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New initiatives from ECCO

ECCO, the European CanCer Organisation, is strengthening its commitments both to patients and to the education of cancer professionals. Newly formed groups – the Patient Advisory Committee and the Education Committee – are launching, respectively, web-based Patient Information, and a new eLearning programme.

The Patient Advisory Committee (PAC), chaired by Professor Louis Denis (Oncology Centre, Antwerp, Belgium), aims to establish a dialogue with the ECCO Board. PAC will present the patients' view, advise on how to optimise ECCO's patient-centred activities, and guide ECCO's strategic direction. "The patient shall be centred firmly at the core of all ECCO activities," said Professor Denis.

Effective communication is key to achieving its aims. PAC's new online Patient Information section on the ECCO website will be "an interactive, connective platform for patient-centred action within ECCO", he said. It "will offer a broad selection of innovative, reliable and up-to-date information on cancer related issues, expressly collated to meet the needs of patient advocates and organisations".

'WE HOPE TO INSPIRE ALL STAKEHOLDERS TO HEIGHTEN THEIR UNDERSTANDING OF PATIENTS' ISSUES'

Professor Dirk Schrijvers

PAC members will advise on content. Professor Denis: "We hope that our patient information online will stimulate lively cross-interest collaboration and debate in cancer research, treatment and care around Europe, and also inspire all stakeholders in oncology to heighten their understanding of patients' issues to work together and make the difference."

At the same time, the Education Committee, chaired by Professor Dirk Schrijvers (Ziekenhuisnetwerk Antwerpen-Middelheim, Belgium), is setting up a series of eSeminars, as part of ECCO's eLearning programme. Courses will be open to all oncology professionals, and aim to encourage distance learning at minimum cost. Participants will be able to study at home, at their own pace, and gain accreditation points from Accreditation Council of Oncology in Europe on completion.

The first eSeminar, for example, is free of charge. "Specialist updates on management of liver metastases" features case-based presentations from specialists in medical oncology, surgery and stereotactic radiotherapy. Clinicians choose the relevant specialty, view the presentation, and then work through an evaluation. The aim of the course, broadly, is to ensure that participants are aware of the limitations of current treatments, of recent clinical findings, and are able to identify therapeutic and patient considerations for optimising treatment choices. They work towards an evidence-based approach, which integrates new research findings.

'PLEASE CONTACT US WITH SUGGESTIONS FOR ECCO'S EDUCATIONAL PROGRAMMES'

Professor Schrijvers said the Education committee's goal is to offer content-rich material that promotes professional growth through education. "I am keen to witness our eLearning initiative develop and invite you to contact us with any suggestions or ideas you may have for ECCO's educational programmes."

Both the Patient Information section and the eLearning programme are due to become available via the ECCO website (www.ecco-org.eu) this Spring, 2008.

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Launch of European CRC awareness month

MEPs pledged their support for the first European colorectal cancer (CRC) awareness month in March, 2008. The pan-European advocacy group, Europacolon, launched the month at the European Parliament, with the aim of educating the general public about prevention and diagnosis.

An exhibition at the European Parliament included a walk-through model colon, and an educational trailer. Europacolon will be taking both on a tour throughout Europe. MEP Robert Sturdy sponsored the exhibition and said he was delighted to be part of the initiative. "Too many people currently die of this potentially highly treatable disease," he said.

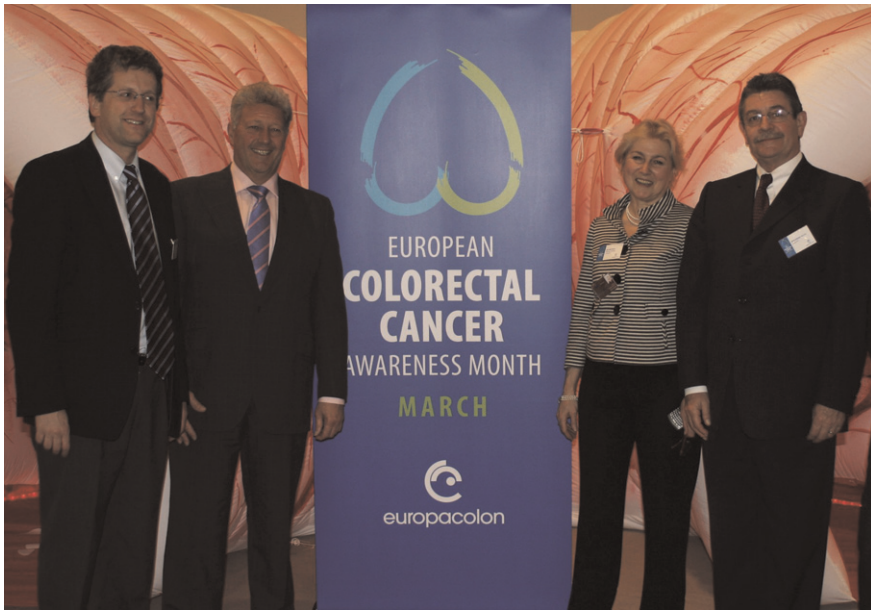
Europacolon was founded by Jola Gore-Booth in 2004 and aims to prevent deaths from CRC, and improve the quality of life of patients by developing patient advocacy groups throughout Europe to increase awareness and improve the management of the disease.

