available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejconline.com

NEWS. . .NEWS. . .NEWS

Molecular testing in CML

Nearly half of European haematologists do not follow European LeukemiaNet recommendations on molecular testing for chronic myeloid leukaemia (CML), according to a survey presented at the 13th European Hematology Association Meeting (*Copenhagen, Denmark, June 12–15, 2008*).

The 'Best to Test' data revealed that 47% of the 550 haematologists and oncologists questioned, from 11 European countries, did not follow European recommendations advising routine monitoring with quantitative PCR every three months. The survey, which involved interviews conducted between November 2007 and February 2008, suggests that 39% of current CML patients across Europe are being monitored inadequately.

Tyrosine kinase inhibitors (TKIs), first introduced in 2001, have revolutionised CML treatment, but resistance to first line imatinib occurs in approximately 25% of chronic phase CML patients, 41% of accelerated phase patients and 92% of blast crisis patients. Resistance often occurs as a result of mutations in the BCR-ABL gene, the target of TKI treatment. Monitoring for treatment efficacy helps to determine whether therapies are effectively controlling CML, and whether patients might benefit from alternative interventions, such as second generation TKIs or bone marrow transplants.

'When patients fail therapy, their leukaemic burden rises from a few cells to millions of cells and this increases their risk of transformation to blast crisis. If patients aren't monitored regularly you miss out on the small window of opportunity to effectively intervene with alternative therapies,' explained Professor Agnes Buzyn (Necker-Enfants Malades Hospital, Paris, France).

The 'Best to Test' survey also highlighted wide discrepancies throughout Europe in the level of monitoring. Only 3% of physicians in Romania carry out molecular testing as part of routine monitoring compared to 47% in Germany, 49% in Italy, 63% in France and 75% in the UK. This is despite 92% of respondents reporting they were aware of published guidelines.

The two biggest barriers to testing identified in the survey were cost and lack of facilitates. Concerns about cost, said Professor Michele Baccarani (University of Bologna, Italy), need to be put firmly in context: the test for mutational analysis costs 400 Euros which is less than one week on a TKI. 'There is a real risk that if you don't test you'll waste a great deal more money on treatments that don't work,' he said.

'THE TWO BIGGEST BARRIERS TO TESTING WERE COST AND LACK OF FACILITATES'

The 'The Best to Test' initiative aims to improve monitoring of CML patients by working in partnership with health care professionals and key CML stakeholders to provide solutions to overcome barriers to testing.

Janet Fricker

(who was sponsored by Bristol-Myers Squibb to attend the EHA meeting)

New drug in palliative care

Methylnaltrexone bromide subcutaneous injection (Relistor) has received marketing approval from the European Medicines Agency (EMEA) for the treatment of opioid-induced constipation (OIC). It is indicated for patients with advanced illness who are receiving palliative care, when response to the usual laxative therapy has not been sufficient.

Professor Lukas Radbruch (University Hospital Aachen, Germany), President of the European Association of Palliative Care said that opioids used in palliative care often cause the unwelcome and distressing side effect of constipation 'so severe that patients can prefer to reduce their opioid pain medication to minimise their discomfort'.

According to manufacturer Wyeth, methylnaltrexone bromide is a first-in-class treatment which blocks the binding of the opioids to peripheral mu-opioid receptors within the gastro-intestinal (GI) tract. It therefore reverses the slowing effects of opioids on the GI tract and bowel without reducing their pain-relieving effect.

Traditional options for the management of IOC include laxatives and stool softeners given as soon as opioids are started. However, the clinical efficacy of these agents is unpredictable, even when used aggressively, and symptoms often continue.

EJC News is edited by
Helen Saul
Tel.: +44 1865 843340,
E-mail address: h.saul@elsevier.com

doi:10.1016/j.ejca.2008.07.034

Cetuximab in NSCLC: caution urged

Claims that the combination of targeted therapy cetuximab (Erbitux) with platinum-based chemotherapy is 'a new standard' in the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) should be viewed with caution, according to a leading oncologist. Toxic effects and costs need to be carefully weighed against a modest survival benefit, he said.

Results from the phase III FLEX trial (First-Line treatment for patients with EGFR-EXpressing advanced NSCLC) were presented at the recent ASCO annual meeting (*Chicago, Illinois, May 30–June 3, 2008*). The trial found that the addition of cetuximab to the chemotherapy extended survival from 10.1 to 11.3 months – an increase of about 5 weeks – which was statistically significant.

Lead author, Dr. Robert Pirker (Medical University of Vienna, Austria) said it was the first time a targeted drug has shown a survival benefit in first-line treatment of advanced NSCLC, including all subtypes of the disease (*J Clin Onc 2008;***26**: *May Supplement Late Breaking Abstract #3*). The results have 'clearly established a new standard in the first-line treatment of patients with NSCLC', he said.

The FLEX trial involved 1125 patients, of whom 94% had stage IV disease. 'Patients with advanced NSCLC have limited treatment options and life expectancy is short, so the survival increase shown in this study is an important step for these patients,' said Dr. Pirker.

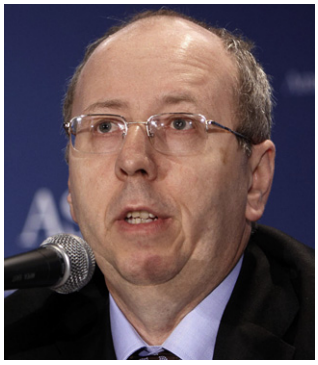

Photo courtesy of ASCO.

