available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejconline.com

NEWS. . .NEWS. . .NEWS

Recognition for medical oncology in Belgium

After 30 years of debate, medical oncology has been recognised as a separate medical specialty in Belgium. The decision is a tribute to increasingly successful cancer treatments and has implications for the recruitment and training of medical oncologists, their continuous education and their role in policy decision-making.

The cause of accreditation of medical oncologist was taken up by the Belgian Health Minister Rudy Demotte. The decision was published on the 14th of June, 2006 (http://www.just.fgov.be/cgi/welcome.pl).

Medical oncologists have applauded the decision. Dr Luc Dirix (General Hospital St-Augustinus, Wilrijk, Belgium),

''POLITICIANS HAVE RECOGNISED THE GROWING SUCCESS OF CANCER TREATMENT''

the current president of Belgian Society of Medical Oncology, said, "It is very positive. We hope that it will encourage more people to train in medical oncology. Young doctors will see that the specialty is recognised by the authorities and take this as an important sign."

The decision taken by Minister Demotte stipulates in some detail the criteria for the formation of the next generation of medical oncologists. Furthermore, it implies that every hospital should employ a medical oncologist, said Dr Dirix. "It is not stated directly but it is implicit. The fact that medical oncology is recognised as a separate specialty confirms that it is quantitatively important and that medical oncologists should be available for patients with cancer."

The decision may have been triggered by the recent progress in cancer treatments, said Dr Dirix: "It is probably this recognition at the political level of the growing success of cancer treatment. Politicians see that there now needs to be an identifiable group of doctors to play an important role in managing this. Increasing drug costs will be a core problem in Belgium as in every country, I presume. More organised decision-making on the use of drugs shouldn't be the exclusive responsibility of medical oncologists but they should be part of the process."

Members of other specialties are less happy with the decision, as it leaves their status unresolved. A proposal to create about a dozen "special competences" in oncology was accepted in 2003. It covered those working in internal medicine and medical oncology; but also those in different specialties such as surgeons, gastroenterologists and gynaecologists who care for cancer patients.

These special competences were discarded when medical oncology became a separate specialty. Efforts were made by the Minister to put arrangements for the other disciplines in place at the same time, but the issue is complicated and has not yet been settled. "Something has to be done for other specialties. It would have made sense to put structures in place for the other specialties simultaneously, but this was not possible. It remains a difficult issue; it is not obvious who fulfils the criteria for surgical oncology, for example. Discussions are on-going, and different criteria such as case-load are being looked at, but it has not been settled yet."

Within medical oncology, the first task is to set up a Certification Board to recognise medical oncologists "so they become identifiable by the authorities. People have been doing this job, but the authorities have not known who they were," said Dr Dirix. Those already working in medical oncology will have

''WE HOPE IT WILL ENCOURAGE MORE PEOPLE TO TRAIN IN MEDICAL ONCOLOGY''

to be signed up; over the past year, Belgian medical oncologists have been encouraged to obtain ESMO certification, and 55% have now passed the examination. Certification also suggests that doctors will have to undertake some kind of continual education.

Further, medical schools will have to incorporate the decision into their curricula. Guidelines proposed by ESMO/ASCO have been adapted and medical oncology training will be comprised of 3 years' internal medicine, followed by 3 years' oncology. "We are hopeful that this will increase the numbers of young doctors in medical oncology," said Dr Dirix.

The Belgian move may help campaigners for recognition of medical oncology in other countries. While it is a separate specialty in much of the former Eastern Europe, in the Netherlands, and throughout much of northern Europe, medical oncology remains a part of internal medicine. "Medical oncology is becoming very important and we hope the decision here may help those elsewhere who are trying to get it recognised as a separate specialty," he said.

EJC News is edited by
Helen Saul
Tel.: +44 1865 843340,
E-mail address: h.saul@elsevier.com

doi:10.1016/j.ejca.2006.07.004

Essential Medicines for Palliative Care

The International Association for Hospice and Palliative Care (IAHPC), in collaboration with other organisations, has compiled a list of 33 medicines essential for palliative care. The work was carried out in response to a request from the world Health Organization (WHO)'s Cancer Control Program.

IAHPC's list is based solely on criteria of efficacy and safety, and is derived from the recommendations and best practice of palliative workers, rather than on evidence-based data. The WHO will now be carrying out cost effectiveness analyses and evidence-based reviews of the recommended medications. The WHO has a Model List of Essential Medicines, but its section on Palliative Care does not at present list any medications.

