast imaging, higher educational attainment and greater innate fear about risk of recurrence. The latter is a major factor for younger women and significant effort should be made to dissuade women with a poor prognostic ipsilateral cancer from undergoing CPM.

Evidence is emerging for a molecular distinction between ILC and IDC which might have relevance to treatment strategies. Giovanni Cirello [Italy] presented data on potential genetic drivers for lobular cancers and asked what distinguishes ILC from IDC at the molecular level. Mutations of CDH1 which codes for e-cadherin were found in 63% and PIK3Ca in 48% of lobular tumours. Others mutations occurred individually in fewer than 15% of tumour samples. E-cadherin loss is the hallmark of ILC and most mutations of CDH1 are loss of function events which all lead to reduced levels of e-cadherin protein. Analyses of gene expression profiling from the Austrian Breast Cancer Study Group 8 trial patients provide some interesting clinical correlates with statistically significant reductions in disease-free (DFS) and overall survival (OS) events for luminal B type lobular cancers treated with anastrozole compared to tamoxifen. Andy Tutt [London] reported results of the phase III TNT trial which randomised patients with metatastic or recurrent locally advanced TNBC (or BRCA1/2 mutation) to carboplatin or

16 year long term follow up of the IBIS-I breast cancer prevention trial
[Jack Cuzik – Queen Mary College, London, UK]



Analysis of the Suppression of Ovarian Function Trial (SOFT) [Prudence Francis on behalf of SOFT Investigators – Bern Switzerland {International Breast Cancer Study Group}]



docetaxol. There was no evidence for any superior response to carboplatin in unselected TNBC and progression-free survival was the same in both groups based on a restricted mean survival analysis with no significant difference in OS. However, response rates were higher for BRCA 1/2 tumours (68% versus 33%) which may benefit from carboplatin and arguably BRCA1/2 mutation status should be known for metastatic disease. The NSABP B36 trial aimed to determine whether 5-fuorouracil, epirubicin and cyclophosphamide (FEC-100) was superior to standard chemotherapy for patients with node negative breast cancer. At a median follow up of 8 years there was no difference between FEC-100 and AC in terms of either DFS or OS. Of note, there were 5 deaths in the FEC-100 arm with higher overall levels of toxicity questioning whether FEC-100 can be justified for (younger) node negative breast cancer patients, many of whom will do well without any form of chemotherapy. The addition of adjuvant capecitabine to ibandronate in older women does not improve disease-free survival.

Jack Cuzik [London] presented longer term follow up data from the IBIS-1 trial which randomised high risk women to either tamoxifen or placebo. During the first 5 years, breast cancer incidence for tamoxifen and placebo arms was 4.6% and 6.3% respectively with the number needed to treat (NNT) to prevent 1 breast cancer = 59. At 20 years, these figures are 7.8% and 12.3% respectively with NNT = 22. Cuzik emphasised that there is continuing benefit from tamoxifen and the curves remain divergent. It is too early to conclude whether chemoprevention with tamoxifen will impact upon mortality and it remains unclear whether tamoxifen should be given for 5 years only or for 10 years, with no clear evidence that durations of >5 years are beneficial in the chemoprevention setting.

The eagerly awaited results of the landmark Suppression of Ovarian Function Trial (SOFT) were presented by Prudence Francis on behalf of the International Breast Cancer Study Group. The primary analysis was a comparison of tamoxifen and OFS compared with tamoxifen and revealed a small but non-statistically significant increase in disease-free survival for the combination of tamoxifen and OFS compared with tamoxifen alone. Subgroup analysis confirmed that patients not receiving chemotherapy had excellent disease outcomes and derived no benefit from either OFS or a combination of exemestane and OFS. For patients receiving chemotherapy, there were improved outcomes with OFS with 5-year breast cancer-free survival rates of 78% (tamoxifen), 82.5% (tamoxifen + OFS) and 85.7% (exemestane +OFS). Furthermore, distant DFS was better for the tamoxifen and OFS arm and larger primary outcome effects were evident for all women age < 35 years. Women who maintained pre-menopausal oestrogen levels benefited most from tamoxifen and OFS and this was most evident for women< 35 years. Hope Rugo [San Francisco] as discussant asked 'how much is enough' for pre-menopausal women with hormone sensitive disease? Firstly, for high risk women (who invariably require chemotherapy), endocrine management should consist of either tamoxifen and OFS or exemestane and OFS. For low risk women, tamoxifen alone for (at least) 5 years is sufficient systemic therapy without any need for chemotherapy or OFS. Those women in the intermediate risk category are perhaps the more challenging in terms of decision-making in this area; age will influence recommendations but Rugo considers it 'reasonable' to offer tamoxifen and OFS to those women who warrant prior chemotherapy. Once again, the estimated absolute benefits from OFS must outweigh endocrine-related side effects.

