José Baselga: playing to Europe's strengths

Marc Beishon

It took José Baselga just a few years to build the oncology department at Barcelona's Vall d'Hebron hospital from a few shabby consulting rooms to a leading centre for research into targeted therapies. Europe has the edge in this type of research because we are better at working together, says Baselga. But we still have a lot to learn from the US.

The European oncology community had better get its act together – or suffer more years of fragmentation, underfunding and overburdensome regulation. It's a strong message delivered by the quietly spoken José Baselga, head of oncology at the Vall d'Hebron hospital in Barcelona, and professor of medicine at the associated medical school at the Universidad Autonoma de Barcelona.

He speaks from a position of considerable strength and experience. Not only did he spend more formative years than most immersed in one of the top facilities in the US, but he has also put Vall d'Hebron on the map as one of the major translational research and cancer treatment centres in Europe – from a standing start.

"We must realise that medical oncology is still a new field – it is not even recognised as a speciality in countries such as the UK," he says. "It is no good pretending we are strong when we actually lack strength at the European level compared to the US. But a lot of top oncology work is European in origin. I don't want to copy what happens in the US but play to our strengths, in particular our capacity for cooperation and partnership. But we need to become far more professional in our organisation, training and fundraising."

All of those factors have been promoted by Baselga in the nine years he has been in Barcelona. Half his time is taken up with the ongoing transformation of what was a tiny oncology effort into a major cancer treatment base for the province of Catalonia, such that 40% of all breast cancer patients in the region, for example, are now seen at the hospital.

The other half of his work is translational clinical and pre-clinical science – probably the area of cancer research that is weakest in general wherever you go. "We have a huge effort here on early clinical development of targeted therapeutics," he says. "We do a lot of pre-clinical and phase I trials on new compounds and we have been blessed to have been involved with a large number that are now on the market."

It all suggests that Baselga is well plugged in to both the many organisational issues that go

ELIGIO PAOLI / CONTRASTO

"I don't want to copy what happens in the US but play to our strengths – our capacity for cooperation"

With his mentor John Mendelsohn (*left*), at the MD Anderson Cancer Center, Houston, Texas, last June, where Baselga was awarded the 2004 Waun-Ki Hong Visiting Professorship

into running a cancer centre, and the clinical research areas most likely to yield promising results. There's always a certain degree of good fortune involved, but what is clear is that he has been able to marry the scientific work he built up from his time in the US with the advantages of working in a public health system in Spain.

Baselga went to medical school at Vall d'Hebron – his background at the university hospital was one factor in his eventual return. "I absolutely fell in love with internal medicine and began to be attracted to oncology." Like many, he saw cancer as a huge challenge. "But the early 1980s were fascinating times – oncogenes were just being discovered and for the first time we had the promise that the molecular basis of cancer was going to be found."

His curiosity led to a request for an 'elective' to a cancer centre, which was granted and Baselga duly asked what would be a good place to go to. "They said 'America,' and I went off to the Memorial Sloan-Kettering Cancer Center in New York, which I'd never heard of."

Initially he was accepted only for a three-month rotation, which confirmed his feeling that oncology was a fascinating subject and one he wanted to pursue. To do so in the US, however, he had to work his way back through internal medicine via internship and residency positions elsewhere in New York, his Spanish qualification not being accepted. He then applied for a three year medical oncology and haematology fellowship at Sloan-Kettering and was successful.

"In the second year of the fellowship I had to choose a mentor and was very lucky to have John Mendelsohn, then chair of medicine – he had produced the first anti-epidermal growth factor receptor (EGFR) antibodies. I became involved in laboratory studies on EGFR antibodies, and gained grants and ran clinical trials."

What happened next was the kind of break

that Baselga would now consider essential for any aspiring medical oncologist. He was offered a faculty position at Sloan-Kettering, but because of visa restrictions he was unable to take up the post until a waiver was arranged. This took about two years. "In the meantime I had no licence to treat patients and that was wonderful because I spent all my time in the lab. What happens with medical oncologists is we get pushed all too soon into clinical duties – which is what we like and what we do best – but it's important to work in the lab too." Today at Vall d'Hebron, he won't give clinical jobs to people unless they have spent at least two years in the laboratory.