To formulate its list, the IAHPC formed a working committee which included board members of IAHPC and external advisors from the field. They agreed on the most prevalent symptoms in palliative care and, based on suggestions from physicians from around the world, drew up a first list of 147 products used to treat these symptoms.

The number of products was reduced following an on-line survey of 112 physicians, who were asked to rate the safety and efficacy of each medication. This modified Delphi process produced a second list, which was presented at a meeting in Salzburg, Austria.

Representatives from 26 international palliative care and pain relief organisations attended the meeting. They were divided among 3 working groups to consider, respectively, medications for mental health symptoms, pain and gastrointestinal symptoms. "Orphan" symptoms such as hiccups were randomly assigned to each group.

The final IAHPC list was agreed at the meeting. It includes 33 medications, of which 14 are also included in the WHO's Model list for the treatment of conditions such as pain or nausea, which are part of palliative care.

Dr Kathleen M. Foley, chair of the Board of IAHPC, said, "The provision of adequate palliative care is dependent on access to treatment and medications and we hope that this list serves as a reference to palliative care providers and institutions around the world. We also hope that the WHO will include the recommended medications in the Palliative Care section of its Model List, consonant to its renewed interest in improving access and availability of palliative care."

The list is to be published in several journals, after which the IAHPC will ask organisations, institutions and individuals to help disseminate and promote it. They are free to use, adapt, change and improve the list to fit the needs of their patients.

IAHPC will encourage countries to use the list as a model and develop their own list of medications for palliative care, tailored to meet the needs of their patients and taking into account their own resources and available medications. Additional debate and discussion will be encouraged to move the list forward, improve it and find ways to improve access to these medications.

Dr Derek Doyle, founding member and advisor to IAHPC, said that research findings, changes in practice and constructive comments from palliative care workers worldwide would be taken into account, and the list reviewed and revised on a regular basis.

He stressed the importance of ensuring that prescribing physicians and pharmacists are made aware of the costs of drugs on the list, compared

continued on next page

Table 1 – The IAHPC list of essential medicines for palliative care

*Amitriptyline**	Depression; Neuropathic pain
Bisacodyl	Constipation
Carbamazepine*	Neuropathic pain
Citalopram *(or any other equivalent generic SSRI except paroxetine and fluvoxamine)*	Depression
Codeine*	Diarrhea; Pain – mild to moderate
Dexamethasone*	Anorexia; Nausea; Neuropathic pain; Vomiting
Diazepam*	Anxiety
Diclofenac	Pain - mild to moderate
Diphenhydramine	Nausea; Vomiting
Fentanyl (transdermal patch)	Pain - moderate to severe
Gabapentin	Neuropathic pain
Haloperidol*	Delirium; Nausea; Vomiting; Terminal restlessness
Hyoscine butylbromide	Nausea; Terminal respiratory congestion; Visceral pain; Vomiting
Ibuprofen*	Pain – mild to moderate
Levomepromazine	Delirium; Terminal restlessness
Loperamide	Diarrhea
Lorazepam	Anxiety; Insomnia
Megestrol Acetate	Anorexia
Methadone (immediate release)*	Pain - moderate to severe
Metoclopramide*	Nausea; Vomiting
Midazolam	Anxiety; Terminal restlessness
Mineral oil enema	
Mirtazapine *(or any other generic dual action NassA or SNRI)*	Depression
Morphine*	Dyspnea; Pain – moderate to severe
Octreotide	Diarrhea; Vomiting
Oral rehydration salts*	Diarrhea
Oxycodone	Pain – moderate to severe
Paracetamol (Acetaminophen)*	Pain – mild to moderate
Prednisolone (as an alt to Dexamethasone)*	Anorexia
Senna*	Constipation
Tramadol	Pain – mild to moderate
Trazodone	Insomnia
Zolpidem (still patented)	Insomnia

* Denotes medication also included in WHO Model List.

EUROFILE

Stem Cell Debate Could Block FP7 Funding

Whether or not research using human embryonic stem cells should be funded under the next EU Research Framework Programme, FP7, has been the subject of debate for months. A long-term failure to agree – which could hold up the entire funding for FP7 – looks more and more likely.

