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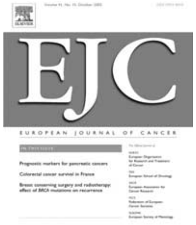

NEWS. . .NEWS. . .NEWS

Radiotherapy after lumpectomy ‘saves lives’

A worldwide overview of randomised trials in breast cancer concluded that radiotherapy following lumpectomy reduces mortality. The 15-year risk of dying from the disease dropped from 36% among women who had lumpectomies alone, to 31% among those who also had radiotherapy.

The Early Breast Cancer Trialists’ Collaborative Group (EBCTCG) conducted an overview of trials of radiotherapy and of different types of surgery. The trials involved 40,000 women with early breast cancer.

A woman’s 5-year risk of local recurrence dropped from 26% to 7% if she also received radiotherapy. For every four recurrences avoided by radiotherapy, in the hypothetical absence of other causes of mortality, one breast cancer death was prevented (*Lancet* 2005;**366**:2087–106).

Similar benefits from radiotherapy were seen in women whose cancer had already spread to the lymph nodes. In this group, local recurrence dropped from 23% to 6% when women had radiotherapy as well as a mastectomy. The risk of dying from breast cancer dropped from 60% to 55%.

For women whose cancer had not spread, and who had a mastectomy, any benefits of radiotherapy were slight and outweighed by its side effects.

Professor Sir Richard Peto (University of Oxford, UK), Cancer Research UK epidemiologist, was an organiser of the collaboration. He said the study provides “the first really definitive evidence” that for women who have had breast-conserving surgery and for those whose cancer has spread to the lymph nodes, radiotherapy reduces the long-term risk of dying from the disease. “The improvement is small but definite and it adds to the improvements in long-term survival produced by chemotherapy and hormone therapy”.

Present guidelines already state that radiotherapy is the standard treatment after lumpectomy, but the treatment actually given depends on discussions between doctors and patients. Non-standard treatment may be offered after discussion: patients may decide against having standard treatment when the benefits of radiotherapy are relative.

A family decision

Family members have an important role in treatment decisions, especially among Hispanic women, according to a recent US study (*Cancer* 2006; doi: 10.1002/cncr.21680).

Researchers at University of California, Los Angeles, interviewed 257 breast cancer patients aged 55 and above within 3–9 months of their diagnosis. They found that older, Hispanic women rely more heavily on family to make treatment decisions than women of other racial groups. About a quarter of African-Americans and whites identified the physician as the final decision-maker, compared to just 10% of Hispanics.

Patients who identified the family as the final treatment decision-maker were more likely to be treated with mastectomy rather than breast conserving surgery. Dr. Rose Maly led the study and concluded that, among older Hispanics, “physicians should acknowledge patients’ family members as potential key participants in medical decision-making, rather than merely as translators and providers of social support”.

Fatigue after breast cancer

Up to a third of breast cancer survivors report fatigue symptoms up to 10 years after diagnosis, according to US researchers. Those with concomitant cardiovascular problems and depressive symptoms, and those treated with combined radiation and chemotherapy, were most likely to suffer (*Cancer* 2006; doi: 10.1002/cncr.21671).

Researchers at University of California, Los Angeles, followed 763 women for up to 10 years after their diagnosis and treatment for breast cancer. The women were interviewed in the first 5 years, and again between 5 and 10 years after diagnosis.

Approximately one third of women reported symptoms of fatigue at each time interval. About one in 5 (21%) complained of fatigue at both. Concomitant depression, pain, heart disease and high blood pressure increased the likelihood of fatigue, as did combined radiation and chemotherapy.

Dr. Julienne Bower led the study and concluded that the findings “highlight the resilience of breast cancer survivors and suggest that persistent fatigue is experienced by a minority of women in the aftermath of cancer diagnosis and treatment”.

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New Italian website for patients with cancer

A new website –www.azaleaweb.it.– has been launched to offer Italian patients with cancer and their families a single source of validated information on treatment and patient care.

"There's a lot of information available on cancer, but not all of it is useful to patients", explains senior collaborator Anna Boglioli (National Institute of Cancer Research, Genoa, Italy). "Much of it is too technical for the general public, possibly misleading if it is on the internet, difficult to access, duplicated, or in a foreign language. The aim of the Azalea project is to provide information that has been validated by a medical panel, at a level people can understand, and in Italian".

