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NEWS...NEWS...NEWS

Europe 'must double cancer research funding'

Europe spends 7 times less per capita on cancer research than the US, according to a comprehensive new survey. Researchers said the funding gap was ''far wider than previously thought'' and ''has major implications for European cancer research policy.''

The European Cancer Research Funding Survey, funded by the European Commission, covered the whole of Europe including accession, associate and applicant States, plus the European Free Trade Area. It was conducted by the European Cancer Research Managers (ECRM) Forum.

The survey identified 139 non-commercial sources of funding and found that the US spends 5 times more per person than the 15 original members of the European Union (EU-15); and 7 times more per person than the 25 current EU members.

Dr Richard Sullivan (Cancer Research, UK) chairs the ECRM Forum and said, ''There's a lot of arm-waving about co-operation, collaboration and improving cancer networks for patient benefit but it's absolutely clear that there simply is insufficient funding. It's not a question of matching US levels, but doubling the amount spent across Europe is feasible.''

''YOUNG INVESTIGATORS JUST WANT TO DO THEIR JOB''

He warned that unless this happens, the knock-on effect will be the loss of scientists and clinicians from Europe. The picture is mixed across Europe and while the UK, France and Germany have lost some researchers, Spain and parts of southern Europe have a greater problem. As top researchers move to the US, Europe is in turn losing the intellectual property rights (IPR) generated by their work. ''In Spain and Italy, young investigators have little access to long-term funding. They're not moving for personal gain, they just want to be able to do their job. It is a real issue.''

As the volume of research dwindles, so does patient care, said Dr Sullivan. ''Good service delivery anywhere is inextricably linked to research activity. Where there is research going on, the way care is delivered, the use of protocols and access to innovative therapies all improves and standards are higher than anywhere else.''

Professor Françoise Meunier, Director General of the European Organisation for Research and Treatment of Cancer (EORTC), and one of the survey's authors, agreed. ''The under-funding of clinical cancer research, coupled with a disproportionately burdensome regulatory environment, is seriously damaging European cancer research and its competitiveness. This is bad news for Europe, but more importantly, it is bad news for cancer patients.''

Launching the survey, one of its initiators, Professor Gordon McVie (senior consultant to European Institute of Oncology, Milan) stressed the ''tough methodology'' employed in compiling the study. Researchers contacted organisations throughout Europe, requesting financial information for the fiscal year of 2002/2003. Follow-up letters were sent twice to non-responders, then at least 2 emails and numerous phone calls. Websites were searched for financial information and all data was reviewed and cross-checked.

Professor McVie said it is the first factual survey. ''It will lay a foundation in fact for all the claims and counter-claims about how well- or badly-off European cancer research is. It will provide a factual basis for further discussion on research funding.''

The survey found that the total spend on non-commercial cancer research for 2002/3 was Euro 1.43 billion. EU Member States accounted for 93%, and the original EU-15, for 98% of the money. The survey also found a huge variation in funding between countries. The UK had the highest absolute spend at Euro 387 million; Malta spent nothing. The European Commission contributed Euro 90 million.

The low spend by accession countries was not surprising, Dr Sullivan said, but did raise questions. Hungary, for example, has a strong tradition of science and technology and has produced great Nobel Prize winners. But its survival rate for testicular cancer is less than 70%. Should basic care be improved, therefore, before research is financed? ''There are some really difficult ethical and practical issues to be addressed,'' he said.

''THERE IS NO PUBLIC HEALTH POLICY IN EUROPE''

Europe concentrates a large proportion of its spending on basic scientific research at the expense of preventive and clinical research. Biology receives 41% of all cancer research funding, compared with 20% for treatment and just 4% for prevention. In contrast, the US spends 25%

continued overleaf

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

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'European cancer research funding survey—*continued*'

on biology, 25% on treatment and 9% on prevention.

Ms Kathleen Vandendael, Executive Director of the Federation of European Cancer Societies (FECS), suggested the emphasis on basic research might be because each Member State is keen to finance its national programme. Le Centre national de la recherche scientifique (CNRS) is financed by France; the Max Planck by Germany. ''Basic research is more easily undertaken at national level rather than clinical research which more often has to be of pan-European nature. This is certainly a question to be investigated and to be worked on.''

Dr Sullivan was ''a little surprised'' that there was not more activity in preventive medicine and translational research. But he said, ''These are difficult domains. They are time-consuming and require a different type of research approach. We need to ringfence money and drive initiatives in public health.''

