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ECCO and ESMO reach compromise

The long-running discussions between ECCO and ESMO have concluded with a decision to jointly host the biennial multidisciplinary meeting. The ECCO 15–34th ESMO Congress will be held in Berlin from 20–24 September, 2009. The 2009 ESMO Congress in Vienna has been cancelled.

The meeting's scientific committee will be chaired by both ECCO and ESMO, and subsequent joint congresses will be held biennially in the 'uneven-numbered' years. ESMO will continue to hold its own congress in the intervening 'even-numbered' years.

A joint statement from the organisations said the meeting 'will provide the best and most updated scientific data for everyone working in cancer and will also strengthen initiatives aimed at providing all cancer patients with equal access to high-quality cancer care.'

ESMO's Board of directors also voted unanimously to become a founding member of the new ECCO organisation, which is comprised of European cancer societies. ESMO will therefore have a seat on the ECCO Board of Directors. The ECCO Board unanimously accepted the proposals.

ECCO President, Professor Alexander Eggermont said he was delighted. 'ESMO and ECCO have been discussing this for some time now, and we firmly believe that joining forces in this way will benefit all our member organisations, European cancer professionals and, most importantly, cancer patients.

'With so much happening in Europe affecting advances in oncology, we need to work together when interacting with European policymakers and industry, so that they take notice, understand and act on our messages. ECCO's mission is to uphold the right of all cancer patients to the best possible treatment and care and to promote interaction between all organisations involved in cancer research, education, treatment and care at the European level. Together with ESMO, I am confident that we will be able to achieve this goal.'

Professor Alexander Eggermont, ECCO President (left) with Professor José Baselga, ESMO President

ESMO President, Professor José Baselga added, 'This uniting of the landscape of European oncology is the result of an agreement on common goals combined with a strong spirit of goodwill and collaboration on all sides. In becoming a founding member of ECCO, we are convinced we will strengthen our ability to represent European oncologists and patients. ESMO is a community of professionals who share the common goal of providing the best possible care for all cancer patients – a mission which is in total harmony with ECCO's objectives.

'This is a win-win situation for ESMO, ECCO and all of our patients. I am looking forward to liaising closely with Professor Eggermont, not only in supporting medical oncology and cancer treatment by multidisciplinary teams, but also in working towards enhancing European conferences as attractive settings to present research done in Europe and worldwide. Looking ahead, we will combine our efforts to make the 2009 ECCO 15 – 34th ESMO Congress the best and biggest European cancer congress yet.'

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6th European Breast Cancer Conference (EBCC-6) Berlin, Germany; 15–19 April, 2008

MRI before surgery 'should become standard'

Early use of magnetic resonance imaging (MRI) in women diagnosed with breast cancer can often lead to a better adapted surgical approach to the tumour, Dr David Martinez-Cecilia (Hospital Universitario Reina Sofia, Cordoba, Spain) told the meeting.

He and his colleagues studied 249 patients who were undergoing surgery for breast cancer, and carried out routine MRI as soon as a biopsy showed malignancy. If additional lesions were discovered, a further biopsy was carried out on them.

The MRI detected 20 additional malignant lesions in 18 patients, and for 15 of these patients, surgical treatment was changed. Surgery was also altered in patients in whom the MRI showed a larger tumour than that originally identified (*EBCC-6, 2008 Abstract # 16*). An analysis of surgical outcomes found that the changes in surgical treatment were beneficial in 22 patients (9%), non-beneficial in 6 patients (2.4%), and uncertain in 4 patients (1.6%).

'We would like to see MRI become a standard preoperative treatment for breast cancer, along with biopsy, mammography, and ultrasound,' Dr. Martinez-Cecilia said.

Pregnant patients 'Should receive standard treatment'

A data-collection exercise among German women who were pregnant when diagnosed with breast cancer suggests that pregnant women may safely benefit from the same breast cancer treatments that are given to non-pregnant women (*EBCC-6, 2008 Abstract # 61*).

Dr. Sybille Loibl (University of Frankfurt, Germany) analysed data on 122 pregnant patients diagnosed with breast cancer between April 2003 and December 2007. Four weeks after delivery, the outcome in babies whose mothers received chemotherapy was not different to those whose mothers did not.