In June, 2006, the new Italian research minister, Fabio Mussi, announced that Italy would no longer block funding for such research. This would dismantle the previous blocking minority of six member states in the Council. Members of the International Society for Stem Cell Research and the European Consortium for Stem Cell Research, applauded what they called "an honourable decision" that would ensure that "Italy is no longer blocking scientific progress for universal benefit."

Later the same month, the European Parliament voted to continue the status quo under FP6, allowing the EU to fund stem cell work permitted under member states' own legislation. Many began to believe that things were looking hopeful and that a way out of the impasse would be found.

But now things have changed again. Lithuania and Slovenia look likely to join Germany, Austria, Poland, Malta, Luxembourg and Slovakia to form a blocking minority that could hold up the legislation. With 90 Council votes needed to prevent agreement, between them these member states have 91. This effectively means that the whole research budget for FP7 could be blocked indefinitely.

Even the Parliament's stance is far from being a foregone conclusion. The Strasbourg plenary on June 15, 2006, narrowly rejected amendment 319 which would have restricted funding to research on stem cell lines created before 31 December 2003 – the date at which a previously agreed moratorium for such funding expired. The voting was 274 against and 255 in favour with 35 abstentions. But MEPs were asked to vote on another amendment (354), which would have barred all funding for stem cell research, and this split the vote. If all those who had supported amendment 354 had supported 319, opponents would have had a majority.

Interestingly, the vote seemed to be divided more along national than party lines. The proposers of the two blocking amendments were both from the European People's Party (conservatives), but some Socialists supported 319 and two British Conservatives – Malcolm Harbour and John Purvis – were responsible for drawing up the successful amendment aimed at maintaining the current rules, which was adopted by 284 to 249 votes, with 32 abstaining.

Angelika Nieblier, a member of the Parliament's Industry, Research and Energy Committee, who proposed amendment 319, thinks that many Parliamentarians remain unconvinced. "They believe that FP7 funds should only be used for projects that are not prohibited in some member states", she said.

''FP7 SHOULD NOT FUND PROJECTS BANNED IN SOME STATES''

Whether Parliamentarians are thinking along the same lines as those who elect them is unclear. To try to find a compromise on the issue before the vote, Science and Research Commissioner Janez Potočnik was asked to permit the early release of the results of a special Eurobarometer on biotechnology to indicate the public opinion on this issue. "55% of Europeans approve embryonic stem cell research under the current government regulations, 17% under some extra conditions, 9% declare not to approve it under any conditions and 15% say they don't know," he said.

Whatever happens, it looks as though the blocking minority of member states will hold out on the issue. Some member states believe that Germany has brought pressure to bear on the smaller nations, with Slovenia's decision being a particular surprise. The views of the German research minister, Annette Schavan, would seem to bear this out: "We reject the funding of embryonic research and incentives for the killing of embryos." In November, 2005, Germany was one of six signatories to the Declaration of Ethics, which calls on European institutions to prevent research projects involving human embryos and human embryonic stem cells from receiving funding under FP7. Germany was intending to consider the draft legislation and debate it with other member states in July, 2006, she said. Not everyone in Germany agrees with Schavan's views. Ernst-Ludwig Winnacker, president of Deutsche Forschungsgemeinschaft (DFG) the German basic research public funding agency, would like to see an easing of restrictions governing the import of stem cells. He pointed out that, in any event, plans for FP7 would ban the most hotly-debated applications of stem cell research, reproductive and therapeutic cloning.

Others have been more outspoken. Bob May, a member of the European Research Council's scientific council, said that the "tyranny" of the blocking minority should not be allowed to hold up FP7. "Once you allow that particular minority to subvert the basic agenda of the EU then there is no end to it – who knows what comes next?"

Mary Rice
Brussels

Essential Medicines for Palliative Care – *CONTINUED*

with more expensive competitors with equal therapeutic benefit.

"Every effort should be made to get charities supporting palliative care to encourage recipients of their funds to use the drugs on the essential medicine list in preference to more expensive ones with equivalent therapeutic benefit," said Dr. Doyle. "All trainees in palliative care – whether medical, nursing, pharmacy, clinical psychology – should be made aware of the IAHPC Essential Medicines List for Palliative Care, should expect to be examined on it, and understand why drugs were selected for the list."

A full report of the process involved will be published as a chapter in the next edition of the Oxford Textbook of Palliative Medicine.

