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NEWS...NEWS...NEWS

Cancer care 'must be uniform' across Europe

Mortality rates across Europe vary and we need to change this, said cancer survivor Ms. Karin Jöns (German MEP and Chair of EuropaDonna Germany), speaking at 29th ESMO conference (Vienna, Austria, 29th October –2nd November, 2004). Unfortunately, for some Member States it ''is more important to build roads than implement screening programmes'', she said.

The European Council recommends women aged 50–69 years are screened for breast cancer; those aged 25 years and over, for cervical cancer; and both men and women aged 50 years and over, for colorectal cancer. These recommendations are evidence-based, she said, and delegates need to put pressure on their national health services to implement these programmes.

The EU has set aside 500 million Euros to fund cancer research and early detection programmes for the next 5 years. It is also promoting research, health education and data collection, she said. Guidelines for best treatment have been set, for example, for breast cancer, but these are not always adhered to. ESMO announced a set of minimum clinical evidence-based guidelines at the meeting to ensure a common standard of care. ''Patients in Europe should have a similar access to cancer diagnostics and treatment'', said Professor Rolf Stahel (Chair of the ESMO Guidelines Taskforce) announcing these recommendations. We hope they ''serve as tools for physicians''.

Ms Karin Jöns

Ms. Jöns said that pressure needs to be exerted on Member States to encourage them to tow the line. ''Europe often does much more to support patients than their own government does''. The EU will provide funding for palliative and supportive care in 2005, she said. European and national policies need to be closely interlinked. ''Only by pooling resources will we be able to prevent patient suffering''.

Dr. Heinz Ludwig (Chairman of the ESMO Patient Seminar Working Group) said, ''We believe in patient power…. It depends on us. It's our society, we have to shape it''. Ms. Jöns concluded, ''What do people want? Better roads or modern health structures?''

Emma Cannell
Vienna

For the ESMO minimum clinical guidelines, see www.esmo.org/reference/reference_guidelines.htm.

Call for increased investment in radiotherapy

European health ministries were urged to allocate sufficient resources to ensure all eligible patients receive radiotherapy 'in a timely manner'. Professor Michael Baumann (UK Carl Gustav Carus, Dresden, Germany), said, 'Urgent action needs to be taken if all patients are to have equal access to optimal care'.

Speaking in Amsterdam at the 23rd Meeting of European Society for Therapeutic Radiation and Oncology (ESTRO, 24–28th October, 2004), he said that more than half of all cancer patients now receive radiotherapy, but that treatment capacity is exceeded in many countries, making access to treatment a major problem. 'For tumours to grow beyond a curable size takes weeks or even months. But in some countries waiting times of this length are not uncommon', he said.

Few EU countries have enough linear accelerators. In the UK and the Netherlands, increased investment in equipment and training of staff had resulted in substantial improvements. 'Recent figures show improved cure rates across a range of cancers in the UK which is, in part, due to improved availability and access to treatment'.

'Overall, though, in many countries of the European Union, a high proportion of patients requiring radiotherapy receive their treatment not within what oncologists would agree is an acceptable time', said Professor Baumann.

'On behalf of the 6000 European radiation oncologists that ESTRO represents, we would urge European health ministries to move quickly to allocate sufficient resources to make sure that all patients eligible for radiotherapy are treated in a timely manner, according to accepted guidelines,' he concluded. 'It is critical that funds are allocated to ensure that patients receive the best care possible and the best opportunity of surviving their disease.'

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Childhood vaccines 'protect against melanoma'

Vaccination with either BCG (Bacille–Calmette–Guérin) or vaccinia may protect against the development of melanoma, and improve survival, say researchers. Two key papers, published in this edition of *EJC* shed new light on the extent of their effect.

The first, from the EORTC's Melanoma Cooperative Group (*EJC, this issue p. 118*), followed 542 patients in 7 countries for a mean of 5 years. It demonstrated that prior vaccination with vaccinia (in early life) significantly prolonged the survival of patients with malignant melanoma after initial surgery. It halved the risk of death at 5 years. BCG vaccination had a similar, though weaker, effect.

The study adds to increasing evidence that infections and vaccinations play an important role in the normal maturation of the immune system. The improvement in prognosis in the previously vaccinated patients ''was remarkable'', the researchers said, ''and calls for further studies in relation to melanoma and other cancers''.