"I did feel frustrated that I couldn't see patients like all my peers – but looking back it was great because I was so productive in the lab. At the time the HER2 antibodies had come out and John Mendelsohn had received Herceptin [trastuzumab] from Genentech to study. It was fascinating to see its effect on breast cancer cells and we became involved in the phase I and II trials of Herceptin, and I was principal investigator on the phase II single agent trial where we saw the first sign of activity."

After his visa waiver came through Baselga took up his faculty post, continuing his joint lab and breast service work. "I'd done the hard part and got my qualifications, green card and faculty job and I thought I'd now stay in the US. I was publishing well and the research was exciting."

But by then he'd met and married his wife Silvia, a Spanish economist and also from Barcelona. They'd had their first child and she wanted to return home, and fortuitously Baselga was sounded out for the opportunity to head the development of the new oncology centre at Vall d'Hebron. At first, it seemed like a hard decision for him. "I was involved in leading the clinical development of EGFR and HER2 antibodies and was giving up a lot. But there were frustrations in New York about the capacity to do good translational clinical science. It was extremely difficult to enrol patients in clinical trials because of the regulatory atmosphere, and tremendous difficulty in getting funding."

There were also, adds Baselga, difficulties in simply getting people to work together at Sloan-Kettering. "It was very hard for me to have, for example, a good working relationship with the pathology department. I did try very hard to run biopsy driven studies to look for biomarkers of activity in tumours – but I couldn't do it."

He puts this down to the professional and cultural structures in the US – "Still the same today I hear" – and says that team working is much better at Barcelona and indeed in other parts of Europe. "So I came here not only to build the oncology effort but also because I was convinced I could do superb translational science here – and that's been true. If you look at my CV you'll see that my best translational work has been done at Vall d'Hebron. I don't feel deprived of new compounds here – quite the reverse. Just look at the number of trials we are doing here."

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In fact, no fewer than 55 trials were running in early 2005, including 15 phase I trials. This level of activity has not been possible in the US, which has been the subject of much soul searching. While European trials involvement is also patchy, Baselga's experience indicates that the barriers here are more easily overcome.

Baselga does, however, recognise the enormous advantages the US has in basic science and cancer care, albeit marked by a big social divide driven by the medical insurance system. "Memorial is full of excellence – they have many superb research scientists working there. They

At home with his family

have huge funding and vision and also many physicians working in clinical care. Overall, the US model has heavily influenced my career and that of many others in Europe."

The authorities at Vall d'Hebron were fortunate to find Baselga before he became too entrenched in the American research community, although he was young for such a move – just 37. "There's a point of no return once you are on the career path to full professor and your family is settled over there," he says. "Apart from the timing, I also had the advantages that I knew the hospital well, having been a student here, and am from Barcelona. But many times people come back to Spain from the US and other parts of Europe and have failed. If I'd have come back with a US mentality I would have failed too."

Certainly, he knew that the oncology department at Vall d'Hebron was the Cinderella of the hospital – relegated to a few shabby consulting rooms in an old part of the large complex, which is located on the edge of Barcelona. "First I set out to recruit my closest collaborators – people who shared my vision and were prepared to roll up their sleeves, such as the head of research at the oncology department, Joaquin Arribas, who was also at Sloan-Kettering. He was brave enough to come here to build the first oncology lab."

Next, Baselga created a clinical trials programme. "We set out to get involved in some important phase III trials, such as for Herceptin, for which I'm very grateful to Genentech. I met with the faculty and said I'd started the phase III Herceptin trial at Sloan-Kettering and we had an opportunity to translate the protocol here – an opportunity that will very seldom come along. It took many months and we were far behind – but we entered more patients in the trial than Memorial did.

"From the start we built a clinical trials effort in pursuit of excellence and it sent a signal to the oncology community, although we were lucky that the first results were positive and so we got extra visibility – we were co-authors on the *New England Journal of Medicine* papers on Herceptin.

"The other thing I did was try to instil a sense of pride in the staff who had been there for years. We had some great professionals who had little self-esteem – they were just pushing chemotherapy. I said to them: 'This is medical oncology, this is the future and you're good and we have to do a good job' – and they began to join societies and I helped them design trials of their own and get published."