The government-funded project is promoted by the Alliance Against Cancer (www.e-oncology.it) whose aims include improving Italian cancer research and homogenising treatment nationwide. Seven Italian oncology institutes developed the website, coordinated by Ivanna Trucculo (Centre For Oncology Referrals, Aviano, Italy) and Gaetana Cognetti (Regina Elena Institute, Rome, Italy).

Users can navigate the site by body or subject area, via alphabetical headings, or by using the search tool. The site provides easy-to-read articles in Italian on all types of cancer, treatments and patient care, links to various associations, and summaries of clinical trials. Many articles can be downloaded, whereas others are accessed via links to other websites. The site's request system can obtain documents available only on paper (in which case a summary is provided) for the price of a photocopy.

"Hopefully, users will feel empowered with this information and be able to take more control during a very difficult period of their lives", says Boglioli.

According to Debbie Coats, senior information nurse at CancerBACUP, London, UK, 250,000 unique users access www.cancerbacup.org.uk each month. "It shows what a huge demand there is for accurate, sensitive, evidence- based information written from the patient's point of view", she adds.

Adrian Burton

This story originally appeared in Lancet Oncol 2006;7:6.

US approval for Sorafenib

The US Food and Drug Administration (FDA) has approved sorafenib tablets (Nexavar) for the treatment of patients with advanced renal cell carcinoma. Manufacturer Bayer HealthCare said sorafenib is the first treatment for this cancer to be approved by the FDA in more than 10 years.

Sorafenib is a multi-kinase inhibitor that targets serine/threonine and receptor tyrosine kinases in both the tumour cell and tumour vasculature. In preclinical models, sorafenib targeted kinases involved in tumour cell proliferation and those involved in tumour blood angiogenesis. They included RAF kinase, VEGFR-2, VEGFR-3, PDGFR-β, KIT, and FLT-3.

A multicentre, international trial found that treatment with sorafenib was associated with an approximate doubling of progression-free survival among patients with advanced renal cell carcinoma. The drug is also in phase III clinical trials for the treatment of advanced hepatocellular carcinoma, and metastatic melanoma. A phase III trial in non-small cell lung cancer (NSCLC) is planned for 2006.

Bayer HealthCare has filed for regulatory approval with the European Medicines Evaluation Agency (EMEA), and in Switzerland, Australia, Brazil, Canada and Mexico.

Zactima: towards orphan drug status

The EU's Committee for Orphan Medicinal Products (COMP) has recommended orphan drug designation for ZD6474 (Zactima) for the treatment of patients with medullary thyroid cancer. This positive opinion follows the US Food and Drug Administration (FDA)'s orphan drug designation for ZD6474 in follicular, medullary, anaplastic and locally advanced and metastatic papillary thyroid cancer. Final adoption of COMP's opinion is expected from the European Commission early in 2006.

ZD6474 is a once-daily oral therapy that targets key cell signaling pathways involved in tumour growth and spread, including VEGF (vascular endothelial growth factor) and EGF (epidermal growth factor) receptor signaling. It also inhibits RET kinase, which is believed to be an important pathway in medullary thyroid cancer.

Treatment options for medullary thyroid cancer are limited and the prognosis is poor. ZD6474 is being evaluated in patients with advanced hereditary thyroid cancer; a phase II study is ongoing and continues to recruit patients.

Manufacturer AstraZeneca has announced its intention to progress into phase III trials evaluating the anti-tumour activity of the drug in advanced non-small cell lung cancer (NSCLC).

Delay in availability of Gliadel in England

Gliadel Implant, an innovative treatment for grades III and IV gliomas, is now freely available in Scotland, but the treatment is not yet funded for all patients in England.

The Scottish Medicines Consortium (SMC) gave a positive opinion for Gliadel in December 2005 but in England, a ruling from NICE (National Institute for Clinical Excellence), is not expected until August 2006. However, most neurological centres in the UK continue to fight for ongoing funding on a case-by-case basis.

The Implant is carmustine in the form of small biodegradable discs. They are inserted into the tumour site at the time of surgery and deliver immediate chemotherapy. International, randomised, multicentre studies have shown that Gliadel can provide patients with a 5-fold increase in 3-year survival and enable patients to maintain their independence for longer.

European approval was granted in April 2001 for use in recurrent tumours. It is now approved for use in primary diagnoses in France, Luxembourg, Germany, UK, Ireland, Spain, Greece, and parts of Scandinavia. Applications for this use have been submitted in Italy, Belgium, Austria and Switzerland.