'This shows that pregnant patients can benefit from the same breast cancer treatment that is given to non-pregnant women,' Dr. Loibl said.

Mammography to age 75

Breast cancer screening is effective and appropriate in women aged up to 75 years old, according to new data presented at the meeting. Another study found that the best interval for screening is 3 years, countering arguments that women should have mammograms more frequently.

The first study (*EBCC-6, 2008 Late Breaking Abstract # 5*), was conducted in the Netherlands, where, in 1988, screening was extended to women aged up to 75 years, rather than the previous limit of 70 years.

Mr Jacques Fracheboud (Erasmus Medical Center, Rotterdam, the Netherlands) showed that there had been a steady decline in deaths from breast cancer among women aged 75–79. By 2006, breast cancer mortality was 29.5% lower than the average for the period 1986–1997 for this age.

'The reduction in breast cancer mortality shows that the screening has started to have a statistically significant effect,' Mr Fracheboud said. 'It is easier to find breast cancer in older women due to their breast tissue being less dense. But it is not necessarily an argument for continuing screening beyond 75 because many tumours found at this stage are slow growing and may never reach the stage of causing a problem.'

In the second study – the UK Breast Screening Frequency Trial – researchers randomised nearly 100,000 women to have either an annual or a 3-yearly mammogram after the date of the first screening to which they were invited after their 50th birthday. After an average follow-up of 13 years, there were 373 breast cancer deaths among the 49,173 women invited to attend annual screening, and 374 among the 50, 162 in the control group invited to 3-yearly screening. The difference was not statistically significant (*EBCC-6, 2008 Late Breaking Abstract # 4*).

One of the authors, Professor Roger Blamey (Nottingham City Hospital, UK) said, 'There was a lot of criticism of the UK for having a 3-yearly interval when breast screening was set up. These results indicate that our earlier predicted mortality figures were accurate and that there is no evidence in favour of shortening the current 3-year screening interval.'

Specialist nurses 'could save countries millions'

Nurse-led follow up for breast cancer patients was 20% cheaper than a physician-based programme in Sweden, with no difference in patient outcomes. Researchers said that nurse-led programmes 'would enable substantial savings to be made in a country's health budget.'

Dr IngaLill Koinberg (Hospital Varberg, Sweden), who is both a nurse and a medical doctor, presented data on a study with randomised 264 breast cancer patients to 2 different follow-up groups. Women either received routine medical follow-ups by a physician, or, in the nurse-led group, they received check-ups on demand.

The main difference in cost was explained by the fact that there were 21% more contacts with the physician in the physician group than in the nurse group.

The women in the 2 groups did not differ in terms of anxiety, depression, satisfaction with care, how accessible they found the medical centre or in medical outcomes such as rates of cancer recurrence or death (*EBCC-6, 2008 Abstract # 391*).

While acknowledging that the difference in cost per year and per patient between the 2 groups is modest, Dr Koinberg said it amounts to nearly Euro 900 per patient and 5-year period 'offering a substantial opportunity for reallocating resources since breast cancer is the most prevalent tumour worldwide'.

Individual countries need to have coherent discussions about how the organise the follow-up of cancer patients: 'The majority of women treated within the last 5 years attend a follow-up programme. These follow-up programmes consume large resources,' she concluded.

EUROFILE

Spain shines in European frontier research scheme

Cancer research has made its mark in the first round of grants from the European Research Council. Of the dozen or so awards won by cancer researchers, five are at Spanish institutions, and three at the Spanish National Cancer Centre in Madrid.

The European Research Council (ERC) was established in February 2007 with a remit from the EU to support investigator-driven 'frontier' research, at the limits of knowledge and the boundaries between disciplines. To do this it has a budget of €7.5 billion from 2007 to 2013, drawn from the EU R&D programme.

'THE ERC WAS DELUGED WITH 9,167 APPLICATIONS'

The ERC's first funding scheme targets young investigators, between two and nine years of receiving their PhD, with the aim of helping them establish independent groups. These Starting Independent Researcher Grants last up to five years, and can be worth up to €2 million.