A re-introduction of mass vaccinia vaccination is unlikely because of occasional adverse effects, but BCG might be considered, because of the global rise in tuberculosis. Alternatively, determination of the underlying immunological mechanisms could lead to the development of a designer vaccine against melanoma and eventually, other cancers, the group concludes.

The second paper (*EJC, this issue p. 104*) notes that not being vaccinated with either BCG or vaccinia is a new risk indicator for melanoma. The researchers propose that the vaccinations induce or enhance immune surveillance for melanoma. The possible causative role of the HERV-K-MEL antigen is described.

An editorial comment (*EJC, this issue p. 12*) says the ''challenging and exciting observations'' add to the growing conviction that the human body is not defenceless against cancer. The studies provide hope that simple vaccination strategies and effective immunotherapeutic strategies against established cancers ''may not be far away''.

European Society for Medical Oncology, Highlights from 29th Meeting, Vienna, Austria, 29th October–2nd November, 2004

Reports by Emma Cannell, EJC Scientific Editor

Vaccine for lung cancer?

Patients with non-small cell lung cancer (NSCLC) survive 4.4 months longer on vaccine treatment than those treated with best supportive care (BSC). Lead investigator Dr. Charles Butts (Cross Cancer Institute, Edmonton, Canada) said the increase in survival ''is a notable period of time for such an aggressive disease as NSCLC''.

The vaccine (L-BLP25) targets a sugar-protein molecule called MUC1 which is abnormal on many cancer cells: the protein backbone is exposed making it an attractive target. L-BLP25 tags the abnormal cells to help the patient's immune system recognise and eliminate them. The vaccine is packaged in liposomal components to improve delivery to its target (*Annals of Oncology* (2004), **15**, Suppl 3, abstract# 3).

The phase II trial included 171 stage IIIb and IV patients from 17 centres. They had stable disease or had responded to previous treatment. They were randomised to receive BSC with or without the vaccine. BSC consisted of second-line chemotherapy, palliative radiotherapy or other treatments, as indicated by the investigators.

Patients in the vaccine group had a median survival rate of 17.4 months compared with 13 months for the BSC controls. This survival benefit for vaccine-treated patients was even more pronounced for those with stage IIIb cancer, localised to the lung. These patients showed 2-year survival rates of 60% compared with 36.7% for controls. Further, in this subgroup, the median survival has not yet been reached whereas it is 13.3 months for controls.

An update from this trial was expected in December 2004 and Dr. Butts said he hoped that Phase III studies would be launched in 2005. ''It will change the paradigm for how we treat patients as there is no current effective immune therapy for lung cancer'', he said. Dr. Bernhard Ehmer, Vice President and Head of Merck's Oncology Business Area, agreed: ''These phase II data are very encouraging in terms of offering a potentially meaningful benefit to patients in an area where so little progress has been realised despite many years of work''.

Predicting resistance to Herceptin

An assay measuring protein complexes provides clues to Herceptin resistance, US researchers announced. ''Early studies are extremely promising'', said lead investigator Dr. Sharat Singh (Aclara Biosciences, California, USA).

About 30% of breast cancer patients over express the tyrosine kinase receptor, erbB2 (her2/neu) and these patients have poor survival rates. Herceptin, a humanised antibody therapy, targets this receptor and blocks it, stopping cell growth. But about 40% of these patients show resistance to Herceptin for reasons that are unclear. Other members of the erbB receptor family are thought to contribute to disease progression and Dr. Singh proposed that levels of these other receptors might predict resistance in patients.

His group used an antibody-based e-Tag™ technology in breast tissue biopsies from 13 patients (*Annals of Oncology* (2004), **15**, Suppl 3, abstract #53). ErbB protein complexes were detected and helped define the active signalling pathways in these tissues. He hypothesised that patients with high levels of heterodimers would show resistance.

Initial results showed that patients with high her3 levels were poor responders, possibly because her3 is a known strong signalling point. Additional studies are underway. Dr. Singh said he hoped that with further validation the technology could be extended to examine other protein targets and help in determining treatment options for patients.

ESMO highlights continued on page 4

EUROFILE

New Constitution promotes science

For the first time, 'scientific and technological progress' has been acknowledged as a formal objective of the EU. The new Constitution, signed at a summit in Rome in October 2004, puts European research on a fresh legal footing.

