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FECS–*EJC* Awards for best ECCO-12 Abstracts

A study which has changed standard radiotherapy practice in Denmark won first prize for the best abstract and presentation at ECCO-12 (Copenhagen 21–25 September 2003). The joint FECS–*EJC* Award was presented at a FECS Presidential Session at the conference.

The judging panel was comprised of Professor Bill Gullick, FECS President, Professor John Smyth, Editor-in-Chief of *EJC*, and Giel Vaessen, Chair of the ECCO-12 Nursing Committee. Professor Jens Overgaard, Chair of the Scientific Committee, stepped down from the panel because he led one of the short-listed research papers.

Dr Cai Grau (Aarhus University Hospital, Denmark) presented the winning study: the final results of the Danish Head and Neck Cancer Study Group trial (DAHANCA 6&7). It demonstrated that an accelerated radiotherapy schedule was superior to conventional fractionation (*EJC Supplements* 2003, **1**(5), #1065; *The Lancet* 2003, **362**, 933–940).

Dr Cai Grau and Professor Bill Gullick

Patients with squamous-cell carcinoma of the head and neck-1476 in all-were randomised to receive either five or six fractions of radiotherapy per week. They received the same total dose and fraction number. Five-year loco-regional control rates were 70% in the group receiving the accelerated schedule, compared with 60% in the conventional treatment group. Disease-specific survival was also better at 73% versus 66%, but there was no significant difference in overall survival.

Acute toxicity was worse in the accelerated group, particularly mucositis, but the effect was transient and healed within 2 months. "Treatment with 6 fractions per week is superior to conventional fractionation," said Dr Grau. It is now standard treatment in Denmark. The principle of giving the same dose over shorter periods of time "can probably be applied to other trials," he said.

In the discussion, he was asked whether treatment could be extended to seven fractions per week. Dr Grau replied that this had been tried in a Polish trial, but there is a narrow therapeutic window before the toleration level of the mucosa is reached. It can lead to severe acute reactions that do not heal.

Second prize was awarded to the paper presented by Professor Alex Eggermont on the value of interferon-alpha2b in the treatment of patients with stage IIB-III melanoma. Previous studies have shown little benefit, but researchers from the EORTC set up the largest ever adjuvant chemotherapy trial (EORTC 18952) to establish whether alternate treatment schedules were active.

The study included 1388 patients, who all received intermediate doses of IFN-alpha2b over 4 weeks and were then randomised to either 10MU 3 times-weekly for a year; 5MU, 3 times-weekly for 2 years; or observation (*EJC Supplements* 2003, **1**(5), #1067).

Stage IIB patients given the extended treatment over 2 years showed a non-significant improvement compared with the observation group in terms of distant metastases-free interval (DMFI). However, there was no difference for the stage III patients. The 1-year treatment had no effect at any stage.

Overall, DMFI at 4 years in the 2-year treatment group was 7.2% superior to that in the observation arm. Toxicity was moderate, but there

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EJC News is compiled by:
Helen Saul
Tel.: +44 (0)1865 843340
Fax: +44 (0)1865 843965
E-mail address: h.saul@elsevier.co.uk

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New ATAC data provides reassurance on fracture rates

The latest data from the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial provide reassurance on the risk of fracture associated with anastrozole (*EJC Supplements* 2003, **1**(5), #676). A highly significant increase in fractures among women in the anastrozole arm has been shown previously; the latest results show that the relative risk of fracture in these women appears to stabilise with time, said Professor Tony Howell (Christie Hospital, Manchester, UK), Chairman of the ATAC Steering Committee.

The ATAC trial is a multicentre, randomised, double blind trial in 21 countries, including 9366 postmenopausal women with early breast cancer. The combined treatment arm was shown to be inferior to tamoxifen and has been stopped.

At 33 months, there was an absolute difference in disease-free survival of 1.8%, in favour of anastrozole. This widened to 2.6% in follow-up at 47 months. Overall survival data should become available in 2004 and are due to be presented at the San Antonio conference that year.

Risk of bone fractures has been a concern with anastrozole because of the profound oestrogen deprivation it causes. Tamoxifen, by contrast, has a mildly positive effect on bone density.