EUROFILE

Disappointment over Framework Budget

The saga of the budget for the EU's 7th Framework Research Programme (FP7) looks set to run and run. The programme was due to be discussed in the European Parliament in December 2005, but this has now been postponed until March 2006 and it is still uncertain whether member states will have agreed on the amount of money available by then.

Funding will have to be found from the much-reduced total EU budget for the period 2007–2013 salvaged at the last minute by the British Presidency at the end of December 2005. It looks likely that the increase over the FP6 budget will be low, possibly as little as 8% a year, amounting to a total of €50bn in real terms over the next seven years. This is an improvement on the €34bn total of FP6, but very much lower than many scientists would have wished for, and indeed than the €70bn budget originally proposed by the Commission for FP7.

The new budget has also to pay for the establishment and running of the European Research Council (ERC), which is due to start work in 2007. Some scientists are worried that this initiative, much needed to provide funding for basic research at EU level, will also suffer from budget cuts.

The Austrian and Finnish governments, which will hold the EU presidency for the first and second half of 2006, respectively, have said that they will make the speedy adoption of FP7 a priority. This is essential if the programme is to be in place in order to take over from FP6 in 2007. It is also important if progress towards the 'Lisbon agenda', which aims to bring industrial competitiveness levels in Europe up to those which operate in the USA, is to be maintained. But given that the current annual EU research budget is 5% of all public money – very much less than the US spends on its National Institutes of Health alone – this seems more and more to be a question of paying lip service to a good idea.

''ANY BUDGET CUTS CONTRADICT EUROPEAN LEADERS' DECLARATIONS''

Research Commissioner Janez Potocnik and the European Parliament committee on Industry, Research and Energy (ITRE) may be used to finding themselves on opposite sides of the fence on many issues, but on FP7 funding they are in agreement. The underlying problem exposed by the December budget negotiations was that member states essentially saw the EU budget as a financial mechanism of redistribution, he said in a speech in Germany. "The essential question is whether we are ready and capable of going beyond the redistribution logic so that we can define a budget that better responds to the challenge of today's world", he said. "I think that for far too long political leaders in Europe have allowed the debate to turn around net flows".

The ITRE Committee will be the lead committee to consider the legislation to set up FP7 before it goes into the full European Parliament in the Spring. In January 2006 their rapporteur on the subject, former Polish Prime Minister Jerzy Buzek, published a report which was highly critical of the budget deal. This follows a report earlier in the month from the Parliament's Budgets Committee, which rejected the European Council's December agreement, saying that it did not guarantee an EU budget to provide prosperity, competitiveness, and cohesion.

"The European Parliament agreed with the Commission that the budget of the Seventh Framework Programme must be doubled", says Buzek's report. "Any cuts in FP7 budget are against the Lisbon strategy and in disagreement with all the declarations of European Union leaders".

Any reduction in the proposed budget for FP7 puts at risk the success of the European Research Council, undermines the effort to raise EU investment in research to three percent of GDP, and threatens the European research effort in areas where public support is particularly necessary, says the report. "We cannot imagine how possible budgetary cuts could affect such sensitive areas as, for instance, health, energy, or environment". In addition to cancer, cardiovascular disease, diabetes and obesity, and rare diseases, the report suggests including rheumatic and respiratory diseases in the clinical and translational research categories, as well as suggesting that paediatric medicine and research on prevention should be added.

''WE MUST KEEP UP MOMENTUM''

Aside from budgetary problems, the ITRE committee report proposes a large number of amendments to the original Commission text for FP7. One important change concerns the operation of the ERC, which goes beyond the 'high degree of autonomy' proposed by the Commission, saying that it should be established as "a legally independent structure to be established under Article 117 of the Treaty, after a brief transitional phase managed by the Commission and a Scientific Council. The ERC should be accountable to its fund-providers but autonomous in its operations and selection of research projects".

Buzek presented his report to committee members for the first time in mid-January 2006, and they will vote on it before it goes into plenary session in the European Parliament. Potocnik is worried that time is short. "There is a lot of work to do this year; we need to continue to make progress in Council and the European Parliament on all the legislative proposals. It is extremely important that we keep up momentum", he says.

Mary Rice
Brussels

Lifestyle factors ‘affect PSA test’

The reliability of the PSA (prostate specific antigen) test may be compromised by lifestyle and demographic factors, according to US researchers. They found that PSA velocity can be significantly affected by age, race and diet, leading to possible misinterpretation. A single measurement of PSA concentration – the most common use of the PSA screening test – was minimally but significantly affected by age and body mass index (BMI).