With such attractive terms, the ERC was deluged with applications. Out of 9,167 proposals, peer reviewers selected a priority list of 201 that could be covered with the original budget. The ERC also drew up a reserve list of 229 projects, all of which passed the 'threshold of excellence'. Additional resources to support around 99 of these projects have been found, and the ERC is encouraging other funders to consider them as well. So far, research councils in France, Italy, Switzerland and Spain have responded with national initiatives.

Given the fierce competition, it is impressive for any institution to get an ERC Starting grant. The Spanish National Cancer Centre (CNIO) put in three applications, all from its molecular oncology programme, and got the lot.

'I think that the success is based on the subjects of research proposed by our three junior group leaders,' explains Maria Blanco, director of the programme. 'They all work in very new, upcoming and promising research topics in molecular oncology and they all have been trained in the very best and leading labs working in these topics.'

The winners are Almudena Ramiro, who will study AID, an enzyme involved in somatic hypermutation; Eduardo Moreno, who will look at the way cancer cells can out-compete surrounding normal cells; and Oscar Fernández-Capetillo, who will dissect the role of ATR in DNA damage signalling.

The other Spanish winners are both in Barcelona: Eduard Batlle, who works on colorectal cancer at the Institut de Recerca Biomedica, and Joan Seoane Suárez who works on brain tumour genesis and progression at the Institut de Recerca Hospital Universitari Vall d'Hebron.

The rest of the cancer research winners are scattered around Europe, including two in Finland, and one each in Sweden, the UK, Portugal, Belgium, Italy and Switzerland. They are active in a range of disciplines, from basic molecular biology to more applied research with a therapeutic target or method clearly in view.

The winners explain that the Starting grants are attractive because of the amount and the duration of funding.

'Research funding in Finland and many other European countries tends to be quite fragmented,' explains Akseli Hemminki, of the University of Helsinki, who will be researching a method in cancer gene therapy. 'Therefore there is a constant process of writing grant applications, half-way reports etc, and still the grants only allow for hiring of one or even half a person. The ERC gives us stability for five years which is also useful for hiring people – good people tend to like long term contracts. With the ERC grant I can assemble a high quality team to get the job done.'

'IT GIVES US STABILITY WHICH IS USEFUL FOR HIRING GOOD PEOPLE'

Maria Rescigno, of the Istituto Europeo di Oncologia in Milan, agrees. 'This will allow me to have, for five years, the amount of money that I need to do my work.' She will be researching anti-cancer immune responses in the gut.

Most of the cancer winners will invest in new staff, either expanding their groups with post-docs, PhD students or technicians, or changing the balance from PhDs to post-docs. Several say they will expand their facilities or buy new equipment, while meeting the costs of animals and reagents is frequently cited as a decisive impact of the grant.

Some say the effect is to allow their work to proceed much more quickly, while a few say that without the ERC grant their projects would not have gone ahead.

'I wouldn't have been able to launch such ambitious approaches, new approaches, risky approaches without the grant,' says Johanna Ivaska of VTT, the Technical Research Centre of Finland, in Turku, who works on cancer signasones. 'I couldn't have afforded the reagents and also without more long-term funding you have to be more worried about quickly publishable results.'

Martin Bergö, of Sahlgrenska University Hospital in Göteborg, is not so sure. 'For me, and I think for a lot of the other people who got grants, it's more that it allows the research to happen faster. If it wouldn't have happened at all without the grant, I don't think you would have got the grant.' His project looks at the role of CAAX proteins in tumour development.

The next round of starting grants will be announced in the summer of 2008, with the expectation that the ERC will tighten up the eligibility requirements to limit demand. Meanwhile a further ERC funding scheme, for more experienced researchers, is currently assessing its first round of applications.

Ian Mundell
Brussels

Processed food and breast cancer risk

Two French groups have found that raised serum levels of trans fatty acids nearly doubles the risk of breast cancer. Researchers from INSERM (Institut national de la santé et de la recherche médicale) and Institut Gustave Roussy collaborated to examine data from EPIC, a large European study co-ordinated by the International Agency for Research on Cancer (IARC).

The study was conducted on the E3N cohort of French women. The women, approximately 100,000 in all, were born between 1925 and 1950, and have been followed up since 1990.