A particularly controversial topic discussed at this year's symposium was supplementary screening for women with dense breasts. Legislation has now been enacted in the United States mandating

that radiologists make women aware of the potential benefits of supplementary screening for those with dense breast tissue on conventional modality screening with mammography. The state of Connecticut was the first to adopt this legislation and Jean Weigert presented data suggesting that supplementary screening with breast ultrasound can detect an additional 3.2 cancers per 1000 high risk women. All cases with these additional cancers had normal mammograms but dense breast tissue. However, discussant Jafi Lipson conceded that the clinical impact of finding these additional cancers is unknown and some of them might be detected at the next screening round (and still remain impalpable). There are no data on effects of supplementary screening on mortality and the increase in false positive results (5 – 10%) with ultrasound screening represents a particular problem. A recent analysis [Sprague A, et al. Ann Int Med 2014 Dec] concluded that supplemental ultrasound would increase costs with little benefit. Tomosynthesis may offer better prospects for supplemental screening with increase in cancer detection rate but reduction of false positive cases by as much as 15 – 30%.

Several presentations in the final session of the meeting addressed advances in targeted therapies with a focus on biological and endocrine agents. Sarah Hurvitz presented results of BOLERO-1, a phase III randomised controlled multicentre trial comparing daily everolimus plus weekly trastuzumab and paclitaxel as first line therapy in women with HER2 positive advanced breast cancer. Median progression free survival (PFS) in the everolimus arm was not significantly different to the placebo arm and on-treatment deaths in the everolimus group were noted. Mo Rimawi [Houston] discussed targeting of ER escape pathways as a strategy for overcoming endocrine resistance. The hypothetical benefits of co-targeting ER and HER2 pathways with longer duration of treatment was investigated in the TBCRC023 trial which randomised women with HER2 positive breast cancer to either 12 or 24 weeks of dual HER2 inhibition with lapatinib and trastuzumab. Longer durations of treatment significantly increased rates of pCR in the 24 weeks arm compared with 12 weeks of therapy (28% versus 12%). This increase in pCR was almost entirely confined to the ER positive group and therefore more prolonged dual anti-HER2 and endocrine therapy (without chemotherapy) could offer a promising research strategy for ER positive and HER2 positive tumours.

Gunter von Minkowitz presented results of the phase III ICE study which randomised women aged ≥65 years to either ibandronate alone or combined with capecitebine. Three year DFS was equivalent between the two arms but there were more side-effects in the capecitabine arm. Outcomes for moderate or high risk patients receiving ibandronate alone were favourable with 5-year DFS and OS rates of 77% and 85% respectively.

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BNOS 2015 at Nottingham University "Neuro-Oncology Across the Ages – From Childhood to Old Age"

Date: 1-3 July 2015. **Venue:** Nottingham, UK.

Preview

Building upon last year's outstanding success in Liverpool, the British Neuro-Oncology Society's Annual Conference 2015 offers a topical programme relevant to researchers, health professionals, those involved in organising health care and those involved in societal movements.

There will be an Education Day with parallel tracks for clinical, scientific and public participation. This will include workshops, multi-disciplinary team discussions, and patient communication demonstrations. JTV (Formerly Jimmyteens.tv) will be filming the conference in its entirety, which will be freely available subsequently. Plenary speakers will include:

- Henry Marsh CBE; Neurosurgeon, star of the film "The English Surgeon" and author of the memoir "Do No Harm: Stories of Life, Death and Brain Surgery"
- Jonathan Finlay; an international Paediatric Neuro-oncologist, with life long experience.
- Michael Weller; President of European Association of Neuro-Oncology (EANO) and international leader of clinical trials for novel therapies in Glioblastoma.
- Simona Parrinello; prominent bio-scientist in the field of stem cell biology in brain cancer
- Mathilde Chevignard; A rehabilitation physician developing new models of care for young adults with brain tumour in France.
- Katherine Warren; Researcher and clinical trialist from the US NCI focussing upon Diffuse Intrinsic Pontine Glioma (DIPG)
- Helen Bulbeck; Director of Services for Brainstrust and specialist in communication training
- Glenis Wilmott MEP; Labour's Leader in Europe and Member of the European Parliament for the East Midlands. Glenis was

Rapporteur for the revision of the EU Clinical Trials Directive (http://www.gleniswillmott.eu/tag/clinical-trials-directive/)

The Gala Dinner will be preceded by a "Question Time"- style debate concerned with: UK brain tumour services - Are they fit for purpose for all ages? Are they delivering care and outcomes comparable to the rest of Europe, at an affordable price?