After a median of 31 months of treatment, the incidence of fractures was nearly 60% greater in the anastrozole arm. A similar difference was seen at 37 months but, at the most recent, 48-month follow-up, the increase in risk was down to 34% higher for anastrozole.

The maximum difference between the two treatments was seen at 18 and 24 months but 6-monthly fracture rates appear to reach a plateau after 24 months and then stabilise. Professor Howell said "We have no idea why the fracture rate stabilises but clearly this is important for patients. It is possible that it will climb again but since the curves have been parallel for some time this seems unlikely."

Bone density measurements will be taken at the end of the trial, he said.

Endometrial cancer and cognitive decline

Anastrozole may have other, more positive, side effects, Professor Howell said, and may protect against endometrial cancer and cognitive decline (*EJC Supplements* 2003, **1**(5), #767).

In the tamoxifen prevention trials, which compared tamoxifen with placebo, women on tamoxifen had a 2.4-fold increase in their risk of endometrial cancer. In the ATAC trial, women on tamoxifen were at 5 times the risk of those on anastrozole. This suggests that anastrozole may be protective, said Professor Howell. Results from IBIS-11, which compares anastrozole with placebo in prevention, will be needed to confirm this, he said.

Tamoxifen was thought to help cognitive function, and there has been concern that the decreasing oestrogen levels seen with aromatase inhibitors (AIs) such as anastrozole might increase risk of dementia. However, the results of the Women's Health Initiative Memory Study (WHIMS) comparing combined hormone replacement therapy (HRT) with placebo for up to 4 years suggested that HRT may increase risk of dementia and cognitive decline. This suggests a decrease in oestradiol might in fact be protective. This is speculation, Professor Howell said, and a study is underway in 700 women recruited from the main IBIS II trial to examine the question.

Emma Cannell

FECS–*EJC* Awards for best ECCO-12 Abstracts

(continued from previous page)

was no survival advantage in any of the groups studied. Professor Eggermont concluded, "We still have no standard treatment for melanoma in the adjuvant setting."

In joint third place was a presentation by Mr M. Johnson (King's College, London) on a tool to develop clinical competencies in nursing education (*EJC Supplements* 2003, **1**(5), #1064) This tool "introduces a reflective element and reduces the subjectivity of the process," Mr. Johnson said. He said it had been significant in expediting learning and establishing guiding principles for developing the necessary competencies.

Professor Bengt Glimelius (University Hospital, Uppsala) presented the other third-placed paper which demonstrated survival gain for patients with stage III colon given 5-fluorouracil/levamisole. Combined data from Nordic trials found an approximate 8% survival benefit for those receiving chemotherapy after surgery, compared with surgery alone. He said the survival gain is "considered clinically relevant by the profession and most patients" (*EJC Supplements* 2003, **1**(5), #1066).

Patients starting treatment more than 56 days after surgery had no apparent benefit whereas those treated earlier did. There was also a reduced benefit in those treated for less than 6 months. No meaningful benefit was detected in colon stage II or rectal cancer stages II and III.

Emma Cannell

Erratum

The story in *EJC News* (*EJC* 2003, **39**(14), 1970) on FECS' New Board of Directors should, of course, have included a photograph of FECS' new President, Professor Harry Bartelink. Our apologies to all concerned.

Harry Bartelink

EUROFILE

Protests mount at EU funding decision

Members of national and European Parliaments have joined the protest against the European Commissions Public Health Directorate (DG-Sanco)'s decision to exclude major cancer projects from its most recent funding round. The decision as it stands could lead to the demise of European Networks for Breast Cancer (EBCN), Cervical Cancer Screening (ECCSN), Cancer Registries (ENCR) and the European Prospective Investigation into Cancer and Nutrition (EPIC).

Mr David Byrne, EU Commissioner for Health and Consumer Protection, will take the final decision. Belgian Minister of Social Affairs and Public Health, Mr Rudy Demotte, wrote to him pointing out that, in the past, these networks "were considered to be first order priorities within the EU and were labelled as scientifically outstanding.

