Where are the consensus guidelines for women with metastatic disease?

New conference will tackle this neglected topic head on

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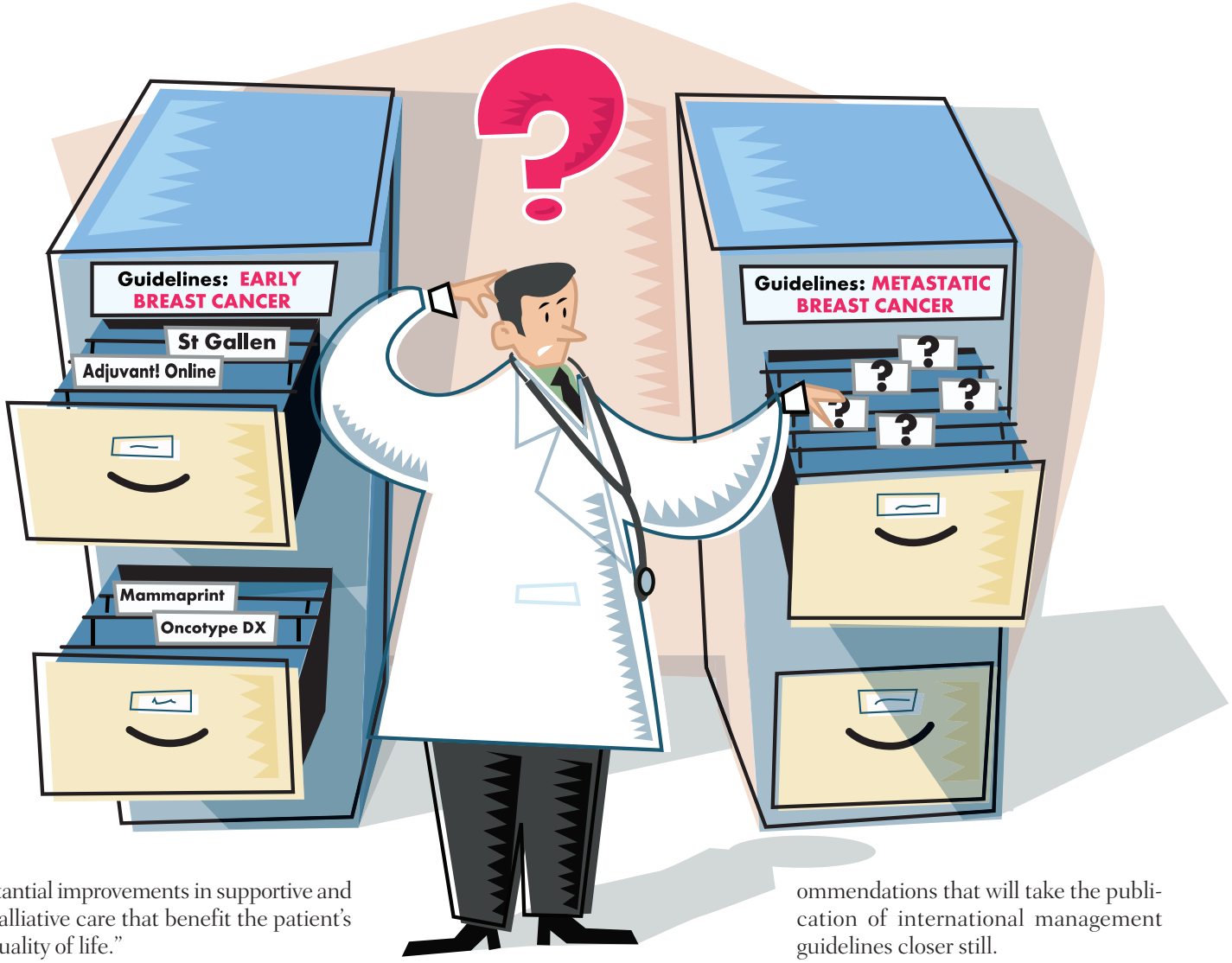
Women with advanced breast cancer can live a full and active life. But median survival is still hovering around three years and the pace of progress is frustratingly slow. A new conference now seeks to develop a more evidence-based approach for treating and caring for women with metastatic disease, so they can benefit from the progress in knowledge and technology that has done so much to improve outcomes in early breast cancer.