Data on lifestyle factors such as diet and hormonal treatments, and health status, has been collected by self-administered questionnaire every other year since 1990. These data were complemented by biological measurements, obtained for 25,000 volunteers, from a blood samples taken between 1995 and 1998.

'WE RECOMMEND LIMITING CONSUMPTION OF PROCESSED FOODS'

Scientists assayed various biomarkers of diet in the blood. They compared serum fatty acid levels among women diagnosed with breast cancer after blood sampling; with those of breast cancer-free controls.

Women with elevated serum levels of trans fatty acids had almost twice the risk of developing breast cancer, compared to women with lowest levels (*Am J Epidemiol 2008 doi: 10.1093/aje/kwn069*). 'At this stage, we can only recommend limiting the consumption of processed foods, the source of industrially-produced trans fatty acid,' the authors wrote.

The study failed to find a protective effect of omega-3 fatty acids from fish on breast cancer risk. This effect has been clearly demonstrated in Asian countries, where fish consumption is much higher than in Europe or in North America. But the highly-powered French study did not find a protective effect 'probably due to considerably lower per-capita consumption of fish', the researchers found.

Risk of second cancer after non-Hodgkin's lymphoma

Survivors of non-Hodgkin's lymphoma (NHL) are 1.65 times more likely to develop other cancers than the general population who have never had NHL, say German and Swedish researchers. They found that the younger the patient at diagnosis, the higher the risk of developing subsequent secondary cancers.

Researchers from the German Cancer Research Centre, Heidelberg, Germany, the Karolinska Institute, Sweden, and Norrlands University Hospital, Umea, Sweden, identified 28,131 people from a wide age range, who were diagnosed with primary NHL. They were followed to see if they developed a second primary cancer.

They found an increased risk in 16 of the 25 most common solid tumours. The highest risk observed was for spinal meningioma (standard incidence ration SIR = 40.8), followed by cancers in the nervous system excluding the brain (18.1).

The overall SIR for solid tumours declined with increasing age at diagnosis. The risk was 4.52 times that of the normal population for people diagnosed with NHL below the age of 20. This dropped to 3.03 for those diagnosed between 20 and 39 years, and to 1.59 for those between 40 and 49 years (*J Clin Oncol 2008;**26**:1850–7*).

The authors say the results provide valuable insights into the carcinogenic process: 'The initially high relative risks in young patients probably reflect the sensitivity of the growing organism to an aggressive and potentially carcinogenic therapy.'

The only decreased risk was observed for endometrial cancer, which was half as frequent among NHL survivors as among the general population. It could be that the castrating effects of NHL therapy explain reductions in risk of this hormone-sensitive tumour, the researchers wrote.

The tumour tool is largest 21 to 30 years after diagnosis, which has implications for the timing of medical surveillance schemes. 'Longer follow-up of patients will be needed to fully characterise the long-term effects of NHL therapy,' the authors conclude.

New guidelines on extravasation management

NEW guidelines on the management of extravasation were launched by the European Oncology Nursing Society (EONS) at its 6th Spring Convention (Geneva, Switzerland; 27–29 March 2008).

Leading oncology nurses who helped to draw up the guidelines hope that they will create a consistent approach across Europe to managing extravasation and help to destigmatise nurses' experience of the condition in clinical practice.

Speaking at the EONS Spring Convention, Yvonne Wengström, chair of the guidelines task force, said: 'These guidelines are much needed because extravasation is under-managed in many European countries, partly because most nurses do not receive specific training in this area.'

Wengström (University of Stirling, UK), Past-President of EONS, said the 'very practical guidelines' would 'help to create a consistent approach to management and support nurses who may experience extravasation'. Guideline task force member Helen Roe, chair of the UK Oncology Nursing Society (UKONS) Chemotherapy Forum, agreed: 'These guidelines may help to destigmatise this issue. I am amazed when experienced colleagues say they have never seen an incident of extravasation. The guidelines may give colleagues permission to talk about this.'

Extravasation is estimated to occur in 0.1% to 1% of all anthracyline treatments.

The guidelines are available for download from the EONS website: http://www.cancerworld.org/CancerWorld/getStaticModFile.aspx?id=1987. They bring together information on the recognition, diagnosis and prevention of extravasation in cancer therapy and highlight the management strategies for vesicant, irritant and non-vesicant extravasation. They also include guidance on the use of antidotes.