The Constitution, which has yet to be adopted by individual Member States, contains references that give EU research policy a new and more solid base. ''It does not simply make research a tool for the competitiveness of the EU by promoting applied research, but broadens the Commission's competence, making research a shared competence'', said a spokesperson for DG Research.

Research is mentioned right at the beginning of the new Constitution. The first paragraph of Article 1–3 of the Constitution, which covers the objective of the Union, states: ''The Union works for the sustainable development of Europe based on balanced economic growth, a highly competitive social market economy … It promotes science and technological progress''.

An addition to the original text states that EU research activities 'will pay due respect to the fundamental orientations and choices of the research polices of the Member States'. A separate annex guarantees animal welfare in the context of formulating and implementing research policies.

The European Research Area (ERA), which aims to create a genuine internal market for research and technological development, is referred to specifically: ''The Union shall aim to strengthen its scientific and technological base by achieving a European research area in

'THE EUROPEAN RESEARCH AREA IS A REALITY'

which researchers, scientific knowledge and technology circulate freely, and encourage it to become more competitive, including in its industry, while promoting all the research activities deemed necessary by virtue of other Chapters of the Constitution''. European law will be necessary in order to set it up, the Constitution stipulates.

Former Commissioner Philippe Busquin, a protagonist of the ERA, was also reported to be pushing for a doubling of the EU research budget for the period from 2007 and 2013. If he had his way, funding would double from the current 5–10 billion euro at the beginning of the next decade. Such a figure would represent 10% of public research spending within the EU.

Member States are beginning to lend their support to a collective research capacity. French Research Minister Francis d'Aubert is on the record as saying that EU powers should put European research ahead of national policies. European funding agencies could be set up rapidly if there was enough political will, he said at a conference during the summer, 2004.

'CRITICAL MASS IS TOO OFTEN OVERLOOKED'

''We need Europe, we need European construction because it is the right level'', he said. ''We need the human resources, territory and power. Critical mass is a crucial factor which has been overlooked all too often in favour of network building''.

More recently, though, a British civil servant argued that the ERA had in fact been in place for many years, and simply needed more focus. The ERA was a continuous evolution rather than a new space, said Margaret Dennis (UK Department of Trade and Industry), and the EU should drop the idea that it must be created from the top down. Bottom-up initiatives should be encouraged to bring about the completion of the ERA, but the main focus must be users, she said.

Former Commissioner Busquin and his successor, the Slovenian Janez Potocnik, seem to disagree with this approach. Busquin said recently: 'The concept of a European Research Area that I launched is a reality. It has really become a point of reference in all the Member States, within the scientific community and in industry. That's not bad for starters!' The consequence of this, and of his obtaining a pledge from all EU Heads of State to increase research spending so that it is as close as possible to 3% of GDP by 2010, is that research and innovation are on the political agenda both at European level and in many Member States, he says.

Potocnik showed himself to be a strong supporter of Busquin's vision at his hearing before the Parliament. He clearly pleased the Industry Committee, which also looks after research questions. The chair of the committee, Giles Chichester, said in a letter to Josep Borrell, the Parliament President, that: 'The nominee was perceived as honest, sensitive to the human factor, with excellent communication skills, knowledgeable and well prepared, but also willing to listen and discuss possible points of disagreement'.

'The clear manifestation of his political will in favour of doubling the EU research budget [...] was very positively received. Equally appreciated was his openness to dialogue with the Parliament and his willingness to admit shortcomings in the current Framework Programme and initiate the necessary reforms', continued the assessment.

With this kind of commitment at the top of the Commission and the support of the new Constitution, can we expect to see research take centre stage at European level? If it does not, it would not be because of a lack of will at pan-European level; rather that some Member States want to continue to pull the strings in their own interests. But after so many years of lip service to the need for scientific innovation, the signs for researchers look genuinely encouraging this time.

Mary Rice,
Brussels

Cardiovascular disease in testicular cancer survivors…

Testicular cancer survivors treated with cisplatin may have an increased risk of cardiovascular disease. ''We need to establish good follow-up routines to identify patients at risk'', said lead investigator Dr. Hege Sagstuen (University of Tromsoe, Norway).

