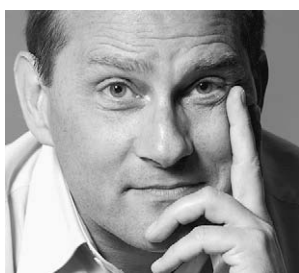


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## News & Views

# An interview with Alexander Eggermont

Janet Fricker



Taking a “helicopter view of oncology” has become the main role of Alexander Eggermont, the first president of the newly reformed European CanCer Organisation (ECCO), who is the driving force behind a new initiative to provide European governments with a “rationale” voice on oncology.

But Eggermont, as head of the department of Surgical Oncology at the Erasmus University Medical Centre, who also holds a Chair of Experimental Surgical Oncology endowed by the Dutch Cancer Society, has done his fair share at the coal face of scientific endeavour. His multiple scientific achievements include helping to establish a TNF based isolated limb perfusion program in Europe, a significant contribution to drug development and clinical trial methodology, particularly in the fields of melanoma and sarcoma, and the establishment of a world class laboratory in tumour patho physiology. Eggermont’s prodigious publication output includes 500 peer reviewed publications, book chapters and monographs.

Professor Eggermont, “Lex” to his friends, is a firm believer of there being a time in life for everything, and that now is his time for shaping the future of oncology. “When I was young I was damned good at the particular line of research I pursued. But with age I slide into a different functioning, and learn that I can have a far greater overall effect with broader brush political strokes than precisely defined areas of research,” he says. “Occasionally one brilliant individual may stumble on something, but in general it’s the interactive process that is leading to the real advances in oncology.”

In a profession whose members are renowned for their dynamism, Eggermont has distinguished himself on the world stage as having a “phenomenal” amount of energy, and

enthusiasm for his projects. Every initiative is considered on individual merit, and triaged on the battlefield of oncology for its contribution to the greater good. Eggermont is invariably known as the person who gets things done, a legacy, he says, of a hyperactive childhood. With a wry laugh, he declines to tot up the number of days he now spends travelling to the US each month for assorted drug development initiatives and international meetings.

Born in Amsterdam in 1952, the son of two language teachers, Eggermont distinguished himself at school, achieving a top school baccalaureate. At the age of 18 he was awarded a Fulbright scholarship to study biochemistry and musicology at the Wesleyan University in Connecticut, USA.

As the ultimate polymath, a student who had the good fortune to be talented in languages, music, literature, and science, it must have been difficult to focus on medicine. “I was cut out to do basic science, but decided to go into medicine to keep my options open. I wanted to do something that would be more interactive at the personal level,” he says.

Returning to the Netherlands Eggermont enrolled at medical school in Amsterdam, then in 1975 won a French government scholarship to study internal medicine at La Pitié-Salpêtrière, in Paris, and French literature and musicology at the Sorbonne. “I was studying at three different universities from 8 in the morning until 10 at night, but still finding time to play in a blue grass band on the weekends,” he says.

The start of his clinical rotations marked the end of this “free floating” time, and he focused exclusively on medicine to the exclusion of everything else. “I’ve never once regretted it. Medicine is a tremendously interesting field, combining fundamental biology, and real innovation with human interest,” he says.

In 1981 he began to work on his PhD thesis looking at interferon and interferon-inducers in the treatment of cancer at Erasmus University, Rotterdam, combining this with his surgical training at University Hospital Rotterdam-Dijkzigt. At the first glance of it surgery appears a surprising choice for someone who had shown such an early interest in basic science.

E-mail address: [janet.fricker@tesco.net](mailto:janet.fricker@tesco.net)

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“For me surgery is the most exciting speciality in medicine, and provided me with the adrenaline rush that part of my personality craved,” he says. “It was a perfect fit with my basic science work which provided the continual challenge of innovation. More than anything else I am obsessed by what medicine will be like in the future.”

Perhaps the most major influence on Eggermont’s career development was the 15 months he spent in the lab of Steve Rosenberg, one of the pioneers of tumour immunology research, at the National Cancer Institute in Bethesda, Maryland, on a Fogarty fellowship. “It was such a golden opportunity. The critical mass of having so many really good people together in one environment created such a feverish environment, and helped me to learn an incredible amount in a short space of time,” he says.

He still holds enormous respect for Rosenberg, undoubtedly one of the main mentors of his career. “He’s the most cited scientist in the cancer world. I don’t think that I’ve ever seen anyone manage time so effectively and still be a nice person. He runs an incredibly tight ship without being a dictator.”

From his American colleagues he learnt the importance of becoming extremely focused scientifically at an early stage in his career, and developing super expertise in one particular clinical area. “The pressure in Europe would have been to stay broad and go for general surgery. But by making myself into a real expert in melanoma I was able to distinguish myself scientifically.”

Returning to Rotterdam Eggermont completed his thesis and armed with an impressive track record of publications from NCI, attracted research funding from the Dutch Cancer Society. He started the slow process of building his research lab up from scratch, at the same time taking a staff surgeon’s post at the Daniel den Hoed Cancer Centre, where he focussed on soft tissue cancers – melanoma, sarcoma, and breast.