Salvage radical prostatectomy is second chance of cure

Salvage radical prostatectomy should become the treatment of choice in selected patients after failure of radiotherapy, say Belgian researchers, who have analysed their own 15-year data (Eur J Surg Oncol published online Jun 29, 2006; DOI: 10.1016/j.ejso.2006.05.015).

In the 11 patients who underwent salvage radical prostatectomy, biochemical disease-free survival was 55% and overall and cancer-specific survival was 91%, after mean follow-up of 6.9 years. Mean age at surgery was 60.5 years and mean time to salvage surgery was 36.9 months. Continence was no worse with salvage radical prostatectomy than with initial radical protatectomy, and bladder-neck stricture was the most common postoperative complication.

Salvage radical prostatectomy offers patients a "second chance for cure", in carefully selected patients, the researchers conclude.

Lead author Jochen Darras (University Hospital Leuven, Belgium) says that with increasing popularity of radiotherapy, a substantial rise in the incidence of recurrent prostate cancer after radiotherapy was to be expected. "In the last 5 to 10 years, brachytherapy has become more and more popular as a treatment for localised prostate cancer. Logically, within the next decade, a certain number of these patients will suffer from recurrence. I think that a salvage prostatectomy can offer them a second chance for cure, while hormonal therapy will not cure them."

Darras adds that the perfect candidate is a young, healthy, and motivated patient, who is willing to cope with possible side-effects (incontinence, impotence), life expectancy of more than 10 years, initial and presalvage prostate-specific antigen concentration (PSA) of less than 10 μg/L, and an initial clinical stage no higher than T2.

James Eastman (Memorial Sloan-Kettering Cancer Center, New York, NY, USA) agrees with this conclusion: "The key is patient selection to optimise the likelihood of cure and preparing the patients for potential [postoperative] complications. External beam [radiotherapy] and brachytherapy are excellent options for prostate cancer. There will, however, be a certain percentage of patients who fail radiation therapy. As more men opt for initial treatment with radiation therapy, the absolute number of men who fail will increase, thus, the number of men who are potential candidates for salvage radical prostatectomy will increase."

However, data from larger patient series at Eastman's institution suggest that outcomes after salvage surgery are much improved with low presalvage serum PSA, preferably less than 4 μg/L.

Emma Wilkinson

*This story originally appeared in Lancet Oncol 2006;**7**:622.*

Heart damage "worsens over time"

Long-term follow-up of children and young adults who had doxorubicin treatment for bone tumours suggests that the damage gets progressively worse as the years go on. Researchers from the University of Groningen, the Netherlands, say that all patients treated with anthracyclines should have life-long cardiac monitoring.

They followed 22 patients, who were treated between 1977 and 1999, for a median time of 22 years (15–27.5 years). Their median age was 39 years. In the most recent assessment, 45% had diastolic dysfunction, compared with 18% in 1997. Further, 27% had systolic dysfunction, compared with 9% in 1997; these patients also had abnormalities in the motion of the heart wall with suggestions of ischaemic heart disease in two patients.

Lead author Dr Inge Brouwer said, "Our results suggest that after treatment with anthracyclines there is an ongoing deterioration of cardiac function and it is possible that this deterioration will continue, although we don't know if and when there will be further progression."

"It is important to be ready to treat cardiovascular risk factors and to encourage patients to make helpful lifestyle changes."

Extended indication for anastrozole

The aromatase inhibitor, Anastrozole (Arimidex), has been approved to treat breast cancer in women who have already received 2 to 3 years of adjuvant tamoxifen. The new indication covers its use as an adjuvant treatment for postmenopausal women with early hormone receptor positive breast cancer. It was previously licensed only as a primary adjuvant treatment.

The approval was granted through the EU's Mutual Recognition Process, with the UK acting as the reference Member State. The new indication is therefore granted in the EU Mutual Recognition Markets: the UK, Germany, Austria, Portugal, Italy and Spain.

Tamoxifen and Mortality

Tamoxifen as a breast cancer prevention drug has little impact on overall mortality for most women classified as high risk, say US researchers. Only those at the highest risk (greater than 3% 5-year breast cancer risk) – and those who had previously had a hysterectomy – experienced increased life expectancy.

Dr Joy Melnikow (University of California, USA) and colleagues used a modelling strategy to look at data from the large US chemoprevention study into tamoxifen. They considered tamoxifen's effect on survival, rather than on breast cancer risk (CANCER 2006 DOI:10.1002/cncr.22075).