At the same time Baselga was working on obtaining more resources and funding – and the rapid ramp-up of trials work was a key factor. "In 1996, we were number 23 of all the research groups at Vall d'Hebron in terms of impact [i.e. papers and citations]; by 2002 we were number one and were given more resources. It's been a huge victory – and now we are also the largest oncology trials site in Spain by far."

Between 15% and 20% of patients are now in trials – "It's easier to do research in a public health system, and Spaniards are interested in participating. We also make sure that patients in trials are very well taken care of – they get the best nurses and superb physicians." With approval and budget restrictions, enrolling in trials is also the only way that some patients can access treatments such as taxanes, he adds.

Essentially, Baselga has continued his work on molecular targeted therapies and signal pathways at Vall d'Hebron. "When I started here the only agents available were anti-EGFRs and Herceptin, but then came the tyrosine kinase inhibitors and we jumped on them, doing a lot of studies on selecting the best dose and patient

populations." His recent and current work now read like a roll call of new agents – trastuzumab, cetuximab, gefitinib, erlotinib, EMD 72000, *Ras* inhibitors and a variety of anti-angiogenic agents – and his team has pioneered combined molecular blockades, for example anti-EGFR and small molecules.

"We now only get involved in phase I trials where we are part of the science – I'm not interested in pushing drugs and seeing whether they are tolerated or not, which is the classic model of phase I development. I think our obligation is to understand why an agent is working and selecting the right patients for treatment."

Facilities at Vall d'Hebron now include six labs and a refurbished and expanded oncology department. Baselga says he has strong pathology and diagnostic departments and the key differentiator compared to other translational centres is multidisciplinary integration. It's a far cry from when he started – medical oncology was merely a referral point for chemotherapy. Now every tumour case is discussed in multidisciplinary teams with oncology playing the central role.

A new breast cancer centre will open next year – as he is a breast specialist it is natural that this has been a focus for expansion, but as he points out research is now much more targeting the molecular features of cancer and not its site. "I don't feel restricted to one tumour type. Yes, we do a lot of trials on breast cancer, which is my main area, but also on colon, lung, and head and neck cancers – wherever we see an opportunity we will try and adapt to that disease."

The new breast centre, he adds, will be a "paradigm and laboratory" for future expansion. "If it is successful we will open centres for gastrointestinal, prostate and other cancers – the future for big academic hospitals is to create tumour-focused multidisciplinary teams." Breast is a good place to start, he says, as many patients need chemotherapy prior to surgery, and pathologists, radiologists and genetic counsellors are all also involved – "So it is obvious we all have to work together." (And, pragmatically, it is also a cancer with a strong advocate community and fundraising potential, he notes.)

If all this sounds like a smooth progression, Baselga notes that in the early days many basic problems had to be sorted out. They included convincing the hospital to upgrade the oncology facilities from one of the worst to among the best; being open with patients about their condition, and not allowing families and consultants to hide the truth; and abolishing waiting lists (no mean feat given there are 3,000 new patients visits each year and 30,000 follow-ups).

Another issue familiar to many around Europe has been persuading surgeons to specialise only in particular tumours – that's been agreed at Vall d'Hebron, but is not the case yet in outlying hospitals in Catalonia.

Motivating the medical oncology staff has also not been easy. "For example, I've had to force people to learn English so they can travel and participate in international forums, and internal sessions are also conducted in the cancer community's lingua franca." Baselga is a great advocate of networking and personal bonding with European colleagues. With funding from a Spanish bank he's also inviting experts to come to Barcelona to give talks, but is equally keen that staff get to know them over lunch and dinner.

It's part of his drive to make the most of opportunities for co-operation within Europe. Outside of individual centres, Europeans can often organise trials on large patient populations much quicker than counterparts in the US

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– studies on adjuvant Herceptin being a case in point, he notes. But the agenda for medical oncology is much broader and more challenging.

The community needs to lobby for medical oncology to be recognised across Europe as a key discipline, feels Baselga – medical oncologists must be the pivotal players in multidisciplinary teams. As he points out, only doctors with a background in internal medicine can hope to understand the molecular basis of cancer and in what combinations, settings and population groups to administer treatment. "The quality of cancer care relates directly to the strength of medical oncology in any centre – there's no question of that. If you look around Europe, there is a tremendous imbalance of quality of care – because we don't have a strong speciality."