This year, a new, regular conference will convene that will challenge a long-standing and often forgotten issue in oncology – that there is little we can do to greatly improve the outcome for advanced breast cancer. Despite the plethora of meetings, research and experts already focusing on breast cancer, metastatic disease has been neglected for treatment and management guidelines in favour of the early stages because of its difficulty and complexity.

That is simply not good enough, say the clinicians behind the First Advanced Breast Cancer International Consensus Conference (ABC1), to be held in Lisbon this November. Not only are there many questions unanswered about how to manage advanced disease, they say, but also the many women faced with metastatic illness deserve a much more positive, evidence-based approach, and support systems that lessen the all too frequent isolation felt by people with an incurable condition.

"It is metastatic disease that kills patients so we will never cure breast cancer unless we focus much more on its advanced stage," says Fatima Cardoso, who will co-chair and host the conference as head of the breast cancer unit at the new Champalimaud Cancer Center in Lisbon. "Already a small subset of those with metastatic cancer show promise for a cure if we identify and manage them correctly," she adds. "For the majority of patients, however, the aim is to improve length and, especially, quality of life. If we could transform it into a chronic condition it would be a major step forward. But we cannot just give up on aiming for a wider cure – and to do that we have to convince investigators and the industry that it is worthwhile to invest in high quality clinical and translational research that could lead to major gains, as we have done in early-stage disease."

She points out that results from work in early-stage breast cancer are seen as meaningful when they translate into years or even decades of survival, but in the metastatic setting gains are mostly weeks or months at best. "The median survival of advanced disease has improved from two to three years in a decade, and that is not acceptable in my view. But we have made far more sub-



stantial improvements in supportive and palliative care that benefit the patient's quality of life."

The concept behind this new addition to the cancer conference calendar arose from a taskforce on metastatic breast cancer set up in 2006 by ESO and the European Breast Cancer Conference (EBCC). In 2007 the taskforce published a set of recommendation statements in *The Breast* (vol 16, pp 9–10) on managing metastatic breast cancer, with a view to developing detailed guidelines and supporting papers in the following years, with consensus sessions at every EBCC. "At the session on advanced disease at the 2010 EBCC we had 1000 people who came on the last day of the meeting – but a few hours every two years when we bring people together is just not enough for what we need to do," says Cardoso.

Now the aim is for a panel at the new conference to develop consensus recommendations that will take the publication of international management guidelines closer still.

As Cardoso explains, the idea is to establish a conference similar to the St Gallen meeting held every two years in Switzerland, which publishes a consensus paper on early-stage breast cancer treatment. "Studies show that countries that have applied the guidelines developed at St Gallen have improved their survival, and that's what we want for advanced disease too."

But she recognises that it will be a

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challenge. "There are of course already a few national and regional guidelines for metastatic disease, but they are not well followed and too many oncologists have given up on the idea that they can help." And there are limitations to existing guidelines, such as a lack of depth on specific needs of advanced breast cancer patients in the light of recent knowledge, she adds. These limitations must be addressed, and doing so at an international level will greatly improve the chances of the 'sceptics' in the cancer community taking guidelines seriously, Cardoso feels.

The sceptics' case is mainly that there are too many variables in advanced breast cancer patients for guidelines to be worthwhile, particularly after the usual first-line treatments have been applied. Then it becomes more 'art' than science. Cardoso disagrees. "It is not different from early stage disease, where in any case you need to adapt guidelines to the patient in front of you by, for example, balancing the side-effects according to the chances of a cure.

"In metastatic disease you have to add quality of life factors and possibly prolongation of life, but not a cure in the majority of cases, so the balance is different and more difficult. But if we are talking about increasingly personalised treatment in the early stages, more than ever now we must also apply the same approach in the metastatic setting."

A marker for personalised management in metastatic disease is the initial set of 12 statements published in *The Breast* (vol 16, pp 9–10), which includes not only brief notes on treatment options applicable then but also the need for psychosocial support, informed decision

A life worth living. The needs of women living with advanced breast cancer – for a longer life and a better quality of life – have tended to be overshadowed by the heavy focus on early disease

making, quality of life assessments and enrolment in well-designed trials. Not surprisingly, given the complexity, a multi/interdisciplinary team is crucial (and this is the first recommendation).

