Tanja Čufer: all the confidence of new Europe

Marc Beishon

Tanja Čufer, based in Slovenia's main cancer centre, is fighting on every front, championing academic research, arguing over the structure of her country's cancer services, agitating for holistic patient care. Far from playing catch-up with the West, she believes countries like hers can help Europe shed the baggage of the 'old fashioned' disease-oriented approach.

New resources to fight cancer – such as buildings, medical personnel, more beds, new equipment – are always welcome at a cancer institute. But on their own they do not represent state-of-the-art of treatment and care. That requires commitment to the best education for incoming young staff, knowledge development for all, high clinical standards, and a level of research that helps to ensure that new techniques are properly investigated and introduced.

It is a theme that Tanja Čufer, senior medical oncology consultant at Ljubljana's Institute of Oncology, cannot stress highly enough as she watches the latest phase of building work going on around her. Over the last 10 years, a modern facility has slowly risen within the grounds of Slovenia's principal cancer centre, where some of the buildings were constructed more than 100 years ago – with one dating back over two centuries.

"The institute was one of the first comprehensive cancer centres in Europe and has a history of conducting good science," says Čufer, who has worked there since 1986. Yet she has had to struggle over many years – during turbulent times and against entrenched interests – to get medical oncology established and to improve cancer care. "New facilities are nice to have, but we need also to maintain those high standards of knowledge and science – and since Slovenia became a democracy, there are competing views and interests about where we need to go with public programmes such as cancer. There is a view that the institute should focus more on primary prevention and treat all people in Slovenia. Or should it be, as I wish, a university centre for education and implementation of new methods of diagnosis and treatment, spreading knowledge and good practice to other hospitals in the country."

There is much at stake for Europe as a whole regarding the future of the countries in Central and Eastern Europe (CEE). As Čufer points out, pioneering multidisciplinary centres such as Ljubljana and the National Oncology Institute in Budapest, Hungary, can provide models for other parts of Europe where oncology specialisms are less well developed. As a recent accession country to the

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European Union, Slovenia's European Parliament members are also bringing great enthusiasm for raising oncology standards in the EU. Most importantly, the involvement of the CEE's cancer centres in Europe-wide research is crucial to improving outcomes in countries with some of the poorest cancer prevention and treatment records.

Čufer notes that no country, even one as small as Slovenia (which has just 2 million citizens), can afford to opt out of front-line clinical research. "If we wait for America and other large countries to develop and implement new treatments we could end up spending a lot of time and money on not very good care," she says. "Medical oncologists, in particular, need to work in research to get acquainted with the efficacy and side-effects of new drugs, such as trastuzumab. Only then, when the drug is available off the shelf, can you treat properly."

It's an approach that the founders of the Ljubljana Institute of Oncology would no doubt approve. Its origins go as far back as 1946, when it was launched as a multidisciplinary centre, and even further back to 1937, when it was known as the Regional Institute for Research and Treatment of Neoplasms. In 1950 the institute set up a cancer registry for Slovenia, one of the first national registries in the world. Fittingly, in September this year Ljubljana will host the annual meeting of the

Slovenia was one of the first CEE countries to recognise medical oncology as a specialty

International Association of Cancer Registries.

For Čufer, one of the most important traditions of the institute is its affiliation with the medical school at the University of Ljubljana, where she is also professor of oncology, and the fact that it was one of the first universities to introduce an oncology curriculum at undergraduate level (in 1947). It is no surprise that of all the top oncologists interviewed recently by *CancerWorld*, she is probably the most active lecturer and teacher, spending at least one day a week on lectures, seminars and journal clubs alone. It was a desire to be part of a profession that has a strong teaching component that spurred her to choose medicine.

"There was no magic moment when I thought I wanted to be a doctor, but I was always interested in natural science, and wanted also to help people and educate others – with medicine you can join all three together." Čufer selected internal medicine as a post-medical school specialty, and was soon attracted by the young science of medical oncology. There were few local mentors – most of her inspiration has come from afar, and she mentions Branimir Sikic, an oncologist with roots in Croatia but based at Stanford, where she spent time as a clinical observer.

