What's coming up in colorectal cancer?

Mary Rice

A panel of experts is predicting that colorectal cancer patients will soon feel the benefits of the sort of individualised therapies that are beginning to be used in breast cancer. More effort is needed to promote a multidisciplinary approach, improve staging and raise awareness of the benefits of screening.

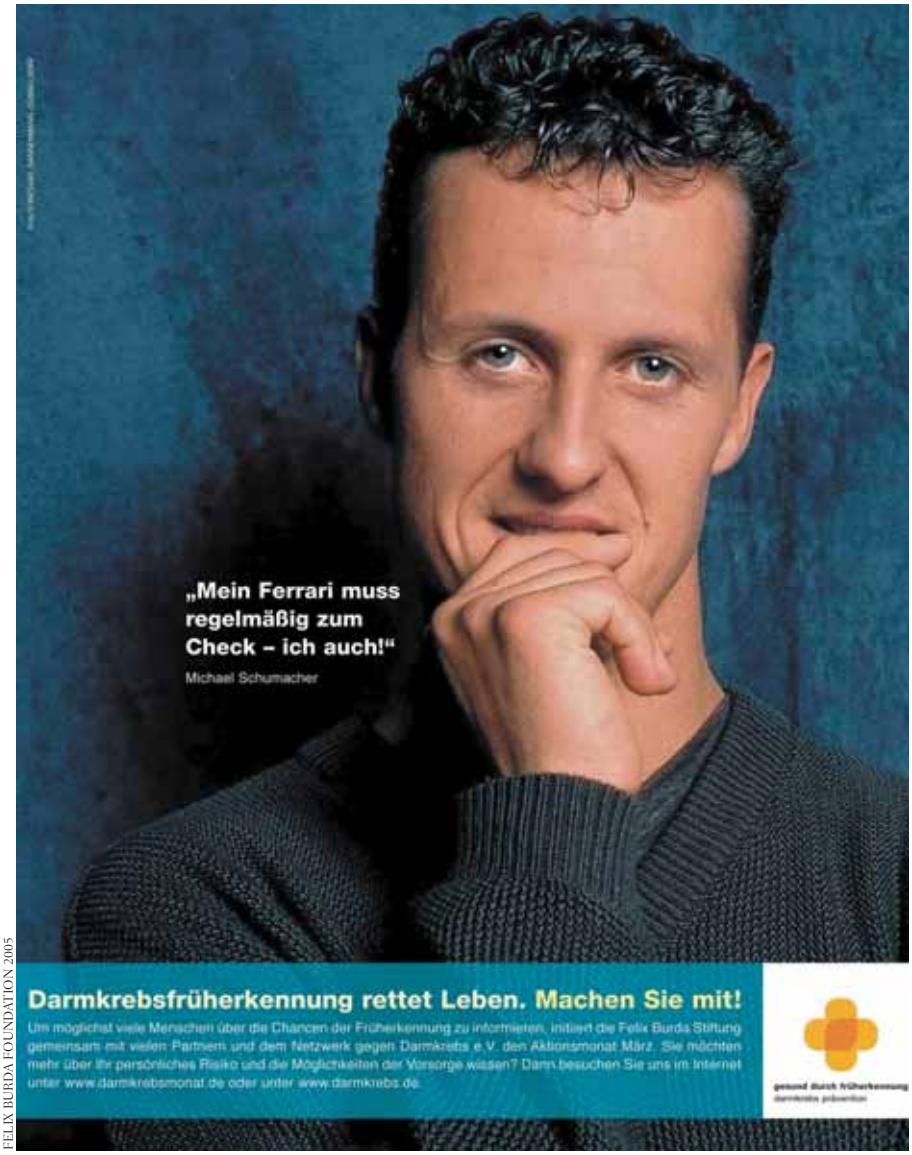
Some catching up to do compared with some other cancers, but otherwise treatment for colorectal cancer is making good progress. This was the overall view of the experts gathered in Barcelona for the first Colorectal Cancer Observatory, organised by the European School of Oncology. Clinicians and patient representatives from Europe and the US were asked to predict how they saw treatment, diagnosis, screening and patient advocacy evolving over the coming 12 months, so that all participants could see their work in the context of a wider arena.

The single most important thing that could happen to improve colorectal cancer treatment, said Observatory chair Mario Dicato, of the Centre Hospitalier de Luxembourg, would be improving our ability to predict risk of progression. "Because we are not as advanced in this field as they are in breast cancer, for example," he said, "it is certain that a number of patients are still under- or over-treated. We are still unable to delineate clearly between sub-groups at different risk. We do not have predictive markers for the use of Avastin [bevacizumab] in the same way breast cancer patients have for Herceptin [trastuzumab], and this is bad both for patients and for healthcare systems, which have to foot the bills for treatment that we know is sometimes unnecessary. The current problem is knowing for whom it is unnecessary."

Europe-wide guidelines for colorectal cancer were called for by Cornelis van de Velde, of the Leiden University Medical Centre in the Netherlands. Some countries have no guidelines at all, he said. For a start, multidisciplinary treatment planning should be made mandatory for everyone. Staging is also a big problem.