"It is crucial we get across the message that colorectal cancer is curable if diagnosed and treated early and appropriately.", she said.

Former EU Health Commissioner, Markos Kyprianou, said: The launch of the first European Colorectal Cancer Awareness Month will ensure Europe's second biggest cancer killer is at the top of the health agenda, which is the first step to reducing deaths in Europe.

"Primary prevention alone is not enough. We need effective screening and early detection programmes to enable prompt diagnosis and treatment to reduce the overall burden of CRC in the European population. Although there is consensus between the Member States and the Council of the European Parliament in promoting CRC screening as a public health policy, implementation of the screening programmes vary between Member States," he said.

At the launch, Professor Panos Kanavos (London School of Economics, UK), presented preliminary findings from a registry on CRC services in Europe. The variable quality of data collection "presents a significant barrier to policy development, co-ordination and assessment", he said. The LSE work demonstrated that screening policy is fragmented within and between European countries due in part to inconsistent screening methods, poor compliance to existing programmes, and a lack of awareness. The majority of European countries lack the human resources, skill-set and new technology necessary for population-based screening programmes. Member States need to develop "a consistent and comprehensive cancer strategy and treatment plan". Professor Kanavos concluded: "Europe is lagging behind the US in its attitudes to the management of this disease and it is time we stood together to call for more stringent strategies."



Left to right: Professor Eric Van Cutsem (University of Leuven, Belgium), medical director, Europacolon; Robert Sturdy, MEP; Jola Gore-Booth, Europacolon founder and director; Dr Keith B. Spencer, non-executive director, Europacolon.

Infused 5FU 'better than bolus'

Infusional fluorouracil (FU) conveys a survival advantage over the bolus form, when used with irinotecan-based regimens in the treatment of first-line metastatic colorectal cancer (mCRC), US researchers say. Updated results from the BICC-C study (*JCO* 2008;**26**(4):689–90) found that an irinotecan/bevacizumab combination used with infused 5FU was associated with a significant improvement in overall survival compared with the same irinotecan/bevacizumab schedule, but bolus 5FU.

The investigators, led by Charles S Fuchs (Dana-Farber Cancer Institute, Boston, USA), set out to compare the safety and efficacy of different irinotecan regimens in first-line treatment of mCRC. However, they amended the trial to include bevacizumab after it received FDA approval. Altogether, 57 patients were randomly assigned to FOLFIRI (irinotecan plus infusional FU and leucovorin) combined with bevacizumab. Another 60 patients were assigned to irinotecan plus bolus 5FU/LV (mIFL), again combined with bevacizumab.

Patients in the FOLFIRI arm had a median overall survival of 28.0 months compared to 19.2 months for patients in the mIFL group (p=0.037). The proportion alive at one year was 87% and 61%, respectively (p=0.01).

"Consequently, when using an irinotecan-based regimen in the treatment of first-line metastatic colorectal cancer, an infusional schedule of FU should be the preferred approach," write the authors.

Education and cancer mortality

Socioeconomic inequalities in cancer mortality "will probably decrease in the future," according to a pan-European group of researchers. Time trends in cancer mortality suggest a narrowing of the gap in mortality according to educational level.

Researchers used longitudinal mortality data sets for the 1990s to compare socioeconomic inequalities in total cancer mortality among men and women aged 30–74 years.