The conference will be held at the East Midlands Conference Centre on the outstanding University of Nottingham Campus with accommodation at the De Vere's Eco-Award Winning Orchard Hotel or the University Halls of Residence.

The welcome reception on Wednesday 1st July is to be held at the historic Wollaton Hall, set in 500 acres of parkland and home to ancient royal herds of red and fallow deer. This Grade One listed Elizabethan mansion was completed in 1588, remodelled in the late 18th and early 19th centuries. It is now home to the city's natural history museum and setting for films, most recently as Wayne Manor in the Batman movie "The Dark Knight Rises".

For further information visit: www.bnos.org.uk

Beatson International Cancer Conference

Date: 5-8 July 2015. **Venue:** Glasgow, Scotland.

Preview

The Beatson International Cancer Conference series is designed to be a relaxed and friendly meeting where delegates and invited speakers have a chance to interact on both a scientific and social basis. We encourage the speakers to stay for the duration of the conference to ensure this interaction.

Aims of the conference

Most solid tumours originate from cells that form the membranes (or epithelia) that line organs such as the lungs, breast, pancreas and prostate. Normally, these epithelial cells have a very well-organised and tightly polarised structure – with a basal membrane on one side, an apical membrane on the other, and intercellular junctions that separate the two. As epithelial cells become cancerous, they lose this well-organised polarised structure to replace it with a different variety of polarity, and this switch enables malignant cells to break away from the epithelium and to invade into other tissues to form metastases. This conference will highlight recent exciting research into the molecular and cellular events that contribute to loss of epithelial polarity during carcinogenesis, and how cancer cells acquire different types of polarity that enable them to migrate and invade. Moreover, we will focus on the avenues for development of agents to target cells with aberrant polarity and a potential route to treatment of metastatic disease.

The opening session of the conference will be held at the Cancer Research UK Beatson Institute with all other sessions being held at Glasgow University. There are several events arranged to give you a taste of the culture and warmth of the West of Scotland and the scientific content of the conference is guaranteed to stimulate.

Jim Norman, Chairman, Scientific Organising Committee, Cancer Research UK Beatson Institute.

For further information
E: conference@beatson.gla.ac.uk
or visit: www.beatson.gla.ac.uk/conf

CDDF 8th Alpine Conference

Date: 2-4 March 2015. **Venue:** Innsbruck, Austria.

Greater interaction is needed between the European Medicines Agency (EMA) and different health technology assessors across Europe for effective delivery of approved drugs, was the recurring message from speakers at the 8th ALPINE Cancer Drug Development Forum (CDDF) meeting, held in Innsbruck, in March, 2015.

"The Alpine meeting provides a unique forum for stakeholders including regulators, academia, industry and patient groups to come together and hear presentations on a wide range of drug development topics," said Professor Heinz Zwierzina, one of the conference chairs from Innsbruck Medical University, Austria. "Discussions and delegate feedback allows us to identify key topics to be addressed in future CDDF workshop meetings."

The prospect for a centralised, EU-wide Health Technology Assessment (HTA) process Bruno Flamion, a past chair of the Committee for Reimbursement of Medicines in Belgium, told delegates, is now 'on the table'. Such developments, he explained, have been made 'workable' by directive 2011/24/EU from the European Parliament and Council on application of patient rights in cross border healthcare.

"The idea of HTA is to provide policy makers with accessible, usable evidence based information," said Flamion, from the University of Namur, Belgium. However, the reality is that with 28 European member states each conducting separate HTA pricing/ reimbursement assessments the system has become fragmented. Differences include France considering the value of new therapies in the context of drug budgets; the UK considering value in terms of health care budgets; and Sweden considering value in terms of wider societal budgets. "In future we may see patient participation increase harmonisation of HTA evaluation. They want access to products based on efficacy and safety and have a right to ask for this," said Flamion.