Dr Hege Sagstuen

In a large retrospective follow-up study from Norway, Dr Sagstuen's group measured blood pressure and body mass index in 1289 survivors of unilateral testicular cancer (*Annals of Oncology* (2004), **15**, Suppl 3, abstract# 419). Patients were treated between 1980 and 1994 and observed for 5–20 years.

Patients treated with cisplatin had increased blood pressure compared with population controls (n = 2847) and with patients treated by surgery or radiotherapy. The increase was most marked among those who received higher total doses of cisplatin (>850 mg). There was also a higher prevalence of hypertension, again, especially in the higher dose group. The association between treatment and obesity was less clear, with the higher dose group showing a tendency only to be more obese.

Norway has one of the highest incidences of testicular cancer. Patients are generally aged between 25 and 35 years and, as survival rates after treatment are >95%, long-term treatment-associated side-effects are important. Studies have suggested that patients may develop hypertension and obesity as late side-effects of cisplatin, but the data reported are controversial. Dr. Sagstuen's study is one of the largest examining the association of treatment with these risk factors for cardiovascular disease.

''Blood pressure should be measured regularly in these patients and, if elevated, should be treated according to guidelines'', she said. ''Patients should be encouraged to follow a healthy lifestyle''. Dr. Carsten Bokemeyer (University of Tbingen, Germany) agreed: ''We should still search for less toxic, equally effective treatments and we have to alter our focus of follow-up in these patients''.

The mechanism of increased risk is unknown, but according to Dr. Sagstuen, is unrelated to serum testosterone levels. Renal damage associated with cisplatin therapy may be involved, but this is purely speculative, she concluded.

…and breast cancer patients

By contrast, a study in postmenopausal breast cancer patients suggests that longer treatment on tamoxifen may protect patients from developing cardiovascular disease. The Swedish Breast Cancer Group, which reported in 1996 on the superiority of 5 years of tamoxifen over 2 in terms of overall survival, presented new data.

Dr Bo Axel Nordenskjold

The same study found (in 4175 patients) that those receiving 5 years of tamoxifen had a 17% lower death rate from cardiovascular disease and a 31% lower death rate from coronary heart disease than those receiving only 2 years of treatment (*Annals of Oncology* (2004), **15**, Suppl 3, abstract# 206).

''Tamoxifen prevents coronary heart disease. Our data strongly support the use of tamoxifen in the adjuvant treatment of breast cancer patients'', said lead investigator Dr. Bo Axel Nordenskjöld (University Hospital, Linkoping, Sweden). This effect was seen because of the large study size and long follow-up of these patients, he said.

Professor Monica Castiglione (International Breast Cancer Study Group, Bern, Switzerland) said the Scottish Group (who compared tamoxifen given postoperatively versus at relapse) found similarly that use of tamoxifen reduced myocardial infarction.

However, where the Swedish group found no significant increase in thromboembolic events with prolonged use, the Scottish study found tamoxifen was associated with a significantly raised incidence of thromboembolism.

Professor Jan Vermorken (University Hospital, Antwerp, Belgium) said, ''These are important findings and suggest we need to carefully monitor what happens when tamoxifen is replaced by one of the new aromatase inhibitors in the adjuvant setting; not only with respect to unwanted side-effects to the bone and lipid profile, but also with respect to the cardiovascular system''.

ESMO highlights continued from page 2

ESMO recognises centres of excellence in palliative care

ESMO has designated 8 centres of medical excellence in palliative care, in order ''to enhance and promote the care and quality of life of patients'', said Professor Raphael Catane, Chairman of the ESMO Palliative Care Working Group (Sheba Medical Center, Tel Hashomer, Israel).

''Optimal care for patients with advanced cancer requires close integration of oncology and palliative care services. ESMO has established this accreditation programme to encourage excellence with regard to these aspects of cancer care'', he said.

He hoped all cancer centres in Europe would be able to join eventually, and said applications are increasing. The first 8 centres, in Belgium, Ireland, Switzerland, Germany, Italy and the UK, had to meet 13 criteria (*see www.esmo.org/WorkingGroups/designatedCenters.html*). Applicants were recommended by the ESMO National Representatives and approved by the ESMO Executive Committee.

Dr. Nathan Cherny (Shaare Zedek Medical Center, Jerusalem, Israel), said that although ESMO has a policy of minimum standards, the Society's aim in giving such accreditation was to provide an optimal level of care and support for patients.