Tests of PSA concentration alone have been blamed for causing too many false positive results and leading to unnecessary tests such as biopsies and transrectal ultrasounds. Investigators continue to refine the tests with calculations such as PSA velocity, PSA density and age-specific PSA. However, understanding of the effect of diet, race, weight and other factors, is limited.

Researchers at the Fred Hutchinson Cancer Research Center (Seattle, USA) reviewed PSA and PSA velocity data from 3341 cancer-free men. They found that PSA velocity was significantly affected by age, race and diet, potentially affecting its clinical interpretation (*Cancer* 2006, doi:10.1002/cncr.21603). PSA velocity decreased as men aged, and increased with higher total energy diets. PSA velocity in African Americans was on average almost twice the level of that in Caucasians, and was lower among users of high-dose calcium supplements.

Large weight fluctuations also had an impact and men who gained with had lower PSA velocity. Those who lost weight had increased PSA velocity.

As in other studies, single determinations of PSA concentration increased with age, and decreased with obesity. These differences, while statistically significant, were considered minimal and would have little influence on clinical interpretation of PSA value.

However, the impact of demographic and lifestyle factors on the clinical interpretation of PSA velocity was considered significant. The research team, led by Dr Alan Kristal, concluded, “Race, smoking, age, energy intake, calcium supplement use and weight change were associated with substantial differences in PSA velocity and clinical interpretation of PSA velocity could be biased by these factors”.

Two-tier screening for colorectal cancer

Two rounds of faecal occult blood tests (FOBT) could substantially decrease the need for colonoscopy in screening for colorectal cancer, Scottish researchers say (*Lancet* 2006; doi:10.1016/S1470-2045(05)70473-3).

The standard guaiac-based FOBT has a fairly low clinical sensitivity and specificity. About half of those positive for guaiac FOBT are negative for neoplasia on colonoscopy. The research suggests a two-tier approach, which could select more appropriately those who should receive colonoscopy.

Individuals who had a positive result from guaiac FOBT were invited to give two samples, from separate stools, for the more expensive immunochemical FOBT test, while awaiting colonoscopy. The immunochemical findings were compared to the results from colonoscopy.

The study included 800 people; of whom 173 had two negative immunochemical results (N/N); 129 had one positive and one negative (N/P) and 498 had two positive results (P/P). Colonoscopy found that only one of the N/N group, and one of the N/P group had colorectal cancer. This compares with 38 of the P/P group. It means that a negative immunochemical FOBT (N/N or N/P) was associated with a less than 1% chance of invasive cancer.

There was also a positive relation between strength of positivity on guaiac FOBT and the results of the immunochemical test. Most participants with a strong positive on guaiac FOBT were P/P on immunochemical FOBT; and the authors suggest that, in a screening programme, this group should bypass the immunochemical test and proceed directly to colonoscopy.

Overall, the authors found that a population with a high probability of cancer and high-risk adenomatous polyps can be identified using immunochemical FOBT. It confirms that “a negative result on immunochemical FOBT means colonoscopy – a procedure not without risk – need not be done, particularly since participants would be offered conventional retesting in 2 years’ time”.

They conclude that a population-based screening programme for colorectal cancer could be based on a combination of initial guaiac FOBT for all, followed by immunochemical FOBT for those with weak positive guaiac FOBT.

“Although immunochemical FOBT is more sensitive and expensive, use of this strategy for those who are weak positive on initial guaiac FOBT would decrease the need for colonoscopy. These data have important implications for national screening programmes, in terms of reducing the costs, inconvenience, and associated morbidity, without compromising screening effectiveness”, they conclude.

Radiotherapy: ‘National policy required’

A consistent national policy for radiotherapy in the UK is required, say specialists (*BMJ* 2006;**332**:107–9). The policy should be one “that is not bound by political time frames and funding cycles”.

The exciting potential for heavy particle therapy in the management of cancers should not divert attention from the inadequate treatment capacity of many UK radiotherapy departments. Many have substantial waiting lists despite efforts to prevent these from occurring.

Those with managerial, political and clinical responsibility for radiotherapy services “find themselves between a rock and a hard place”, according to the authors, from Leeds, UK. “They have the unenviable task of juggling competing clinical priorities and pressures from stakeholder groups in an environment that emphasises equity and speed of access as well as the primacy of patient choice. There is no apparent national guidance or precedent for the unpleasant choices that may have to be made”.