"WHAT IS HAPPENING IS REALLY SILLY"

"The Belgian Government insists on a revision of the primary decision of DG Sanco in order to maintain the level of inter-European exchange of expertise in the field of cancer control surveillance in current and new member states."

Mrs Ulla Schmidt, German Minister of Health and Social Affairs, urged Commissioner Byrne "to strive to obtain continued EU funding" for the projects and said that "the further positive effects which could be expected from such successfully initiated projects — particularly in light of the previous expenditure — will otherwise be lost."

Mrs Karin Jöns is German Member of European Parliament (MEP), President of Europa Donna in Germany, Chair of the European Parliamentary Group on breast cancer and drafts person of the report "Breast Cancer in the European Union", adopted by the European Parliament in June 2003. She has written to the Commissioner twice, drawing attention both to recommendations in the European Code against Cancer on cancer screening, and reminding him of his own previous statements in support of ENCR and EPIC. She has not until now wanted to speak publicly. "I did not put out a press release because I hoped we could find a solution in a diplomatic manner. That is always the best way. But my patience is running out" she said.

She believes that it is still possible for the Networks to receive funding in the 2003 round, but says, "It's a question of willingness. Do they politically want this?"

The funding decisions were the first to be made since the end of the "Europe against Cancer" programme, which ran from the mid-1980s and ring fenced money for cancer projects. Projects applying for funding in the current 2003–2008 Public Health programme will have to compete for funding against those in other disease areas.

As a consequence, applications are no longer reviewed by a panel of independent cancer specialists. Dr Elio Riboli, European coordinator of EPIC, said the applications this time were evaluated only by regular staff at the European Commission, who overturned the previous assessments given to these projects. "EPIC, ENCR, ACCIS and Eurocare were always given very high evaluations. They were top priority activities for the EC in cancer because of the clear public health interest. We understand now that the public health programme is more intervention-oriented. But on the other hand, one must feed interventions with strong European data. The networks provide information on cancer incidence, determinants of risk and so on. The more you know about the risk factors for disease, the more effective your interventions are likely to be. That was our philosophy."

"MY PATIENCE IS RUNNING OUT."

One cancer project, Eurochip, coordinated by Dr Andrea Micheli in Milan, was funded. It synthesises information on oncology indicators and has an input from other projects including ENCR, ACCIS and EUROCARE, and directly from various countries. It is not clear how this project will be carried out with the allocated money, given that much of its source material is likely to be unavailable in an appropriate, comparative form.

Dr Jan Willem Coebergh (Erasmus University Medical School, Rotterdam), is *EJC*'s Epidemiology and Prevention Editor, and a member of several steering committees of the affected projects. He said, "I am really surprised by the decision, and the arbitrary nature of the procedures for making it. What is happening is really silly because the momentum of the collaborative effort — which is a marked and extra workload for many people — will be lost. So much quality control needs to be done to achieve comparability."

He said that the networks had been told to look for money under Framework 6. "We spent an enormous amount of time applying as a Network of Excellence with additional requirements in molecular pathology. But it demands that we are a network only of centres of excellence. The variation in incidence and survival throughout Europe means that broad coverage is needed from all countries and as a result, some of our partners are excellent, others are not. So we were not eligible. It was a tremendous amount of work and we are left feeling misjudged."

The timing of the decision is extraordinary, given that the European Council is to recommend that all member states organise screening programmes for breast, cervical and colorectal cancer. This is due to be discussed by national Ministers of Health at a meeting in Brussels in December 2003, and will apply also to the 10 countries about to join the EU. The *EJC*

Continued overleaf

Clinical trials 'in danger'

The true value of new and existing drugs may never be discovered if the European Union (EU)'s Clinical Trials Directive is implemented as it stands, according to Professor Jaap Verweij (Erasmus Medical Centre, Rotterdam), *EJC*'s Clinical Oncology Editor. The Directive, which was drawn up with industry-sponsored research in mind, has failed to take academic research into account, he said.

Speaking at a press conference at ECCO-12, he praised the work done by the pharmaceutical industry, but said, "It stops at the moment a drug is registered, while the true value and role of a new drug is usually determined in academic clinical research."