Benefits include grants for fellows and special subsidies for trainees. Dr. Cherny hopes accredited centres will ''act as a magnet to other people who can take this model back to their own centres''. In the past, patients could experience feelings of abandonment and neglect, particularly when their disease became terminal. ESMO wanted to promote change as this ''was not our philosophy of care as an organisation'', he said.

PODIUM

Cancer centres – unite!

Professor Thomas Tursz, medical oncologist and researcher, is Director of the Institut Gustav-Roussy, France, and President of the French Federation of Comprehensive Anticancer Centres (FNCLCC). His research has focused on virology and immunology in cancer; he pioneered the use of immunotherapy using cytokines and has received numerous prizes for his work. He is Chairman of the Organisation of European Cancer Institutes (OECI).

Professor Thomas Tursz

What does the OECI do?

The OECI has existed for 25 years. It was created by a number of institute directors from various European countries who met to share experiences and discuss cancer centres' strategies. One well-defined aim was to establish links with centres in Eastern Europe, which was quite isolated at the time. But it became more of a private club than a living organisation.

What has changed?

The concept of the comprehensive cancer institute is better and more widely known and the need for exchange and cooperation is becoming much more important. Innovation in cancer research has made the development of translational research extraordinarily important, and this requires cooperation between centres.

What is your vision for OECI?

OECI's goals are multidisciplinarity, global quality and translational research. OECI promotes coherence between disciplines and aims for multidisciplinary working within cancer centres, teamwork in which professionals share competences, technology and expertise. Further, cancer centres have to take on the challenge of caring for patients from diagnosis through to their return to normal life. Oncology is a global discipline involving physical, psychological and social aspects of care. Finally, cancer centres must be an interface between research and the clinic. More than 40% of people with cancer are not cured, and it is a fantastic challenge to translate research into clinical advances.

Why the emphasis on translational research?

Reports of advances in basic research have led to great hope. In practice, cancer treatments change slowly, patients are still dying, and politicians and the public are disappointed. But basic research moves in giant leaps, such as, in the last 20 years, the discovery of genes and oncogenes. It is a bit like Pasteur's discovery of microbes which completely changed the way people thought, classified and considered infectious disease. It took another 60 years for Fleming to discover antibiotics.

Oncology now is probably closer to Fleming than to Pasteur, but we need to be professionally and strategically organised to make sure that the period between discovery and new treatments is as short as possible.

How will OECI contribute to this?

OECI promotes assessment of quality. We are discussing and coming to a consensus on criteria for each aspect of oncology, in collaboration with societies such as ESTRO, ESMO and EORTC. We will need new criteria for evaluating aspects of oncology such as the integration, multidisciplinary working and the impact of translational research on the life of the centre. It is important that criteria are generated by professionals and not superimposed on us by bureaucrats and administrators.

How will you introduce assessment?

OECI is working towards accreditation of its centres. It will define the requirements of a comprehensive cancer centre and they will be assessed. The quality of care offered will be assessed (by validated questionnaire), but also whether the centre is working in a network, sharing data, technology and people. Accreditation will be voluntary at first to develop the model and then adapted to test the model in other centres.

Where will this lead?

To the notion of the comprehensive cancer centre, which houses all the technology necessary to treat a patient and in which basic and clinical research is integrated in a way that leads to translational research. In which there is synergy between specialties.

What barriers do you foresee?

Economics. Centres in Western Europe are subject to enormous financial constraints but they have to ensure that this does not lead to a general decrease in the quality of research. Another problem is variation in the organisation of care. Scandinavian countries have networks; elsewhere there is open competition between centres. But we have a common purpose; we need a consensus on quality across Europe.

Is this a political role?

The organisation of oncology may vary but patients' requirements are similar and OECI is trying to build a coherent system. Europe is a great place to promote high quality care and innovation and the centres together have the critical mass to achieve this, but they need more co-ordination and more sharing of resources. United, they can become an extraordinarily strong political voice for better oncology.

How optimistic are you that this can be achieved?

There is no other way. The solution to oncology does not lie in one country or centre; we have to come to a supernational model. The role of the centre needs to be defined at a European level. In 10 years' time, accreditation of comprehensive cancer centres and a network between them could be a reality.