Professor McVie was more forthright. ''Governments if they are responsible for anything should be responsible for public health and education. There is no notion of public health policy in Europe. There is in the States and they put in funding to back it up. How can a group of governments not have a policy on public health? It is absolutely scandalous.''

Busy health professionals do not have time to stand back from emergency situations and look at how to prevent cancer. Ideas in preventive medicine are lacking because the research has not been done. ''Ideas don't come out of the woodwork,'' he said.

On a positive note, of 139 funders identified by the survey, just 25 accounted for 80% of the total spend. Dr Sullivan said this contradicts the frequent complaint that European cancer research is fragmented. It also presents the opportunity for partnership between the major funders in Europe.

The act of conducting the survey had itself brought the major European funding bodies together round a table, he said, which has not been done before. It has clarified how each works, allowed the sharing of ideas and paved the way for further collaboration. ''It is a really positive step forward. This would not be top-down but bottom-up, and would allow us to support the great clinicians and scientists we have in cancer research. Cross-border collaboration between funders could allow us to reduce regulatory burdens and unnecessary bureaucracy, which would be an achievement.''

He hopes the survey can continue with 2003/4 data, so that trends in spending will be monitored in future.

The full report can be downloaded from www.ecrmforum.org.

Swiss approval for erlotinib

The Swiss health authority Swissmedic has approved the use of erlotinib (Tarceva) for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of at least one prior chemotherapy regimen. This is the first European approval for the drug, and follows US approval for the same indication in November 2004.

Erlotinib targets the human epidermal growth factor receptor HER1. It inhibits the tyrosine kinase activity of the HER1 signalling pathway inside the cell. Manufacturer Roche says that the drug has also shown survival benefit in a phase III study in locally advanced or metastatic pancreatic cancer patients.

The Swiss approval is based on a phase III study comparing erlotinib with placebo for the treatment of patients with advanced NSCLC, following failure of first or second-line chemotherapy (*Proc Am Soc Clin Onc 2004 # 7022*). Patients in the erlotinib arm survived 6.7 months, compared with 4.7 months for those receiving placebo. Erlotinib is an oral tablet indicated for daily administration.

Brazil approves research with embryo stem cells

Brazil will allow therapeutic research with embryo-derived stem cells after a congressional vote on March 2, 2005. The debate preceding the authorisation of its Biosafety Law attracted much public attention and overshadowed the approval of research into the commercialisation and cultivation of genetically modified organisms (GMOs).

The law was passed with a majority vote – 352 against 60, with one abstention – and will take effect only after presidential sanction. But, the government has already announced that it will give Brazil $5 million (about US$2 million) to research projects on human stem cells.

Eduardo Campos, Brazilian Minister of Science and Technology notes that ''Brazilian researchers have already used stem cells in cardiovascular studies.'' ''This regulatory milestone will allow Brazilians to continue their research'', he adds.

Research will be allowed on stem cells from frozen embryos stored in fertilisation centres for at least 3 years or on unviable embryos. Parents must consent to donate any embryos, and estimates suggest that about 30 000 frozen Brazilian embryos are available. The law forbids the use of embryonic and germ cells for therapeutic embryo cloning and genetic engineering, and imposes fines and prison sentences of up to 3 years for infractions.

The new legislation gives deliberative power to the Brazilian National Biosafety Technical Commission, which approves all research on GMOs. A new Brazilian National Biosafety Council will propose further regulation for activities related to GMOs.

The Brazilian Catholic Church, a strong opponent of the new law, says using stem cells from embryos for research is ''unprecedented in human history and unethical.'' According to Cardinal Geraldo Agnelo, President, Brazilian National Bishops' Conference, ''the debate should continue, as the legislative process through which the proposal will become law is not yet completed.''

Claudio Csillag

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EUROFILE

Dissenters win Radical Overhaul of the Services Directive

The European directive aiming to provide an open market in the provision of services has been one of the hottest potatoes in the current legislative programme. Criticism of the Services Directive has come from all quarters, with some parts of the medical profession being particularly outspoken. The result is that the directive is likely to be redrafted, after heated discussion in the European summit at the end of March 2005.

One of the voices raised most loudly in dissent has been the British Medical Association, which has been pushing for health and healthcare services to be removed from its scope. ''We sympathise with the aims of the Commission to improve competitiveness and growth but remain to be convinced that these goals should apply to health services based on solidarity, equity and universality'', said a spokesman.