Concerns over delayed radiotherapy may influence the choice of treatment. In early breast cancer, for example, local control and survival following breast conserving surgery with (delayed) breast irradiation may not be equivalent to mastectomy.

The authors call for debate at a national level, acknowledging that discussions that “embrace options that represent a retrograde step in cancer care” will be difficult and emotionally and politically charged.

“In the light of growing waiting lists, avoiding discussion of active intervention represents the tacit acceptance of prioritisation by default and is not a responsible approach”, they conclude.

PODIUM

The Voice of Youth

Dr. Fatima Cardoso

Dr. Fatima Cardoso is Assistant Professor at the Chemotherapy Unit, Jules Bordet Institute, Brussels, Belgium. She combines clinical work with her responsibility for phase II–III trials in breast cancer. She is Scientific Director of the TRANSBIG network. Dr Cardoso trained in Porto, Portugal, and is Vice-President and Co-founder of the Flims Alumni Club, a multidisciplinary network of young cancer specialists in Europe.

What issues do young oncologists face that their predecessors didn't?

Oncology is evolving rapidly, more so than many other specialties. Translational research comes with particular legal, ethical and administrative issues – use of biomaterials in research for instance, and the administrative mountain produced by the EU Clinical Trials Directive – but these are problems for everyone, not just young oncologists.

How difficult is it for young oncologists to combine research with clinical work?

It is hard. The general shortage of young people entering oncology, coupled with increasing numbers of cancer patients, means a heavy clinical workload and little free time for research. Most institutions in Europe – with a few exceptions – do not ringfence time for research. It has to be done over and above clinical commitments, and clinicians don't get paid for it.

How easy is it for young oncologists to work in different countries?

There is still variation in the way different EU States view oncology. Some see it as a specialty in its own right, elsewhere it remains a subspecialty of internal medicine. I had to work for an extra year in Belgium to be accorded specialty recognition (having already received this in Portugal). It was particularly disappointing as oncology training in the two countries takes exactly the same length of time. Things may be improving but mobility of workers within the European Union needs to become a reality, not just a concept.

How important is it to have the right mentor?

A good mentor encourages you, makes you look ahead and, in my case, persuaded me to leave the country! Mentors do not have to be famous; rather they have to give you the opportunity to develop your qualities and help you to overcome difficulties. You need guidance, but you also need freedom; it's a balance.

How attractive is a career in clinical research?

There are new problems, but there are also new solutions. In breast cancer, for example, we have international networks and people have learnt to work together in large, collaborative trials, which involve thousands of patients and produce definite conclusions. Similar research networks are being set up for other cancer types; research will only move on at speed if we all work together. If the same question is asked time and again in small trials, it is a waste of human, financial and patient resources.

Having the opportunity to work on these trials is excellent. These are exciting times for research in terms of new agents and the clinical application of new technologies.

Are individual researchers credited for their part in large trials?

They may not be, and this is a problem for young oncologists, who need publications on their CV in order to progress in their career. If you are responsible for a trial in your own institution, or one in combination with 2–3 other hospitals in your country, you may get your name on a paper.

If you take part in a large, international trial, you probably would not even be mentioned in the publication or only in the acknowledgments. However, you learn a lot about getting patients into trials, obtaining their consent, following them up, dealing with the administration and management of trials, which is all very important for clinical researchers. The situation is more difficult for those in mid career, who are past that learning stage but not yet directing their own research programme.

What needs to happen?

Young oncologists cannot expect the system to solve its own problems; we want to be part of the solution. We are trying to do that by forming groups; it is easier to set up a research project within a network, than alone. The Flims Alumni Club (FAC), for example, grew out of the annual Flims Workshop in Switzerland, which teaches young researchers the basics of clinical and translational research and how to set up clinical trials. FAC aims to keep alumni with similar research interests in touch, with the aim of setting up international projects. ESMO also has a young oncologists group, which again, promotes the aim of international collaboration. Young oncologists need the support of established societies to be able to participate in strategic meetings, where key issues in the development of research are being discussed. We want to be involved early on.

What do these groups hope to achieve?

In any profession, progress can only occur where there is a balance between experience and innovation. People who have been working in the same area for a long time may keep having the same ideas and follow the same line of thinking. Sometimes, it takes somebody new, with a different line of thinking and new ideas for things to advance. Young oncologists do not want to teach the previous generation, we just want to participate, to speak and to have our ideas heard, while we learn.