They found no mortality benefit for women at the lower end of the high risk range for breast cancer. When they took into account oestrogen-receptor negative cancers – which has not been done before – mortality rates actually increased slightly until 5-year risk reached more than 2 percent. "The projected benefits of tamoxifen for women at or near the threshold risk for breast cancer (1.67 percent are very small or non-existent," they concluded.

Moreover, the authors point to the "extraordinarily high cost" of the intervention in the US, where average wholesale price for the drug is US $ 1212 per year. They calculate a cost of US $ 1,335,690 per year of life saved.

PODIUM

Two Novel Agents, One Trial

Professor Laurence Baker

Professor Laurence Baker (University of Michigan Medical School, Ann Arbor, USA) is Chairman of the US' Southwest Oncology Group (SWOG) and Executive Director of Sarcoma Alliance for Research through Collaboration (SARC). He recently established a joint US-European investigator-led trial, with 2 experimental arms.

What is the background to this innovative trial?

The Connective Tissue Oncology Society (CTOS) was set up a dozen years ago and includes both Europeans and North Americans. But a line was drawn, with Americans on one side believing that Europeans are slow and conservative, and Europeans thinking Americans are cowboys, always changing the rules. A few years ago, Jaap Verweij (Erasmus Medical Centre, Rotterdam) and I realised mid-argument that we have more in common than we have differences. We have been working towards setting up joint US/European clinical trials.

What effect has working together had?

It has made Americans more careful about definitions – we started to use European definitions – and the Europeans, much bolder about treatment. The Americans also saw the value of European organisations like EORTC, and several of us set up SARC which is not-for-profit, with a broad membership, and has European board members.

How far does the pharma industry influence the research agenda?

Clinical trials in an uncommon cancer like sarcoma are too often directed by drug companies, whose principal goal is to bring a drug to market. Our primary goal is to improve the care of patients. That might include bringing a drug to market, but only if the drug clearly improves care. When our goals overlap, we can work together.

How did the new trial come about?

The first drug – owned by the Spanish company PharmaMar in partnership with Johnson & Johnson – works, however, despite completion of a number of trials, neither EMEA nor the FDA have approved the drug. J&J and PharmaMar eventually came to SARC and agreed to fund an investigator-led trial. This will be our first international trial.

The second drug is owned by a biotech company, Ariad, in Boston. Ariad wanted to run a trial of almost identical design. Both companies used the same specialists to advise them, and we said we would prefer to do a 3-arm study. One arm would be the J&J/PharmaMar drug; the second, the Ariad drug; the third, the control group. This design minimizes the number of people in the control group, so it is to the patients' – and their clinicians' – advantage.

And Ariad agreed?

At our annual meeting prior to ASCO this spring, SARC firmly upheld our position. We run our meetings with drug companies present, because it should be a partnership, not an antagonistic relationship. Our members universally agreed to the proposition of the 3-arm study, run jointly by SARC and European doctors. Ariad was in the position of either agreeing to this, or running its own trial in competition. It felt like an exercise in shuttle-diplomacy, but in the end it was agreed.

How significant a development is it?

Never in the history of drug development has there been a study like this: 2 experimental arms in the same trial. We are hopeful that both drugs will be proven to be of value, and that we'll bring to market 2 new drugs. It will have saved money and it will have saved on the number patients needed to answer these important questions. A senior person at the US' National Cancer Institute has expressed amazement that we are able to do this. We are hopeful that this will be a model for the future; it is very pleasing.

Are there any restrictions on what you can do in the trial?

The compromise is that we can't compare the 2 drugs directly, because that would be disadvantageous for the companies. The investigators will compare drug A to the control and drug B to the control but not A vs B. If we didn't do that, the companies would never have agreed to it.

What can you say about the trial itself?

We have a start date of March 1, 2007. It will be a joint US-European study, designed, controlled and reported by investigators, and used for the purposes of registration in both Europe and US. European investigators will present data to the FDA, Americans will present to EMEA. We want to demonstrate to regulators that investigators are working in partnership. Our next hurdle is to be certain that there aren't details that EMEA or FDA objects to which would hamper the approval process. We don't want to let arguments over a single point override our guiding principles, and we'll appeal to the FDA and EMEA not to either.

Will this trial design be taken up in other areas?

I hope so; lessons can be learned from uncommon cancers. It can be easier to be inventive and to reach consensus because there are fewer people involved. Those in small groups learn that in order to survive, they must work together.