It was the perfect subject for developing and disseminating new knowledge, although on a wider stage she notes that there is considerable work to do, especially in countries in southern Europe such as Slovenia. "I gave a presentation at the recent CEE Cancer Patient Summit, *United Against Cancer*, held in Ljubljana last November, in which I described the huge breakthroughs we have made in long-term survival since 1970, such as in childhood leukaemia, advanced testicular cancer, Hodgkin's and in breast cancer, which is my main specialty. But even today many people here – and that includes some doctors – believe that cancer cannot be cured or even treated." To help combat such lack of awareness, she helped the Institute of Oncology to launch a twice yearly educational magazine in Slovenian that goes to doctors in the country.

The presentation at the summit was about the need to promote independent, academic clinical research to continue the success stories in the fight against cancer, and Čufer's career has focused directly on establishing medical oncology as a specialty in Slovenia and creating as many opportunities as possible for her institute to participate in clinical research.

"Medical oncology was finally recognised in Slovenia in 2000, one of the first of the CEE countries to do so," she says. Having up until then been labelled mainly as an internal medicine specialist, one of her proudest achievements has been to see the first certified medical oncologist pass through the institute's residency programme.

That challenge – to ensure systemic chemotherapy is performed by medical oncologists and not by surgeons or radiotherapists – has occupied a lot of her time over the years. While the institute was progressive in many ways in multidisciplinary working – introducing, for example, a psycho-oncology department in 1983 – it has been harder for medical oncology to make its mark. Surgeons and radiation oncologists have tended to hold sway, and cancer care in the country still suffers from early and sometimes inappropriate intervention by surgeons in other hospitals, before patients reach the institute.

It was when Čufer became medical director for the whole institute for a spell in the mid-1990s that she and colleagues were able to push for more specialisation, succeeding eventually with medical oncology. "We tried also to establish surgical oncology as a defined specialty, but did not succeed – that's also a problem Europe-wide," she notes.

In 1997, Čufer also participated in drawing up a national cancer control programme for Slovenia, at a time when few countries had such a plan – now of course there are highly sophisticated cancer plans in place in England and France. Slovenia's

Championing academic research. Čufer *(right)* made a well-argued and impassioned plea for the importance of academic research at the *United Against Cancer* conference in Ljubljana, November 2006. Speaking from the same platform, her compatriot Janez Potočnik *(left)*, the European Commissioner for Research, acknowledged her concerns and called for a dialogue with academic researchers to find a way forward

programme, says Čufer, now needs to be revisited ten years on – she says it was oriented more to prevention and was drawn up to follow World Health Organization criteria. "We did also adopt diagnosis and treatment guidelines from ESMO [the European Society for Medical Oncology] and ASCO [American Society of Clinical Oncology] but what we need are minimal standards we can actually introduce for the population as a whole in Slovenia. We need also to improve screening programmes and services such as rehabilitation. Finance, organisation and implementation are key now."

Wider political issues concerning cancer control within Slovenia and Europe have been steadily rising up Čufer's agenda. Like many young oncologists in the 1980s, it was involvement with European research groups, in particular the European Organisation for the Research and Treatment of Cancer (EORTC), which gave her experience of that wider stage. Now a general board member of EORTC, she first joined the breast cancer and biomarker groups, and has been a driving force to establish translational research at Ljubljana ever since. "We had good basic research but not so much awareness of the clinical and translational side and it was through the EORTC groups that we were able to set up a framework for the resources you need to run clinical trials, such as data management. For us, the 1990s were a golden age for such research – now of course it is more difficult to gain support for independent academic trials."

However, along with her teaching and patient duties, translational research remains a top priority for Čufer. "My main interests are the prognostic and predictive factors for breast and genito-urinary cancers – most of my work has been on breast and bladder," she says. "For example, under the EORTC biomarker group in collaboration with a German team we have done a lot on proteases, enzymes that destroy the stroma of the cancer and help tumour cells to invade the rest of the body. We found that the level of proteases called uPA and PAI1 is a very important prognostic factor – a high level means a high chance of developing metastases and patients need more and different systemic therapy."

This research has been validated in prospective trials and is now level 1 evidence as a marker in breast cancer, she says. Her group is also participating in the European Union's 6th Framework projects on genomic markers.

Like many oncologists involved in research, she is concerned about the future of academic clinical work. For her, key obstacles at present are the European Clinical Trials Directive and the influence of the pharmaceutical industry, the societal priorities for public health in Slovenia, and changing priorities within the medical profession.