“The early years in a science training are extraordinarily difficult. You have to stick to your guns with great fanaticism because there’s a real danger you can die every year,” he says, adding that the only way to ensure long term survival is to have a lucky break. Eggermont is in no doubt that his own lucky break came when he joined the EORTC melanoma group and met Ferdy Lejeune, an oncologist from the Jules Bordet Cancer Institute in Brussels, then chairman of the group.

Tumour necrosis factor (TNF), identified by Lloyd Old in 1975, is the substance secreted by macrophages that attacked tumours. Initially heralded as one of the most promising “magic bullets” in molecular biology’s assault on cancer, by 1985 the chemical was in the doldrums after animal studies showed it was a mediator of septic shock and caused hypotension.

Lejeune, who had been given a stash of TNF by a drug rep, used it to develop an innovative procedure, known as “isolated limb perfusion” (ILP) in patients with intransit melanoma metastasis confined to the limb. ILP involved tying off the affected limb from the rest of the body with a surgical tourniquet to minimise the systemic effects of the chemotherapy, and subjecting the tissues to a combination of TNF, melphalan and gamma interferon. Since the treated limb was attached to a heart lung machine there was no limit to how long it could be exposed to the drug.

Results showed that in melanoma the combination treatment produced a complete response rate of around 80%, and an overall objective response greater than 90%. In soft tissue sarcomas, the technique resulted in salvage in 80% of cases, a complete response rate of 20% and an objective response rate of 80%. Although the procedure could be used to avoid amputation of the limb, then the most common treatment approach, it had no effect on overall survival in either melanoma or sarcoma.

From the outset detractors told Lejeune that TNF would kill patients, and ascribed his positive results purely to patient selection.

“When Ferdy showed me his angiograms of sarcoma patients administered with the local perfusion system I was totally blown away. The results were so spectacular that I became one of the few believers,” says Eggermont, who at the time was in the process of establishing a big sarcoma practice in Rotterdam.

Never to do anything by halves, Eggermont immediately threw the whole force of his energy behind writing protocols for multi-institutional studies and persuaded his own hospital authorities to implement an ILP-TNF programme. “Ferdy and I divided the work up between us. He ran the melanoma perfusion programme, while I ran the soft tissue sarcoma perfusion programme. It turned out to be a big success, and was the start of a very long standing friendship,” he says.

Ultimately the dynamic duo persuaded Boehringer Ingelheim to invest in the clinical programme, resulting in the development of an appraisal file. Together they have expanded the treatment to a network of about 40 cancer centres around Europe, training many surgeons to carry out the technique.

The money raised from the TNF programme Eggermont ploughed into the laboratory of Experimental Surgical Oncology, which he started to build in 1993 in Rotterdam, to study the vessels that feed tumour cells and drug delivery kinetics. The laboratory perfected the technique of intravital microscopy which allows investigators to directly observe the micro-circulation of tumours in animal models.

The technique allowed them to start to unravel the biology and mechanism of action behind the clinical TNF programme, and to look for ways to optimize treatment. “We elucidated basic mechanisms of action that explained the increased drug uptake of chemotherapy and synergy that led to complete vasculo disruption of the tumours due to the TNF and defined other factors to optimize efficacy for the programme, which would have been impossible to do in the clinic. We were able to show that the approach could also work in isolated perfusion of the liver,” he says.

Today the lab, which has the facilities to explore how new drugs interact with tumour models, is largely self financing, and has grown to include 12 PhD students and 8 technicians.

The success of the programme, Eggermont says, has been largely due to his collaboration with Timo ten Hagen, one of his first laboratory assistants, who now looks after day to day running of the laboratory. This collaboration has undoubtedly freed Eggermont up for the international stage, cutting his teeth at the EORTC, first as secretary of the melanoma group, and then as chairman of the group. There he has been closely involved in spearheading the EORTC phase III adjuvant trial programme in melanoma and various vaccination phase I, II and III studies in melanoma.

Melanoma, he says, is proving a hard nut to crack, and still carries a mortality unparalleled by any other tumour in oncology. “Until recently melanoma was considered one disease, where as now we’re only just beginning to realise that it’s five or six different diseases. So long as we continue bunching all these different cancers together with one drug regimen it’s unlikely we’ll ever see an effect,” he says.

This year at ASCO he hopes to present data on a trial giving interferon exclusively to patients with ulcerative melanoma, a subtype of melanoma, that is showing the suggestion of a response.

“Ultimately, I think if we stick to our guns and tease out all the different types of melanoma we’ll eventually make progress,” he says.

AT the EORTC, where he was president between 2003 and 2006, Eggermont streamlined organisation to produce a leaner, more efficient machine, and encouraged translational research to become a mandatory component of trials. His support for translational research has been enabled by a pragmatic approach to interact with the pharmaceutical industry. “My philosophy at the EORTC has been to run large clinical trials in melanoma, that generate money that can then be used to fund translational research projects,” he says.