Stiina Aarum


Tatiana Prowell

Stiina Aarum, from the European Medicines Agency (EMA), highlighted the need for developers to interact with regulators and HTAs in parallel. Currently regulators and HTAs, she said, often answer different questions and have different evidence requirements. Such variance in standards can result in divergent appraisals of risk benefit versus cost effectiveness. "There's a need for stakeholders to come together early to devise optimised development plans discussing issues such as trial populations, comparators, and endpoints," said Aarum.

The EMA, she said, has completed 34 parallel procedures with HTA bodies from England, Italy, Germany, Sweden, France, Netherlands, Spain and Belgium for a broad range of indications including lung, breast and pancreatic cancers and melanoma. This year, said Aarum, around 23 parallel scientific advice procedures are ongoing.

The adoption of break through therapy designations, Francesco De Lorenzo, President of the European Cancer Patient Coalition (ECPC) told delegates, does not solve the problem of patient access to innovative drugs. "The safest, most effective drug that arrives too late is of no benefit for patients," said De Lorenzo, a colorectal cancer survivor, medical doctor, and former Italian minister of health. Inequalities in cancer care, he said, are a reality for Europe. Average cancer expenditure per citizen varies from€182 in Germany, to €16 in Bulgaria. One possible solution, he suggested, would be for cost-effectiveness to be evaluated as part of the market authorization process. Patients are ready to accept the risk of adaptive licensing/ break through designations, he said, but require good information. "We need shorter simpler consent forms of two to three pages rather than the current 20 plus pages. Governments have to invest more in education and advice," said De Lorenzo.

The FDA wants to proactively engage sponsors to discuss trial designs to improve consistency of Patient Reported Outcome (PRO) data, said Tatiana Prowell, the FDA Breast Cancer Scientific Lead. To this end, the FDA has recently appointed PRO leads for each of its three divisions in the Office of Hematology & Oncology Products.

The 2012 FDA Safety and Innovations Act, Prowell explained, created a mandate to include patient perspectives in drug development. "PRO data can support accelerated or regular approval, but should be held to the same high standards as other endpoints," said Prowell.

Patient-reported symptoms, studies have shown, demonstrate better correlations with disease status than clinician-reported symptoms but issues remain around PRO reproducibility. "Most importantly, can you detect responses to the intervention that represent clinically meaningful changes for patients?"

The demonstration of spleen size reduction in myelofibrosis patients treated with ruxolitinib offers a good example of a successful PRO programme that achieved accelerated approval in a trial involving just 300 patients. Here sponsors engaged early with FDA advisors to discuss trial endpoints resulting in the development of a simple PRO tool including six symptoms of direct relevance to patients. "While it took time for the companies to meet with FDA and develop the PRO tool, the process resulted in a better development and registration strategy," said Prowell, adding that the FDA is in the process of building a PRO research agenda.

Janet Fricker, Medical Journalist.

British Neuro-Oncology Society

Dear Delegate

The British Neuro-Oncology Society is delighted to offer you this year's annual meeting programme in Nottingham, entitled "Neuro-Oncology Across the Ages; from Childhood to Old Age". This meeting has been organised by the Children's Brain Tumour Research Centre at the University of Nottingham.

BNOS is offering three days of conference activity linking the opportunity for syndicates and groups to meet, an education day and 1½ days of intensive scientific communication about the management of cancer within the brain, from the perspective of the patient and their family, the multi-professional team, the research scientists and people involved with organisation of health services and the associated technical drug and therapy industries.

Cancer affects the brain of humans at all ages; in childhood nearly 25% of all primary cancers arise in the brain; in adulthood, whilst only 6% of primary cancers arise in the brain, up to 40% of all cancers may be complicated by brain metastases. The startling fact that brain cancer is the biggest cancer killer, up to 40 years of age, justifies this conference as a priority in the scientific and clinical calendar.

Socially, the Organising Committee has arranged a Welcome Reception at the historic Wollaton Hall on the evening of 1 July. This year we are holding a debate before the Conference Dinner on 2 July to explore the evidence for the effectiveness of clinical services in the UK.

We are fortunate this year in being strongly sponsored by charity and commercial partners. We have a number of keynote presentations by leaders in their field; we will make an award to our Young Investigator of the Year, and we will be offering prizes for the best posters and presentations.

We welcome you to Nottingham! We want your ideas on how to improve BNOS for the future, we invite you to become involved with the BNOS organisation through our sub-groups, and we look forward to working with you over the next three days.

Yours sincerely

David A. Walker.

David A Walker
President of BNOS
Chair of Organising Committee: on behalf of Donald MacArthur, Beth Coyle, Lisa Storer, Ruman Rahman, Sue Franklin