It is an opposite view from the one sometimes heard from surgeons – that medical oncology has become very powerful because it gets so heavily funded by pharmaceutical companies. ESMO (the European Society for Medical Oncology), they argue, already has one of the biggest European meetings. "But compare ESMO to ASCO [the American Society of Clinical Oncology], which has 28,000 attendees at its conference – and just look at how many presentations they have from Europe. I love ASCO – it's been fundamental to my career, it gave me a young investigator award, a career development award, and I'm a board member, but we are not doing our job here if most of our major papers go to them."

It may surprise some to learn that ASCO has grown from about 15 employees to close on 300 since 1996 (and Baselga recalls that when it was small he once got a call from the executive director chasing him for a grant application). Those days are long gone. "Now ASCO has tremendous lobbying power and capacity to produce educational materials, and is funding career development – as well as running a great journal and annual meeting. Given that Europe has twice the population of the US, we should have a society of at least the same size and influence as ASCO, especially to bring on the new generation of medical oncologists." The good news, he adds, is that ASCO does also operate as a global organisation, and would be "very happy to help the European cancer community".

Training of oncologists is an especially important topic for Baselga, who is currently chair of ESMO's young medical oncologists working group. Just as cancer care is far from uniform across Europe, training also varies greatly, which can only delay the establishment of medical oncology as a specialism and the emergence of oncology leaders – of whom there is a dearth, according to Baselga. "Are we taking care of our young doctors and providing enough funding for training? No – but the Americans are." He does currently have an Italian investigator under his wing funded by an ESMO award – "She is a superb oncologist" – but there are few such positions in Europe.

So what other kind of changes does he envisage? "I don't want another ASCO – let's play to our strengths and be the champions of multidisciplinary work. The European Breast Cancer Conference is a good model for a meeting, at least. We currently have two journals in Europe – the *European Journal of Cancer* and the *Annals of Oncology* – we should instead have one strong publication to rival the American *Journal of Clinical Oncology* [JCO]. The careers of young oncologists depend on publication, so I can't fault them for sending papers to JCO – they have to look after themselves."

Lobbying at European and national level will be critical to addressing resourcing gaps – and Baselga isn't alone in wanting a professional lob-

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Speaking at a conference attended by Spain's Queen Sofia at the Real Academia de Medecina in Barcelona, October 2004

bying and fundraising operation. "We need minimum standards for cancer care agreed by law and to create a European movement against cancer." In Catalonia, Baselga is playing his part – dinner with the president of the region helped cement 12 million euros for his new research laboratories, and he's a regular on TV, including a 'telethon' fundraising programme that involved patients speaking up about their treatment. He has also set up a research foundation (Fundació Privada d'Estudis i Recerca Oncològica – FERO), through which the breast centre and a new head and neck cancer lab are being funded, and he hopes to set up scholarships and young investigator awards.

Medical oncologists also need to speak out more about their achievements. Baselga often talks of breakthroughs in clinical research – again, this is something to learn from the US. "There is a psychological issue here with the way medical oncologists communicate – we are making breakthroughs all the time. Breast cancer mortality is dropping 2–3% a year. Colon cancer response rates used to be 12–15% with available chemotherapy – and now with new agents the response to metastatic disease is 84%. Herceptin increases survival of HER2 positive breast cancer by 45%. If these aren't breakthroughs, what are?"

Americans are rather more gung ho. "The Breast Cancer Foundation has a powerful logo, the MD Anderson Cancer Center's logo is 'Making Cancer History'. Memorial Sloan-Kettering says it has the 'best cancer care anywhere'." That's the kind of branding he'd like to see more widely applied, and with the "phenomenal progress" being made with the many new compounds he's involved with, there is no shortage of achievements to trumpet.

With so much to work on he's probably glad of the distractions of home life. He's now a father of four children aged 12 and under – and they sound like an outward bound family; "My wife and I are mad on skiing, hiking and biking." Family life should keep him in Barcelona for the foreseeable future – but he gets plenty of big job offers from other cancer centres, especially in the US, who want the best person to lead their clinical research, so the attractions of Europe may not be enough to keep him for ever.

When he's not reading medical papers, Baselga likes to pursue his keen interest in modern history. One senses that, at just 45, Baselga has every chance of making a history of his own.