Large variations were observed for the impact of educational differences in total cancer mortality, but 3 distinct patterns emerged. In Denmark, Norway and Sweden, the relative index of inequality (RII), calculated according to educational level, was significant at around 1.3–1.4 in both men and women. In France, Switzerland, Belgium and Finland, the RII was 1.7 in men but lower, around 1.2, in women. In Spain, Slovenia and Turin RII varied between 1.3 and 1.9 among men, but there were no differences among women (*BJC 2008*;**98** *(5): 1012–9*).

Lung, upper aerodigestive tract and breast cancers explained most of the variations. "The gradual spread of the smoking epidemic explains why southern populations still show much larger inequalities among men than women," the authors write.

The findings suggest "a large potential for change", the authors write. Recent studies have suggested that less educated younger women may have rising rates of breast cancer mortality. Further, as southern European countries have still to experience the last stage of the smoking epidemic, these women may also have increasing rates of lung cancer mortality.

"Given these trends, variations between countries and genders in socioeconomic inequalities in cancer mortality are likely to reduce" the authors conclude: "Consequently, tobacco control, alcohol policies and breast cancer screening should ensure that they reach lower, as well as higher, socioeconomic groups."

More intense chemotherapy in neuroblastoma

Increasing the dose of chemotherapy and reducing the interval between treatments increased survival among children with high-risk neuroblastoma, according to the results of a pan-European study.

A 10 year trial recruited 262 patients with stage 4 neuroblastoma from 29 centres in Europe. All patients were over the age of 1 year (median 2.95 years). The study was co-ordinated by the UK's Children's Cancer and Leukaemia Group (CCLG).

Researchers studied the effects of administering chemotherapy every 10 rather than 21 days, at 1.8 times the conventional dose. They found that 5-year event-free survival (EFS) rates were 30.2 percent in the rapid-treatment group, compared with 18.2 percent among patients receiving standard treatment (*Lancet Oncology 2008*;**9**:*247–256*). Rapid scheduling did not increase toxicity.

There was no significant difference in overall survival at either 5 or 10 years, but the researchers said that the increasing difference in EFS after 3 years "suggests that the efficacy of the rapid regimen is better than the standard regimen."

Treatment for advanced neuroblastoma occurs in phases; and reducing the intervals in the initial chemotherapy meant that myeloablation was given earlier. This "might contribute to a better outcome," researchers said. Cancer Research UK, which funded the trial, said that, following these results, the more rapid chemotherapy regimen is being rolled out across Europe.

Lead author, Professor Andy Pearson (Royal Marsden Hospital, Sutton, UK), said, "Our study is the foundation of the current European study of high-risk neuroblastoma, which has already recruited over 10,000 children and is investigating new therapies, hoping to improve further the outcome of these children. In the future, improvements will occur by developing new anti-cancer drugs."

An accompanying editorial (*Lancet Oncology* 2008;**9**:*195–6*) was in agreement: "Ultimately, better approaches for the treatment of minimal residual disease are needed to conquer this lethal malignancy."

MRI Directive postponed

The European Parliament has voted overwhelmingly to postpone for 4 years the implementation of the EU Directive on electromagnetic fields. The EU Physical Agents (Electromagnetic Fields) Directive 2004/40/EC was due to be implemented by April 2008, but would have had the unintended effect of halting the use of magnetic resonance imaging (MRI).

Welcoming the move, Professor Alexander Eggermont, President of ECCO said, "The Directive would have posed particular problems to those healthcare staff that care for patients such as children, the elderly, or those who have been anaesthetised, and who need help and comfort during scans. It would also have stopped the use of MRI for interventional and surgical procedures.

"ECCO will now be involved in the scientific consultations that the European Commission will be undertaking to amend the Directive, in order to ensure that major advances that have been made in cancer care are not put into jeopardy," he said.

Accelerated approval of bevacizumab

The US' Food and Drug Administration (FDA) has granted accelerated approval for bevacizumab (Avastin), in combination with paclitaxel, for the first-line treatment of patients with locally recurrent or metastatic breast cancer. The approval was based on the E2100 phase III study, which showed that the addition of bevacizumab to paclitaxel doubled progression-free survival in patients with metastatic breast cancer, compared to paclitaxel alone.

A full review of 2 further phase III trials, AVADO and RIBBON-1 by the FDA will be required for the accelerated approval to be converted into a full approval.