On the last point, she says that younger people are not enthusiastic about giving up their time. "They want to know what their responsibilities are on what they are paid for," she notes. Generally,

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there is a shortage of people to help her run the trials she wants to conduct now compared with the situation ten years ago.

As for the Clinical Trials Directive – which coincidentally came into force on the day that Slovenia joined the EU – Čufer is not quite as pessimistic as some about prospects for the academic community. For sure, reports are coming out about a great increase in the cost of running non-commercial trials and a cut back in international cooperation, thanks to concerns about countries interpreting the rules in different ways. "Without pressure from the pharmaceutical industry, the EU directive would not be a threat," she says, "but as it stands it's a tool to move research from academia to industry. That's because it is so much easier for researchers and institutes to take part in industry trials."

However, she considers that there are ways that the pain can be eased. For example, in Slovenia, as in some other countries, comparator drugs are still available off the shelf via insurance. There is also scope for rules to be harmonised among countries. Čufer supports the EORTC line on the directive, that a clear distinction should be made between commercial and academic trials. "In other words, we need trials for drug development and trials for therapeutic strategies that usually demand a multidisciplinary approach." A way needs to be found, she says, for industry to pool funds for independent research – as EORTC notes, just one commercial trial can cost a lot more than many academic studies put together.

"I do feel that things will move our way in small steps. The European Commissioner for Research was at our CEE patient meeting last November and said he is in favour of discussing the way forward with academic researchers." In her capacity as an EORTC board member, Čufer is hoping to help recruit more trial centres in the CEE region and strengthen educational activities on good clinical practice and trial methodology.

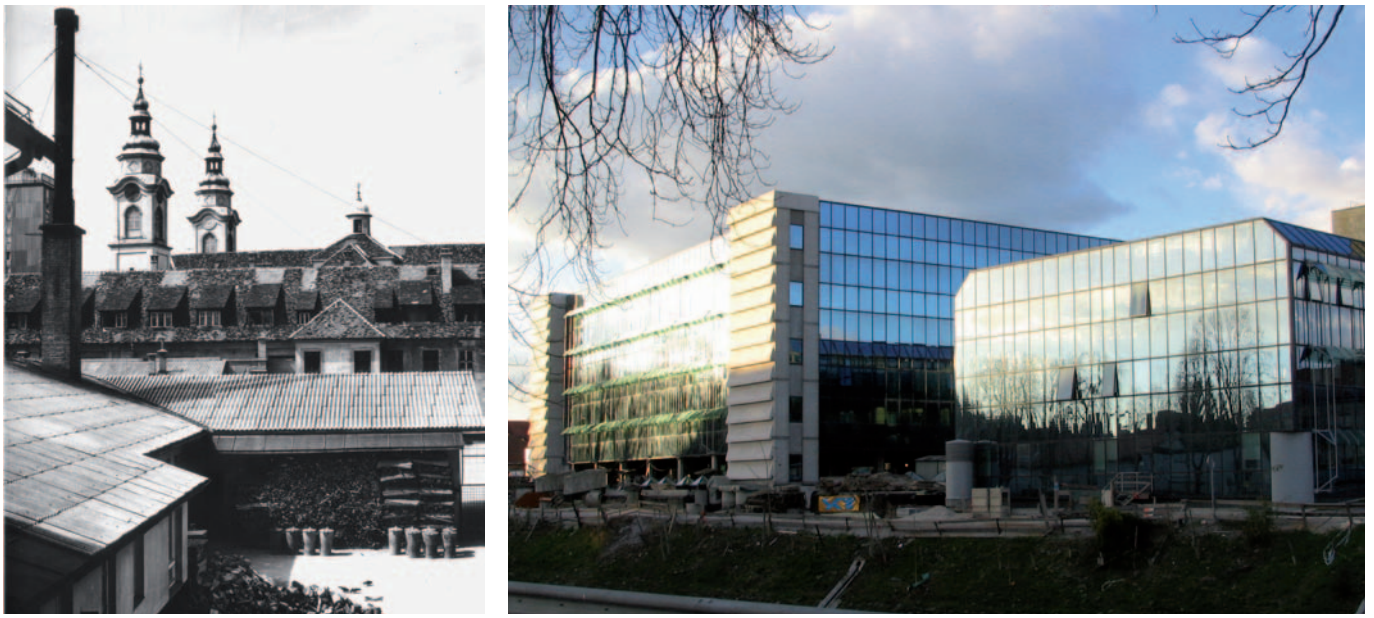
One way this is happening is through the auspices of the Central and East European Oncology Group (CEEOG), set up in 1983 and run for a long time by Sandor Eckhardt from the National Cancer Institute in Budapest, but now headed by Jacek Jassem in Gdansk, Poland, which has grown to include more than 35 centres in the region.