Another initiative dear to his heart was the creation of the Network of Core Institutions (NOCI), which he spearheaded with current EORTC President Martine Piccart, who invented the NOCI concept. The NOCI consortium agreement, which has now been signed by 25 big European academic institutions, provides privileged access to bio-banking materials and a set of general rules to tackle the challenges of translational research, and to facilitate collaborations, including intellectual property, publication and access rights.

Recently much of his time recently has focussed on the newly reformed European Cancer Organisation (ECCO), of which Eggermont became the first president in September 2007. Formed from the six societies of the Federation of European Cancer Societies (FECS), ECCO set out to open up and expand the structure with additional full and associated member organizations to develop a broad forum for a single voice on European cancer about important issues such as support for clinical research and the need for national cancer plans.

“The idea was to revamp, renovate and expand an old and outdated structure, adding lobbying and advocacy to the educational remit and establish a much broader base,” says Eggermont.

Above all Eggermont has become aware of the importance of getting complex messages about cancer across to Europe’s policy makers, and of getting oncologists to speak with a cohesive voice. The complexity of Europe means that politicians from all the different countries need to know who to consult about the important issues in their country. “The priorities for places like Bulgaria and Moldavia in how to organise infrastructure and access to oncology care are completely different from places like Switzerland or Sweden. It’s just not the case that one model fits all. Politicians need to know who to contact for insider knowledge,” he says. “But without guidance there’s a danger they could just pick people at random from the phone book and get extremely confused by the conflicting sound bites.”

To this end ECCO is establishing the European Academy of Cancer Sciences, to be launched at the ECCO 15–ESMO 34

meeting in Berlin (20–24 September, 2009). Initially, the Academy plans to sign up 20 pre-eminent names in oncology, many of whom are Nobel prize winners, such as Paul Nurse and Harald von Zur Hausen and fathers of Oncology in Europe such as Umberto Veronesi, to act as policy advisers to launch this academy. This, says Eggermont, is just the start, eventually they hope that the committee can be expanded to 400 or 500 cancer scientists with representation from each country in Europe.

Such initiatives, he hopes, will go some way to help break down perceived conflicts of interest between scientists and politicians. “Far too few politicians are scientists, it’s a type of world they don’t feel comfortable with, and all too often feel distrust instead of admiration. This is really sad because that politicians need to realise that it is only scientists who are going to solve big issues like cancer and the green house problems. Politicians on their part are needed to build public awareness and created politically supported programs,” he says, adding that he was greatly cheered by Obama’s inaugural speech. “The fact he said science should be brought in a central position in society in the first two minutes was completely spot on, and we wait for European politicians to follow suit,” he says.

But Eggermont feels disquiet that under the banner of personalised and targeted therapies, advances in oncology may have been oversold to the public.

“The tumours that involve just one type of pathway, like GIST and CML, are sadly rare,” he says. “In reality the majority of tumours are extremely complex, involving multiple pathways. Rather than solving the problem it’s likely that we’ll just discover the next level of complexity.”

Eggermont also values his involvement with the American Society for Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO), where he has chaired the Melanoma Program Committee and international Affairs Committee. “The two things that I’ve really learnt from US colleagues are the importance of speed in decision making and of finding creative ways to put money into important projects. The real advantage of international collaborations is that it allows you to cherry pick the best aspects of each culture,” he says.

Today Eggermont is renowned for managing to juggle an extraordinary number of activities, keeping all his balls precariously balanced in the air. This flexibility, he says, is largely achieved by keeping his own diary. “At any moment there can be a last minute change in the agenda on the way to the airport so I need to be in control of myself,” he says, adding that one of the main advantages is that it allows him to consider every activity on its individual merit. “If I consider that something is more important than another project I’m immediately able to prioritise and move it up the agenda.”

Recently he carved four weeks out of his schedule to chair the Deutsche KrebsHilfe International Comprehensive Cancer Center Accreditation Committee that has established a network of nine comprehensive cancer centres in Germany. He’s also relishing the prospect of a new project with the European School of Oncology where he will be setting up outreach programme to EuroAsia and the Arab world. “The plan is to set up good organisational structures, rather than to give lectures. As the old saying goes: “It’s better to teach people to fish than to bring them a fish,” he says.

Asked what he does to relax, Eggermont somewhat surprisingly says "surgery". Even today with his busy transatlantic schedule, he continues to perform the isolated limb perfusion programme, operating for one day every three or so weeks. "The operating theatre is my sanctuary. It gives me protected time away from other interruptions. In surgery you start a job and finish it that day providing instant gratification, unlike the research where progress usually comes in small incremental steps."

In any free time family takes priority. Every year he blocks out six to eight weeks in his diary for holidays with his wife

Carola, their 20 year old son Rogier, a medical student, and their sixteen year old twin daughters Celeste and Eline. Holidays are spent skiing, scuba diving, and visiting a range of different cultures to give the children a greater understanding of the world. He is full of admiration for his wife's double agenda, combining running the family with a busy career as an endocrinologist.

With his fingers in so many various pies does Eggermont ever have a sense of spreading himself too thin? "I'm fortunate in not having had too many things go into apoptosis. As long as things are work there's just no sense in letting them die," he says.