Vulval cancer management could use sentinel nodes

Sentinel-lymph-node dissection has been shown to be safe and clinically useful in early-stage vulval cancer, in a multicentre observational study (*J Clin Oncol* 2008;**26**:884–89).

"The sentinel node concept has been useful in both breast cancer and melanoma", says first author Ate van der Zee (University Medical Centre, Groningen, Holland). "For the first time we have shown that it is also safe and associated with significantly decreased morbidity in early-stage vulvar cancer."

In the study, sentinel-lymph-node procedures were done on 403 patients from March, 2000, until June, 2006. Of those, 276 patients with a node- negative biopsy were observed for 35 months, and 202 had a follow-up of 2 years. After 2 years, eight (3%) groin relapses occurred in assessable patients, including two with multifocal disease. When patients with multifocal disease were excluded, the proportion of failures decreased to 2.3%.

"This study adds a lot to the literature", notes Michael Frumovitz (MD Anderson Cancer Center, Houston, TX, USA). Presently, sentinel-node biopsy in the USA is not widely used, Frumovitz continues. He believes that most

'IT WON'T BE LONG BEFORE SENTINAL NODE BIOPSY BECOMES THE STANDARD OF CARE'

US gynaecologists and oncologists will wait for the findings of the Gynecologic Oncology Group (GOG)-206 validation study before they adopt the procedure wholeheartedly. These findings are expected within a year. "With the data from this new study and the upcoming GOG study, it won't be long before sentinel node biopsy becomes the standard of care in vulvar cancer", says Frumovitz.

van der Zee emphasises that sentinel-node biopsy in vulval cancer should be done by an experienced multidisciplinary team—including a surgeon, a nuclear medicine specialist, and a pathologist. In the study, inaccurate interpretation of the preoperative lymphoscintigraphy by the nuclear medicine specialist, and the staging by the pathologist, resulted in three recurrences. "At each level, the quality of the procedure must be high, because false-negative results have such serious consequences for patients", cautions van der Zee. He believes that gynaecologists and oncologists should do at least ten sentinel-node biopsy procedures followed by lymphadenectomy to learn the technique. "It's important that the surgeon as well as the other members of the medical team should master the learning curve", adds van der Zee. "For a rare tumour such as vulvar cancer this means that treatment should be centralised."

Barbara Boughton

*This story originally appeared in Lancet Oncology 2008;***9**;324.

Multiple targeted agents in advanced breast cancer

Biologic agents acting on multiple targets may offer improvements over existing targeted therapies in metastatic breast cancer, according to speakers at the 1st Asian Breast Cancer Conference (New Delhi, India; February 9–10, 2008).

Professor Martine Piccart (Institut Jules Bordet, Brussels, Belgium), current President of the EORTC, said that several multi-targeting biological therapies are in development. "It is hoped these can improve on the median overall survival of 2–3 years in advanced breast cancer achieved to date with agents such as trastuzumab, lapatinib and bevacizumab," she remarked.

Of around 10 investigational multi-targeted agents in clinical development for metastatic breast cancer, sunitinib malate (Sutent), a small molecule oral tyrosine kinase inhibitor, currently approved for treatment of metastatic renal carcinoma and gastrointestinal stromal tumour (GIST), is currently the most advanced, speakers said. All act primarily against angiogenesis via the vascular endothelial growth factor (VEGF), but are also active against one or more other targets, and may have additional anti-tumour effects. Others include recentin (AZD2171), AMG 706 and pazopanib.

Sunitinib has shown promise in phase I and II trials for treatment of advanced breast cancer and is now being investigated in 4 phase III trials for the condition, Professor John Crown (St Vincent's Hospital, Dublin, Ireland), told the meeting. "Sunitinib targets class III and V receptor tyrosine kinases, all VEGF and platelet-derived growth factors (PDGF), the stem cell receptor c-KIT and FMS-like tyrosine kinase-3 (FLT3). It also targets class XII RTK neurotrophic factor (Rearranged during Transfection; RET)," he said.

VEGF is a well-recognised biological marker in breast cancer and has important interactions with the HER2/neu system. Tumours expressing PDGF are associated with poor prognosis: PDGF acts to stabilise new blood vessels via smooth muscle cells, pericytes and fibroblasts. The c-KIT receptor is becoming increasingly recognised in triple-negative breast cancers that oncologists find difficult to treat, he said: "Some HER 2/neu and hormone-receptor-negative patients show response to sunitinib."