If anything, oncology organisation within the region is increasing during the period of accession to the EU of several countries. Just to confuse matters, there is also the Central European Cooperative Oncology Group (CECOG), based in Vienna, and founded in 1999 (see *Where East meets West*, p32). The previous year, Čufer had helped Branimir Sikic and other colleagues to establish the Central and Eastern Oncology Congress, now held every two years in Opatija, Croatia. "We felt we needed an educational congress for CEE countries. It is primarily a meeting for young oncologists where they can learn more and present their own work.

"Of course the big American and European meetings are crucial, but it's important for local people to gather together and share knowledge. That's just not possible at say an ASCO meeting. The possibilities and priorities for the CEE area are different and we have to recognise limitations."

Another meeting that Čufer highlights is the Interconference Breast Cancer Meeting in Sarajevo, Bosnia (renamed from the Sarajevo Breast Cancer Conference), which runs in the years between the main European breast cancer meeting, and again is mainly educational. The conference is a collaboration between pan-European groups such as the Federation of European Cancer Societies (FECS) and more regional organisations such as CECOG and the Bosnian Oncology Society. "It's very important to develop this event to cover different cultures, and to acknowledge that Bosnia and its science went through a terrible time in the last decade. I think too that people from Islamic countries may feel more comfortable coming to Sarajevo."

Čufer is a regular speaker at such events and,



Ahead of the pack. Launched as a multidisciplinary treatment facility in 1946, the Ljubljana Institute of Oncology is one of Europe's first comprehensive cancer centres . The old Šempeter Barracks (left), where the hospital started its life, is now known as Building A. Patients are cared for in a beautiful modern edifice on the same site (Building H, right)

on the educational front, has also made considerable input to oncology training in Slovenia and at European level. One barrier that needs to be broken down in Europe, she feels, is that some countries still have a common clinical oncology training programme. "The US has been much more pragmatic in my view, as training has followed specialisms for some time, in particular medical oncology or radiation oncology. As the disciplines have grown so much it really is impossible to cope with learning more than one specialty."

There's a solid undergraduate oncology programme at the University of Ljubljana, and the residency specialisms are now medical oncology and radiation oncology, and as Čufer says, medical oncology is increasingly being taught separately around Europe. However, in practice, some countries are still very much wedded to training 'clinical oncologists', usually combining medical and radiation disciplines, while in some cases she comments that practitioners can be far removed from her idea of an oncologist. "In Germany and Austria, for example, some surgeons and gynaecologists are actually administering systemic chemotherapy. I find this unbelievable. I simply cannot imagine how they can follow all the new developments, say, in treating breast cancer. It is an old-fashioned disease-oriented approach, and is more a problem of western Europe – the CEE countries are not so set in their ways and are open to new ideas."

Čufer is firmly behind ESMO's drive to help put an end to this situation by getting medical oncology recognised as a specialism in the European Doctors Directive. "I was involved in the proposal that all countries should adopt medical oncology in the directive, which was put to the European Parliament in 2005 – and we lost by a few votes. Our Slovenian members voted for – but members from some of the larger countries voted against." Another vote on this issue is expected this year.

Čufer speaks highly of ESMO's curriculum and exam in medical oncology and the recertification test, MORA (Medical Oncologist's Recertification Approval), which she helped draw up. As she points out, it would have been overkill to write a theoretical exam for the small number of medical oncology residents in Slovenia, so the country is using the ESMO exam coupled with practical work to award national board certification.