OBSERVATORY PANEL

- **Mario Dicato** (chair), medical oncologist, Luxembourg
- **Lynn Faulds Wood** (co-chair), patient advocate, UK
- **Philippe Rougier**, medical oncologist, France
- **Hans-Joachim Schmoll**, medical oncologist, Germany
- **Margaret Tempero**, medical oncologist, US
- **Cornelis van de Velde**, surgeon, the Netherlands
- **Chris Verslype**, medical oncologist, Belgium



FELIX BURDA FOUNDATION 2005

"My Ferrari has to be checked out regularly. Me too!". Michael Schumacher does his bit to promote screening in this campaign run by the Felix Burda Foundation in Germany, but much more needs to be done to raise awareness about Europe's second biggest cancer killer

Accurate staging is vital, he stressed, both pre-operatively, by radiology, and post-operatively by the pathologist. "At the moment it is imprecise. Patients are still mis-staged, particularly in stages 2 and 3, and this hampers the chances of targeting and optimising treatment," he said, adding that pre-operative MRI, essential for staging, is obligatory in some countries, while in other countries it is simply not an option.

But despite having some catching up to do, things are moving at a great rate, he said. "In 1988 there was an editorial in JAMA which looked at whether chemotherapy had a role in colorectal cancer. This was followed by a study that showed that it had survival benefits in patients with lymph node metastases. This seems extraordinary now, but in fact it was only following in the same pattern as breast cancer, and we can expect to see the same kind of progress both in diagnosis, treatment, and survival benefits."

Laparoscopic surgery will become an integral part of colorectal cancer surgery, he predicted. "Currently some people get it and some don't – and this is true even within countries, for example in the UK. The pioneers who thought it would enhance survival have found that this is not the case, but with careful technique the results can be equal to open surgery, at less burden to the patient. It takes more operating time, but is easier to recover from, and the quality of life benefits to the patient are considerable."

Providing better information to patients so that they can be properly involved in the decision-making process could also bring benefits all round, he said. "For example, people are very much opposed to the idea of having a stoma. But to avoid this we have to do highly technically demanding operations, which can sometimes make the patient incontinent. We need to get better at explaining to patients exactly what is involved when there is a choice of procedures, so that they can fully understand and pick the one that is better for them. A stoma can avoid many problems, but because this is not always properly explained, patients sometimes choose an alternative that has a far more deleterious effect on their quality of life."

Margaret Tempero, from the Department of Medicine, University of California at San Francisco, USA, also emphasised the importance of markers for improving decisions on whether or not to treat. She predicted

METASTATIC CRC

In metastatic CRC in the coming year Schmoll predicts:

1. In chemotherapy backbones

- 5FU/oxaliplatin will continue to be an ideal backbone for chemo/targeted combinations
- CapOx and XELOX (oxaliplatin/capecitabine combinations in different schedules) will be used more frequently due to promising data, in particular on safety
- XELIRI (irenotecan + capecitabine) will disappear
- Data on the relative benefits of CapOx vs FU/oxaliplatin will be available in June

2. In targeted therapies

- Bevacizumab will be used more in combination with FOLFOX (oxaliplatin+5FU+leucovorin) and possibly also with CapOx in the 1st- and 2nd-line setting
- Cetuximab will be shown to have strong efficacy when used in combination with chemotherapy in 1st-line treatment, but it will remain unclear whether it is equally effective as FOLFOX/bevacizumab
- Small molecule vascular endothelial growth factor [VEGF] tyrosine kinase inhibitors will not yet be on the market

ADJUVANT THERAPY

In adjuvant therapy in the coming year Schmoll predicts:

- The use of oxaliplatin-based combinations will strongly increase following supportive data from the NSABP C07 study and 4-year MOSAIC update
- Safety data support the use of XELOX, but this combination will not be used in an adjuvant setting at least until 2007, when we will have early data on its efficacy
- For patients who are not candidates for oxaliplatin, FOLFIRI will still be an option (better than 5FU alone)
- Oxaliplatin remains favourable with any 5FU backbone

that research into the management of colorectal cancer will undergo a dramatic shift as genomic predictors of outcome emerge from the analysis of candidate biomarkers in banked tissue. "This will prompt prospective trials to validate the biomarkers as diagnostic indicators to treat or not to treat. A second wave of research on biomarkers predicting sensitivity or resistance will lead to tailored treatment selection," she said.

Lynn Faulds Wood, representing the European Cancer Patient Coalition, and a former colorectal cancer patient herself, set out the wish list for patients over the next year. Public health campaigns must be a priority, she said: it is the second biggest cancer killer across Europe, yet there is very low awareness of the disease and its symptoms. It would help if agreement could be reached on a single name for the disease, which, she pointed out, is "confusingly known around Europe as colorectal, colon, and bowel cancer".

Widespread implementation of screening programmes would be the best way to save many thousands of lives over the next few years, she said, while better access to various forms of treatment would bring improvements for patients. Some patients have to wait months for radiotherapy. Access to life-prolonging and potentially life-saving drugs is too slow, with official approval taking many months longer in Europe than in the US. And better access to carefully targeted therapies is needed.

Hope was held out on that last sentiment by Hans-Joachim Schmoll, of the Martin Luther University, Halle, Germany. He believes that in the next 12 months combinations of chemo-therapy and targeted agents will increase long-term survival rates in metastatic colorectal cancer. New drugs based on oxaliplatin will play an increasing role in adjuvant therapy.

Such expert predictions are useful both in keeping people informed and in giving them a better understanding of what their colleagues in different disciplines are doing, concluded Dicato. "I believe that by helping us understand what is likely to evolve in the next few years, we can benefit not just ourselves, but also patients and healthcare systems. In particular, the promise held out by micro-arrays and targeted treatment in colorectal cancer is something that should be better known by a wider public."

"In the next 12 months combinations of chemo and targeted agents will increase long-term survival"