Rhonda Siddall was sponsored to attend the meeting by TopoTarget A/S.

PODIUM

Cross-over trials 'dilute the data base'

*Jonas Bergh (Karolinska Institutet, Stockholm, Sweden) is professor of clinical and molecular oncology, and a member of the Oncology Scientific Advisory Group for the European Medicines Agency, EMEA. He personally has concerns regarding early-interim analyses and cross-over designs (see also EJC 2008;**44**(7):972–7).*

What is the positive side of a cross-over trial?

Cross-over trials typically randomise patients to receive either experimental therapy or best supportive care/standard therapy. At the time of failure of therapy, patients are offered the treatment in the other arm. So potentially patients all receive the experimental therapy either at the time of randomisation or when they fail on best supportive care/standard therapy. All patients therefore receive reasonably good therapy and it may better address the ethical concerns for the individual patient.

So what is the problem?

Cross-over studies dilute the effect of the experimental therapy because potentially all patients receive it. Surrogate markers such as response rate, tumour shrinkage or lack of any new lesions, may reveal the efficacy of the drug, but you often do not get strong data on the hard endpoint of overall survival.

It presents an ethical dilemma regarding forthcoming patients. It is important that therapies offered to patients are well-described and well-evaluated. Individual patients should always receive the best treatments available. But where the initial study on a drug had a cross-over design, we may always be left with uncertainty over whether a drug is as good as is believed.

Has this happened?

Docetaxel was developed in the 1990s and tested in advanced breast cancer in two phase III studies. The studies demonstrated similar efficacy in terms of tumour shrinkage, and time to progression but only the non-cross-over study (*JCO 1999;**17**:1413–24*) found a significant survival gain. I participated in the cross-over study (*EJC 1999;**35**:1194–201*) which did not find the survival gain, but demonstrated the other efficacy parameters to be similar. We looked at the studies together and explained why the cross-over study did not find the survival gain. But without the non-cross-over study, the data on that drug would have been considered to be weaker.

Is the cross-over design valid?

It is valid from the point of view of an ethical patient study. But where we have a new drug, we have to find out whether it works. If, we think the combination of a new tyrosine kinase inhibitor with a cytotoxic agent might be better than the cytotoxic agent alone, we really have to find out. The combination arm may be more toxic and we need to know whether the toxicity is worthwhile; it is reasonable to look at a hard endpoint. In the long run, we must strive to have solid data.

A similar problem arises from large studies with planned early interim analyses. If you're comparing an experimental drug versus no therapy, and a routine early test for efficacy is positive, the study is closed and patients in the non-treatment arm are offered the agent. The chance to establish the efficacy of the drug is lost forever.

Do licensing bodies look on cross-over trials more favourably than funding bodies?

We have to be realistic, some funding bodies and societies are afraid of soaring health costs. The upfront costs some compounds (they may in the end be very cost-effective) is one reason why we look for hard data on their efficacy, because they are often not particularly toxic. So after trastuzumab was approved as adjuvant therapy in the US and Europe, some funding bodies took a long time to pass it because trastuzumab is associated with marked costs; the toxicity and safety issues were not disturbing.

Is there a danger we'll have no solid evidence base in future?

No, but we have to be aware about strategies, especially if we in the next step run non-inferiority trials. If one drug's reputation is established on loose ground, then, when companies conduct non-inferiority trials, all they will have to prove is that the new agent is not worse than something which may not work anyway. It is very harmful.

Are you saying we should not do cross over trials?

The fewer cross over trials we do, the more solid the data. In principle, it would be much better to have no cross over studies, just as, in principle, efficacy interim analysis should be "forbidden", especially in studies of metastatic disease. But there has to be a balance. It's easier to do a non cross over study if you know very little about the drug you are studying. If there are many phase II studies suggesting that a drug is interesting, it is more difficult to insist on a best supportive care arm. There's a more difficult ethical dimension if you know more.

It's a balance of patients', physicians' and society's requirements, but all clinical trials are run according to the declaration of Helsinki, which clearly states that a patient's interests always take precedent over the interests of science or of society.

Helen Saul