The exam also helps promote mobility for medical oncologists, she adds, and she makes special

The team. Medical oncology tutors and fellows enjoying the sunshine at their Spring barbecue

mention of one of her students, Boštjan Šeruga, who came second out of 193 entrants in ESMO's exam held at the society's 2006 meeting in Istanbul and who is taking up a fellowship at the Ontario Cancer Institute under one of Čufer's close friends, Ian Tannock, a leading Canadian researcher. This was a great achievement for Slovenian oncology, but it's said that Čufer asked him why he hadn't come first – a tribute to the high standards she has set and only an affectionate rebuke.

Like many very experienced oncologists, she emphasises the importance of learning how to 'fine tune' treatment for individual patients, paying particular respect in this regard to the skills of Martine Piccart, head of medicine at the Jules Bordet Institute in Brussels, where Čufer was a visiting professor in 2004. "A usual weakness of younger oncologists is that they are not aware enough of the need for supportive and palliative care. With cancer becoming a chronic disease, often over a long time for some people, we have to find ways to apply systemic, supportive and palliative treatment at the right time. This is where the art of medicine comes in. I always say, 'Don't be an artist before you have a great deal of knowledge and a lot of skills' – it's about working beyond guidelines, applying your knowledge to balance quality of life and survival for an individual."

Čufer has written papers and spoken at several conferences on supportive and palliative care issues, and she has also helped to establish national guidelines for pain control in Slovenia. "We did not even have proper access to opiates for palliative care – there was a fear of morphine addiction and there were restrictions on companies supplying these drugs," she says. "I put a lot of effort to get morphine introduced into the country."

She is firmly against any separation of supportive/palliative care from primary oncology practice, and encourages her students to look at the full spectrum of the cancer cycle in the institute's wards. She also notes that palliative care is sometimes needed ahead of chemotherapy, for example in patients with Hodgkin's lymphoma affecting the mediastinum. However, she points out that it is a challenge to develop the evidence base for supportive and palliative care, given that individuals vary widely in responses and lifestyle, and because of difficulties in follow-up.

In a 2002 paper and presentation on symptomatic and supportive care in metastatic disease, Čufer provided a broad overview of guidelines and issues ranging from preventing emesis, to pain control to fatigue – topics that oncologists often find hard to deal with. The overriding message is that it is the patient and all their symptoms, and not the tumour, that must be treated (see *Eur J Cancer* vol 38 Suppl 3).

This and all the other medical oncology expertise Čufer has built up at Ljubljana, particularly the research, is not unusual in CEE countries, she says. "Oncology knowledge has been quite high.

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Now it is organisation that is lacking." Countries such as Slovenia, she adds, tend to have a model of social medicine that has little room for priority setting, leading to false perceptions that social security systems will pay for everything.

"I always say that cancer is a catastrophe and we must make priorities for it, as in western countries. It is also true that patients are not aware enough of their rights and responsibilities – they do not want to take an active role in their treatment.

"In the past I tried to push too strongly for change – it's hard to stand still when you see no real obstacles to progress. But I've learnt that it takes time to establish standards in a country like Slovenia." When one considers, for example, that major standards such as informed consent and protocol review boards used not to be in place for research, undoubted progress has been made, and despite her current frustrations, Čufer is again cautiously optimistic.

"I'm looking to Europe now to establish common minimal standards for all countries, both old and new Member States, in prevention, treatment and palliative and rehabilitation services," she says. "I also feel we should establish more cross-border cancer care. I don't believe people who say there are too many cultural differences between countries to make common, realistic standards too difficult to achieve." A case in point – she is one of a cadre of professionals putting their name to a position paper on *Guidelines on the standards for the training of specialised health professionals dealing with breast cancer,* on behalf of the European Society of Mastology (*Eur J Cancer*, in press).

She adds, "For us in Slovenia, our best investment is in young healthcare professionals and making it possible for them to spend time in other countries. The problem here is there just are not enough knowledge and opinion leaders."

For her own part, Čufer encourages problem-based learning at the university – Slovenian children are rather too well schooled in learning by rote, she says – and her time could hardly be more committed to promoting the next generation of oncologists.

To let off steam, she goes hiking and skiing, and is married outside of medicine to Bogomir, a computer engineer, and has a son, Gregor, who has just graduated in political science.

In 1997, the Institute of Oncology produced a 60th anniversary book to celebrate its achievements, which noted that its location was once a military barracks. Čufer will be staying in Ljubljana to continue the battle against cancer – and the powers that be – for the foreseeable future.

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