Research into rare cancers will suffer disproportionately. Gastrointestinal stromal tumour (GIST), for example, affects only 5000 people a year in the whole of Europe, including Russia. Glivec, which was registered in 2001 for the treatment of chronic myeloid leukaemia, was tested by the academic community in GIST, and registered in 2002 after only 2 years based on 147 patients. "At this point, Novartis was happy because the drug was on the market but the academic community was interested in further testing because, while we knew 400 mg daily was active, we also knew we could give 800 mg without too many problems."

International studies were set up by the academic community in Europe and the States, comparing 400 mg given once or twice daily. Within a year, 946 patients were recruited in the EORTC study, and maximum follow up is currently just over 24 months. The higher dose adds approximately 6 months to progression-free survival, which is highly significant.

Professor Verweij said, "Without this trial we would never have known that there is a difference in progression-free survival, in favour of the higher dose. No pharmaceutical company would ever be interested in a disease that is so rare. This could only come out of an academic trial."

Françoise Meunier, Director-General of the European Organisation for Research and Treatment of Cancer (EORTC), said the Directive was aimed at facilitating new drug development in Europe and was drawn up by DG-Enterprise, rather than DG-Research. In fact, it covers all clinical research and a key problem is the Directive's requirement for a 'trial sponsor' to take on all responsibility for trials, including legal responsibility and insurance coverage, required by ethics committees.

The GIST trial described by Professor Verweij was coordinated by EORTC and involved 56 centres in 17 countries. Anyone sponsoring such a trial in future would have to negotiate 17 different insurance policies for trial recruits, as there is no harmonisation between requirements imposed by different Member States. The Directive will increase costs to the sponsor by a factor of 4–6, and at least double the administrative burden of trials, said Dr Meunier. The pharmaceutical industry has structures to deal with the new requirements, but academia does not.

Nor does the Directive anticipate the types of question asked in academic research. "We are bound to the same rules for new drugs as for drugs which have been on the market for 20 years. If we wanted to evaluate the use of aspirin in colorectal cancer — which is not so stupid — we would have to report the serious adverse effects of aspirin, because the trial would be covered by this Directive," she said.

EU funding *continued*

Special Issue on "Cervical Cancer Screening in the European Union" (*EJC* 2000, **36**, 17 and comment *EJC* 2002, **38**, 321–326) "showed a fantastic variation in screening procedures with little relation to impact except in a few countries with organised screening programmes," Dr Coebergh said. "Evaluative and collaborative work is necessary to persuade people in the various countries to do the right things. Otherwise there is a tremendous waste of money."

Dr Marc Arbyn, epidemiologist at Scientific Institute of Public Health (Brussels) and a member of ECCSN, stressed the importance of rigorous guidelines. "The existing guidelines for cervical cancer screening were published in 1993. Since then, a lot of new technologies have been developed and there is concern about how to use them; and whether they should be used in primary or secondary screening. We are undertaking meta-analyses and systematic reviews to establish whether the evidence supports their use. The public and health professionals are waiting for updated guidelines, but we cannot produce them without financial support, and a lot of the work already undertaken will be lost."

He said that in colorectal cancer, the situation is even worse, since there are no guidelines in existence at all. "It is extremely difficult for a country with a liberally organised health care system with established opportunistic over-screening (such as in France, Belgium, Germany, Austria, Luxembourg and the more south-European countries) to move to organised screening. European guidelines and exchange of experience on implementation of those guidelines among EU member states are essential to facilitate the establishment of high-quality screening at adequate intervals. The adherence of new member states to the EU makes the EU networks for cancer screening and surveillance even more necessary."

The funding decisions appear to have been based on a desire by the Commission to move to funding "horizontal" projects which touch on a number of disease areas. Dr Arbyn: "It might be good to give more priority to "horizontal" projects but you can't use it to answer all questions in public health. You have to use both horizontal and vertical approaches; and look for the optimal way to target public health priorities. If you want information on trends in incidence, outcome and mortality, and how these trends are influenced by screening, you need a vertical component."

Those affected by the decision now say there is a big risk that on-going collaborations will fall apart. If that happens, even if new initiaves are taken, it will take years to build them up again.

PODIUM

The Lost Tribe: Who cares?