The root of the problem lies in the desire of the Commission to make it easier for professionals to work across Europe, thus putting into place the final of the four 'basic freedoms' enshrined in the 1957 Treaty of Rome: free movement of people, goods, capital, and services. In effect, the plans mean that health would be treated in the same way as any other commercial service, from IT professionals to estate agents. Under the new rules, service providers registered with their own national regulators would be able to operate throughout the union from their home

''THERE COULD BE A RACE FOR THE LOWEST STANDARDS''

base. This would mean that companies from countries with less strict regulation could run clinics, for example, in countries where standards are much higher, but that those standards would not be enforced for fear of jeopardising competitiveness. ''There is a real danger that there could be a race to the bottom in terms of standards'', said Beverly Malone, general secretary of the UK's Royal College of Nursing, ''with unscrupulous companies setting up in countries with the least rigorous regulation in order to then maximise profits elsewhere.''

The medical profession was not the only one to be concerned. Governments in Austria, Belgium, France, German and Austria were worried that the legislation would lead to 'social dumping', where a professional coming from a country where rates are lower could undercut his colleagues in another member state. Now the Directive is to be radically overhauled, and all the signs are that healthcare will be excluded. It is, after all, a national rather than a European responsibility, coming under the umbrella of subsidiarity – the principle whereby the EU does not take action (except in the areas which fall within its exclusive competence) unless it is more effective than action taken at national, regional or local level.

Initially the Commission put up a fierce fight in support of its plans. In a public hearing organised by the European Parliament in November, a senior official said: ''The commission understands the particular sensitivity of health. It accepts that the implications are not entirely clear and that the text needs to be improved. However, the draft legislation will not require member states to change the way they organise and finance their health systems.''

Healthcare workers remained unconvinced by the commission's explanation. Just two days after the Brussels hearing, representatives from medical associations throughout Europe met and unanimously agreed that the health sector should be exempt from the legislation.

In the light of so much criticism the internal market Commissioner has already announced that the redrafted directive will be likely to exclude healthcare ''and other publicly-funded services of general interest.''

Among those hoping for a change of heart has been the Association of European Cancer Leagues. Advocacy officer, Cécile Dubois, says: ''The Association of European Cancer Leagues believes that the Services Directive in its current form would not serve the cancer patients and cancer-care community. Besides great concerns about

''THE PROPOSED DIRECTIVE WOULD NOT SERVE CANCER PATIENTS''

the country-of-origin principle, which could lead to a lowering of quality standards in health care and social dumping, we do not feel that the Directive sufficiently answers cancer patients' and professionals true needs.

''Rather than a general, across-the-board directive endangering our health care systems, what we would like to see is more attention devoted to specific issues in health care that would really benefit the cancer control community. This could include the development of a solid network of reference centers across Europe, the facilitation of co-operation between care centers in border areas, and encouraging the establishment of social and financial support systems that take into account rehabilitation and reinsertion of the patient during and after treatment.''

One of the arguments put forward by proponents of the directive has been the advantages that patient mobility would bring. Dubois disagrees: ''We do not believe cancer patients truly want more 'mobility'. What they want is the best possible care as close to home as possible, with adequate psychological, social and financial support, and the prospect of returning to a normal social, economic and family life as soon as possible. The directive as proposed by the Commission would not advance this vision, and in many cases, would undermine patients' right to quality care.''

For reasons of political sensitivity, the chances of seeing the revised draft directive before the French referendum on the European Constitution look pretty slim. It will not be until later in 2005 that the medical profession will be reassured – or not.

Mary Rice
Brussels

New hope for glioblastoma patients

Patients with glioblastoma may benefit from the addition of a novel agent, temozolomide (Temodal) to radiation therapy, according to the results of an international study conducted by European Organisation for Research and Treatment of Cancer (EORTC) in collaboration with National Cancer Institute of Canada (NCIC) Clinical Trials Group. Further, researchers established that molecular analysis of the tumour allowed identification of those patients most likely to benefit.

The 2 papers (*NEJM* 2005, **352,** 997–1003; *NEJM* 2005, **352,** 997–1003) report on a study including 573 patients from 85 centres. They were randomised to receive either radiotherapy alone (5 days/week for 6 weeks) or radiotherapy plus continuous daily temozolomide, followed by 6 cycles of adjuvant temozolomide.