Sunitinib is now being investigated in phase III trials in combination with taxanes or capecitabine in advanced breast cancer, both in chemotherapy-naïve and heavily pre-treated patients who have failed multiple chemotherapy regimens. One trial, for example, is investigating a first-line paclitaxel and sunitinib combination against paclitaxel and bevacizumab.

Professor Crown said that the real benefit of multiple-targeting drugs with dominant anti-angiogenic effects could be in patients with early stage breast cancer, in whom therapy might prevent the development of metastatic disease. "Ultimately, they might conceivably have a role as adjuvant and neoadjuvant therapy," he suggested.

Olwen Glynn Owen was sponsored by Pfizer to attend the meeting.

PODIUM

Palliative care at a crossroads

Professor Marie Fallon (St Columba's Hospice Chair of Palliative Medicine, University of Edinburgh, UK) is guest editor of the forthcoming Special Issue, 'Palliative Medicine – the Art and the Science' (*EJC 44/8, 2008*).

How is the changing face of cancer impacting on palliative care?

Progress in cancer management over the last 20 years has meant that many patients are living longer with cancer, while demographic changes have led to an absolute increase in the number of patients with cancer, in particular the elderly.

Palliative care was originally care of the dying, but it is now more integrated with oncology. We are seeing patients at an earlier stage of their illness and providing palliative care in parallel with tumouricidal therapy, rather than just at the end of life. The aim to improve the quality of life of patients living with what may still, ultimately, be a terminal illness.

There has been a move to increase this integration. Many large cancer centres have palliative care teams, and our earlier involvement with patients has encouraged further development of palliative care as we have become more aware of the various challenges facing patients, families and oncologists.

What does palliative care offer patients early in their illness?

People still associate palliative care with end of life care and the traditional approach of keeping patients comfortable with adequate morphine. In reality, palliative care aims to maximise patients' quality of life and to integrate control of distress in the broadest sense of the word with the general management of the patient. Our work still involves pain control, but using modern techniques of pain control with a spectrum of management and therapies. We deal with other symptoms – nausea, vomiting, constipation, breathlessness – and psychological support of patients.

Why (in the Special Issue) do you say palliative care is at a crossroads?

Non-hospice palliative care is at a crossroads because our evidence base is lagging behind that in most other specialties. Resources are finite and health services are under pressure to provide a wide spectrum of treatments and care. We need a good evidence base in order to justify doing what we want to do. Some aspects of care – such as morphine pain control – are not expensive, and are beyond evaluation, but many other specific interventions are not yet evidence-based. We have to justify their adoption into the armamentarium of palliative care. They include the new, more expensive methods of pain control, interventional techniques for symptom control and various models of care aimed at improving psychological distress.

Is it possible to gather evidence?

It can be difficult to do research because in general our frail patients have many problems, and our interventions are often complex. The study design can be a challenge in itself. Patient recruitment, the large attrition rate, and ethical issues can all present difficulties. But research doesn't all have to happen at the end of life. Some issues are specific to the last weeks, days or hours, and they remain a challenge, but the majority of problems can be looked at among patients at an earlier stage of incurable cancer, when they are a little more robust. If you define clearly the problem you are looking at, findings on a particular symptom can be generalised throughout the illness trajectory.

Where has progress in palliative care been exceptional?

The introduction of oral morphine in almost all countries world-wide, the development of the WHO analgesic ladder and, recently, recognition of palliative medicine as a discipline. In the UK, it was designated a specialty with its own training programme in 1989, which has helped to attract young doctors, and promote research.

What is the situation elsewhere?

Canada has a palliative care strategy similar to the UK, and most of the rest of Europe is developing along broadly similar lines, with adjustments for local culture, and structures. In the US, recognition is evolving and the Board of Medicine has recently approved a specific training programme and examination.

What gaps exist in the current provision of care?

Patients who are thought to be cured may be living with treatment effects and have significant on-going problems. There is an unmet need for supportive care among survivors, largely because the problem has not been addressed in a structured, systematic way. In addition, patients who are living with incurable cancer, but are not in advanced stages of the disease can experience a lack of appropriate palliative care.

What do you hope the Special Issue will achieve?

I anticipate that this focused work will be read by oncologists who will gain an up to date understanding of our current knowledge, the research agenda, and the way forward. I hope it will lead to bigger and better collaborations between oncologists and palliative care, which can only improve the services we offer to patients.