Dr Jon Pritchard is Consultant Paediatric Oncologist at Royal Hospital for Sick Children (Edinburgh, UK) and an editor of EJC. He is a founder member of the Nikolas Symposium, and of the International Society of Paediatric Oncology (SIOP)'s Liver Tumour Study Group, and a member of numerous national and international committees and working groups.

Dr Jon Pritchard

How much similarity is there between adult and paediatric cancers?
More than half of all paediatric cancers also appear in adults: leukaemias and lymphomas — Hodgkin's and non-Hodgkin's — and sarcomas of soft tissue and of bone. Conversely, adult carcinomas such as of the kidney, liver, and nasopharynx, are all found in children, albeit rarely.

How much interaction is there between the specialists?
Not enough. I don't know of a core curriculum anywhere in the world where adult and paediatric specialists learn together about cancer biology, epidemiology, imaging, pathology, the basic principles of cancer. And after all, we're all dealing with a malignant process based on the same biological dysfunction.

Paediatric and adult practitioners tend to have separate meetings. It's only in the last few years, including particularly at this 12th ECCO meeting (Copenhagen, 21–25th September 2003) and at ASCO (American Society for Clinical Oncology), that a few paediatric and adult oncologists have got together in the same room to discuss mutually important problems,

Have there been tangible benefits so far?
We're at the beginning of this. Plans for adult and paediatric practitioners to work together in Europe on germ cell and liver tumours were proposed at ECCO-12 sessions.

Does the lack of interaction have an impact on patients?
Very directly. You can have the ironic situation where a 13 year old patient is treated according to an adult protocol in an adult ward in a general hospital; a 15 year old with the same tumour may be treated with a completely different approach in a paediatric ward. Yet it's the same problem, divided arbitrarily by the age of the patient.

There is a 'lost tribe' between adult and childhood and few custom-designed facilities for the teenagers or young adults (or TYAs). Individual patients need to be fitted into the milieu that is best for them, taking into account the quality of care, involvement in clinical trials, but also the design and style of the unit.

What can paediatric oncologists teach their colleagues in the adult oncology world?
The multidisciplinary approach is more mature in paediatric settings. It may have been around for 10 or 15 years in adults but it has been a standard part of the paediatric approach for 30 to 40 years.

Why is that?
The rarity of paediatric cancer has meant we have had to form collaborative groups and develop common protocols. At least 60–70% of children in Western Europe are on protocols and some are on 2, 3 or 4. Less than 5% of adults with cancer, overall, are on protocols, but where there is cross-over between adult and paediatric carers, it is more likely that mutually discussed and evolved protocols will be available for patients in that age group.

We have good structures for long-term follow-up of children which are now more applicable to adult practice, as survival slowly but steadily improves.

What can adult practitioners teach the paediatric community?
Since 99% of cancers occur in adults, the critical mass of work in adult cancer is proportionately much greater in the basic sciences, imaging, pathology and in the clinic. The adult community is also rapidly accumulating experience with novel targeted therapies. Paediatric oncology is a relatively small community and is not sufficiently stretched scientifically or exposed to new ideas.

Now that we can cure about 75% of all paediatric patients, for life, the remaining hard core of paediatric problems present the same as adult cancers do: drug or radiation resistance, or unresectability. We're dealing with the same problems.

What is the aim of *EJC*'s Special Issue on Adolescents?
To highlight the plight of this 'lost tribe' between paediatric and adult oncology, and their need for special consideration, not only as adolescents learning how to cope with the pleasures and traumas of adult life, but also with their disease. Providing special facilities for this age group is not just an option, it's necessary. It will be the norm in 20 years' time.
We hope to raise awareness and encourage others to develop and put forward their own ideas. We want to highlight the spectrum and epidemiology of cancers suffered by adolescents, to focus attention on diagnostics, treatment, the treatment setting and their follow-up as they move into adult life. Their therapeutic requirements, and wishes regarding their management, are different from those of children or of mature adults. We want to help the 'Lost Tribe' find its 'Home Land'.

EJC ***39*** *(18), will be a Special Issue on 'Care of the Adolescent with Cancer'. Guest editors: Maria Michelagnoli, Jon Pritchard, Marianne Phillips.*