At a median follow up of 28 months, median survival was 14.6 months with radiotherapy plus temozolomide, compared with 12.1 months for temozolomide alone. Importantly, the study also showed that the new combined therapy did not impact negatively on patients' quality of life.

Epigenetic silencing of the *MGMT* (O6-methylguanine-DNA methyltransferase) DNA-repair gene by promoter methylation compromises DNA repair and has been associated with longer survival in patients with glioblastoma who receive alkylating agents.

The study confirmed that *MGMT* promoter methylation was an independent favourable factor. Further, patients selected according to molecular profile benefited the most from the combined regimen. Among 206 who could be assessed, those whose tumour contained a methylated *MGMT* promoter had a median survival of 21.7 months on radiotherapy plus temozolomide; compared with 15.3 months on radiotherapy alone.

Trial initiator Dr Roger Stupp (University Hospital Multidisciplinary Oncology Centre, Lausanne, Switzerland) said, ''This is the first trial to demonstrate that we can truly impact this devastating disease with chemotherapy. This is only a first step toward cure of brain cancer patients and should now fuel interest, continued international collaboration and research to further improve the outcome of these patients.''

Dr Monika Hegi (University Hospital Lausanne, Switzerland) said, ''Without the close collaboration between the hospital based research laboratory and the leading clinicians, this interdisciplinary success would never have been possible.''

Another of the investigators, Dr Warren Mason (Princess Margaret Hospital, Toronto, Ontario, Canada) said the study ''represents the most important advance in the management of glioblastoma since radiotherapy was shown to be of benefit over 35 years ago.'' He said MGMT was ''the first clinically relevant molecular marker for glioblastoma'' serving both as prognostic factor and predictor for response to chemotherapy. ''This observation paves the way for using the unique tumour genetic signature as a guide for individualising therapy and optimising outcome.''

''THE MOST IMPORTANT ADVANCE IN GLIOBLASTOMA FOR 35 YEARS''

- The results of the EORTC study were used as the basis for approval by the US' Food and Drug Administration (FDA). In March 2005, manufacturer Schering-Plough announced that the FDA had granted approval for temozolomide for use in combination with radiotherapy for the treatment of adult patients with newly diagnosed glioblastoma multiforme (GBM). It can be used as maintenance treatment after the patient has completed radiotherapy. It also granted full approval for the treatment of adult patients with refractory anaplastic astrocytoma (AA), who have experienced disease progression on a drug regimen containing nitrosurea and procarbazine. This follows its accelerated approval for the treatment of AA in 1999.

In the European Union, temozolomide is currently indicated for the treatment of patients with malignant glioma, such as GBM or AA, who experience recurrence or progression after standard therapy. Schering-Plough has now filed an application with the European Medicines Agency (EMEA) seeking approval of a similar indication for first-line GBM.

Childhood cancer in Europe

The increase in cancer among children and adolescents reported recently (*Lancet* 2004, **364,** 2097–2105 and see *EJC News* 2005, **41,** 3) may be partly explained by improved registration and changes in the population, researchers say.

A group from University of York, UK, wrote that, given the comparative rarity of childhood cancers, ''small changes can have a substantial effect'' (Lancet 2005, 365).

''The fact that increases were seen across virtually all neoplasms reassuringly supports the view that generalised improvements in registration have occurred. Indeed, given the amount of work in this area, it would be worrying if progress had not been made,'' they said.

Dr Dermot Murphy (Royal Hospital for Sick Children, Glasgow, UK) said population mixing may also play a role. For example, a rise in the incidence of leukaemia in the Orkney Islands followed the influx of workers from around the world, attracted by the oil industry. The children of oil workers were exposed to pathogens their immune systems had not previously encountered, and appeared to be more likely to develop leukaemia.

Population migration is another possible explanation, he said. ''Certain tumours are more common in certain ethnic groups. If you look at the Afro-Caribbean population, Wilms' tumour is more common than in the white or Caucasian population. Over the past 20–30 years, Europe has had an increasing Afro-Caribbean population so it would not be surprising if we were to se a higher incidence of Wilms' tumour.''

A third factor could be a result of recent improvements in survival. A small proportion of tumours has a genetic basis. As more children survive cancer and go on to have their own children, these genes will more frequently be passed on to the next generation.

''I doubt whether there has been a real rise in incidence. It may have been generated by improvements in the collection of data, or these other factors could explain it,'' Dr Murphy said.