All these areas, and others, need more research, says Cardoso. The many questions about drugs, in particular, stem from another major obstacle to progress. As she comments, "In drug development, industry and the cooperative research groups tend to see the metastatic research setting only as a bridge to reach the adjuvant stage. This often leaves important management questions for metastatic breast cancer patients unanswered."

It means that even after many years oncologists still have doubts on whether to use certain drugs in sequence or in combination, how many lines to consider, whether maintenance therapy is an option, and so on. With trials linked mainly to a particular single use of a drug, there are huge problems getting funding to do more complex trials, she adds. "I can understand that companies are not interested in supporting this work, but it's harder to accept that even the cooperative groups, which should focus on academic research, are unwilling to do the trials."

The ESO taskforce has, however, now published several review papers on the available data, for example on combination versus sequential single-agent chemotherapy, and on a patient subset who potentially have a chance of a cure because they have only one or a few metastatic lesions, usually on one organ.

But as Cardoso adds, these papers also serve to identify much more research that needs to done, such as quality of life and predictive factors when using chemotherapy regimens, and in the 'curative' paper, crucial questions such as whether to remove a primary tumour in a patient with metastatic disease. A study addressing the latter issue is currently underway in the US with academic funding, and was initially set up as a cooperative study between US and the rest of the world (under the Breast International Group). "But it has been impossible so far to obtain the funds – and perhaps also the willingness – to run this purely academic trial outside the US," she says.

"Another reason we need better

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guidelines is that we can now offer procedures we couldn't do before, such as stereotactic radiotherapy on brain metastases," adds Cardoso. "Technology like this is changing how we can manage these patients."

Along with a lack of interest by industry and some clinicians, Cardoso notes that until a few years ago the patient advocacy groups were not the force they could have been for advanced disease. As she writes in an editorial in *The Breast* (vol 18, pp 271–271), patient groups have focused mainly on the prevention, diagnosis and treatment of early breast cancer, which is "totally understandable" given the larger number of women involved and the difficulty of confronting the invariably fatal side of the disease in the advanced stage. But this has left many women with metastatic disease isolated as "forgotten heroes", as she puts it.

Several initiatives are helping to change this. Stella Kyriakides from Cyprus Europa Donna has been on the ESO taskforce from the start, while an international group for metastatic breast cancer has been set up, the MBC Advocacy Working Group, which has published its own consensus report ('Bridging gaps, expanding outreach' – *The Breast* 18:273–275). This brief report identifies three priorities: improving access to information, resources and support services; raising the profile of metastatic disease within the wider breast cancer community and with the public; and increasing understanding of and access to clinical trials.

A lack of participation in trials was highlighted by an project allied to the MBC Advocacy Working Group, the Bridge survey of 950 women in nine countries with metastatic disease.

In Lisbon, national advocacy groups such as the Breast Cancer Network Australia and AdvancedBC.org in the US will be highlighting work they are doing to support those living with metastatic breast cancer. AdvancedBC.org is run by Musa Mayer, an advocate who has written extensively on breast cancer and has been a pioneer in raising awareness of advanced disease. In a paper published last year (*Seminars in Oncology Nursing* 26:195–202), she examines key lessons learned from surveys of need, such as the Bridge survey. "Patients and families want, need and deserve better services," she says.

See you in Lisbon. Up until now, discussions about treatment of advanced breast cancer have had to be slotted into a single session at broader conferences

In the lead up to the November consensus meeting, Cardoso says more work is being done on themes such as whether it is helpful to detect metastatic disease before it becomes symptomatic, and how to follow up and treat patients, given that tests can be demanding and time consuming. "We are also looking more at the role of maintenance therapy, the number of treatment lines to give and we would like to do much more on psychosocial support for patients and their families."

As she concludes, the pioneers in early-stage breast cancer had their sceptics too. "Just look at Gianni Bonadonna's work on adjuvant chemotherapy in the 1970s – half the scientific world did not believe it would work," she says. "Our work now may seem very difficult but it doesn't scare me."

- A webcast of the workshop on metastatic breast cancer guidelines at the 2010 EBCC is at tinyurl.com/32txp8c (on the ECCO website).
- Both the MBC Advocacy Working Group and the Bridge survey are supported by Pfizer Oncology. See www.bridgembc.com for the consensus report and survey and also Pfizer's media room for more information at tinyurl.com/32wdx7m