PODIUM

The Reorganisation of Cancer in France

Professor David Khayat was instrumental in developing France's National Cancer Plan and is President of France's Institut National du Cancer (INCa). He sits on various French, European and International Committees and has received numerous awards and honours, including chevalier of the national order of Merit.

Professor David Khayat

What exactly is the "War on Cancer"?

On the 14th July 2002 – Bastille Day – President Jacques Chirac announced that he wanted to leave as the legacy from his second Presidency, an appropriate tool to fight cancer. I chaired a committee which assessed aspects of cancer care and research in France.

What did you find?

A significant lack of information on prevention was distributed by public health authorities. Citizens had free access to screening, which was expensive, but it was not organised, co-ordinated or evaluated. Only 25 French departments (out of a total of 100) had organised breast cancer screening and less than 20 had a colorectal screening programme.

Care was provided by cancer centres, university teaching hospitals, private and public hospitals. But they did not communicate with each other and they lacked equipment. The delay after diagnosis before starting chemotherapy ranged from 3 days to a totally unacceptable 180. France had only 8 PET scanners for the whole country. And there was a lack of cancer specialists.

Significant discrimination existed. Patients and survivors lacked access to loans and life insurance.

And in research?

We had 1000 cancer research units and 3500 researchers so the average unit was comprised of 3.5 researchers, which is far too small to compete at international level. Units worked in isolation, and before l'INCa, there was no national platform for research. A total of 1700 clinical trials were running at any one time, but 90% were not able to include enough patients to be completed.

Were there any good points?

France had the longest survival after diagnosis of any country in Europe. People in France had a high chance of getting cancer, but were most likely to get the best treatment.

What has happened since?

In 2003, the committee drew up the National Cancer Plan: 70 proposed measures on prevention, screening, care, social issues, training, and research. President Chirac accepted the advice, and set up l'INCa to implement the Plan. It was given 1.7 billion Euro over 5 years, specifically for upgrading coordination and evaluation.

What is l'INCa's mission?

It co-ordinates and finances cancer research; it is an information centre for patients and professionals; a watchdog on equality of access to treatment and a reference point for standards and best practice guidelines. Centres are evaluated using objective international accreditation criteria and will need authorisation to treat cancer patients – which is given according to type of cancer and of treatment. Some hospitals may only be able to treat breast cancer by surgery. They will have to demonstrate that they take a multidisciplinary approach, have the necessary knowledge, skills and co-ordination, and that patients are satisfied with their care.

How did the Cancer Plan alter the organisation of research?

There are now 7 regional canceropoles, covering France. Each has between 500 and 1500 cancer researchers and the potential of a small country like Denmark. They co-ordinated equipment, knowledge and skills.

Who gives research projects the go-ahead?

L'INCa finances projects through the canceropoles, where co-ordination between clinical and basic research is demonstrated. Researchers share equipment and materials within the canceropoles. Each canceropole has to define a limited number of topics – between 5 and 7 – within which they can compete at an international level.

How has the cancer community at large reacted to such a large-scale reorganisation?

Change has been swift because this is a Presidential endeavour and must be completed within 5 years. French Presidents since Charles de Gaulle have left legacies, from airports to arts centres. The French cancer community is happy with the new system.

What obstacles have you come across in the "War on Cancer"?

The speed with which we have had to work has been an engine, not an obstacle. We haven't faced real obstacles. We had to convince people that something real was happening, that this was not just words. The extra Euro 1.7 billion helped.

Has the "War" made a tangible difference so far?

In 2004, 1.8 million French citizens stopped smoking. By the end of 2003, 100% France was covered by a breast cancer screening programme. By the end of 2005, 100% France will be covered by a colorectal cancer screening programme. Before the end of 2007 we will have 112 second generation linear accelerators and 55 PET scans – that's one per 1 million inhabitants.

Every week, things are moving forward. In March, 2005, we published a document outlining the care that every cancer patient can expect. Each will receive a personalised roadmap: a document explaining what they have and what treatment they are going to receive, stressing the multidisciplinary approach.

For oncologists, how easy is it to train in clinical as well as basic research?

It has become easier. We are funding international postdoctoral fellowships along with the UK, the USA and other countries. Trainees will be able to travel to gain the experience they need.

What is left to do?

Cancer is still seen in bleak, negative terms, and this needs to change. It's a political issue. We can treat and cure patients, but afterwards they are still stigmatised by society, by banks and insurance companies. People lose their jobs, husbands leave wives who have breast cancer. Attitudes won't completely change by 2007, but we're moving in the right direction.