Dr. Robert Pirkel

Dr. Giuseppe Giaccone, chief of medical oncology at the US National Cancer Institute (NCI)'s Center for Cancer Research, told *EJC* that, because the improvement in survival was significant, it is likely that the study will lead to registration. Doctors in the States will probably then use the drug, possibly in combination with other chemotherapeutic agents, and in the maintenance phase of disease.

He pointed out that the chemotherapy used in the trial (cisplatin/vinorelbine) is not widely used either in the States or Europe, and it has not been shown that this agent is effective in combination with other chemotherapy regimens.

The most common side effect associated with the drug is an acne-like rash, which was described by the authors as 'manageable'. But Dr. Giaccone said that the acne could be severe, and unbearable to many. It is difficult to grade toxicity, especially in large studies, he said, and it would be interesting to see in the final paper how toxicity had been handled.

Dr. Giaccone thought it unlikely that the drug would be approved for use by agencies such as the UK's NICE (National Institute for Clinical Excellence), which are bound to take cost-effectiveness into account. But the economics of a drug are increasingly important, even in the States, and he said that he thought cost-effectiveness should be addressed 'even before registration.'

'This is a positive study and therefore deserves consideration. But the drug was used with a chemotherapy regimen that is not used by many people so I think at the very least, there should be another study to confirm the results,' he said. Potentially, biological markers such as EGFR FISH and K-ras mutations may shed some clarity on how to better select patients for this treatment and therefore make the benefit larger for this selected population.

Dr. Pirker said that further studies are ongoing and will evaluate cetuximab in earlier stages of the disease, in combination with chemotherapy or chemoradiotherapy in locally advanced disease, and as an adjuvant treatment in patients with early-stage disease.

Helen Saul

Genetic signature 'may predict aggressiveness' of NSCLC

Canadian researchers have identified a 'gene expression signature' that may predict the aggressiveness of early-stage non-small cell lung cancer. A follow-up analysis of a trial by the National Cancer Institute of Canada (NCIC) Clinical Trials Group identified a set of 15 genes that may help to identify those patients who could benefit most from chemotherapy after surgery. It may spare patients with less aggressive cancer from chemotherapy and its side effects.

The researchers analysed tissue from resected tumours taken from 133 of the 482 patients who took part in a trial that showed a significant survival benefit from vinorelbine and cisplatin in patients with early-stage (I and II) NSCL. They first identified the 15-gene expression in 62 patients who did not receive adjuvant chemotherapy. They used it to predict which patients had aggressive cancers with a high risk of recurrence and death and which had less aggressive disease. The signature was then applied to 71 patients who were randomised to receive chemotherapy in the original trial.

Patients predicted to have aggressive disease experienced the greatest benefit of chemotherapy with a 67% reduction in the risk of death. Chemotherapy did not reduce the risk of death in patients designated as low risk.

Presenting the results at ASCO (*J Clin Onc 2008;***26***: May Supplement. Abstract # 7510*), the researchers explained that while their original trial (*N Engl J Med 2005;***352***:2589–97*) showed that only patients with stage II disease benefited from chemotherapy after surgery, the current analysis suggests that the gene signature may identify patients with both stage I and II disease who may benefit from post-operative chemotherapy.

Rhonda Siddall

(who received a travel grant from Bayer Schering Pharma to attend the meeting)

EUROFILE

A Cancer Action Plan for Europe

The European Commission is beginning work on a Cancer Action Plan, which it will present to EU governments and the European Parliament for consideration in 2009. The plan will address all aspects of cancer control, from prevention to early detection and diagnosis, from treatment and rehabilitation to palliative care.

Both the Parliament and the EU Council of Ministers have given their political backing, and their recommendations are the most significant starting points for the plan.

The Parliament's report on cancer was approved in April 2008. Its top recommendation is that the Commission should set up a Cancer Task Force to spread best practice in prevention, screening and treatment and to provide leadership for improved cancer control. MEPs also called for the Commission to support information campaigns on screening and treatment; provide more research funding, in particular for work on primary prevention screening, early detection and new anti-cancer treatments; and draw up a charter on the rights of cancer patients in the workplace.

'PROBLEMS ARE NOT GOING TO BE SOLVED BY COMMISSION BUREAUCRATS'

The Council of Ministers' contribution came in June 2008, emphasising the primary role of governments in healthcare policy. Its demands on the Commission were lighter, but included initiatives to encourage information exchange, an exploration of voluntary European accreditation schemes for cancer screening and follow-up, and the development of quality assurance guidelines. In research, ministers emphasised better collaboration over increased spending.

Screening is set to be one of the main themes of the Action Plan. A first progress report has recently been completed on implementation of a 2003 commitment by EU governments to introduce population-based screening for breast, cervical and colorectal cancer. Despite improvements, it found that the annual volume of screening examinations in the EU was only half that expected if the tests were available to all appropriate citizens.

In developing the Action Plan, the Commission is keen to look at areas where providing information, sharing best practice and establishing guidelines can play a role. The development of accreditation schemes is likely to be a prominent feature, with discussions already under way on a pilot project for breast cancer services.

However, officials warn that the scope for EU intervention is limited because health policy is mainly a matter for governments. "People have very high expectations, but legally and financially we are not always able to respond," said Nick Fahy, head of the health information unit in the Commission directorate for health and consumers. "We have to work more indirectly by bringing people together and getting those who are appropriate to respond."

This needs to be appreciated by the cancer community when thinking about its approach to the Action Plan, which will open to consultation in late 2008 or early 2009. "To paraphrase JFK, it's not just about what the European Community can do for you but what you can do for the European Community," Fahy explained. "The problems that face cancer and the cancer community are not going to be solved by Commission bureaucrats in Brussels and Luxembourg, they are going to be solved by the cancer community across Europe."

The Organisation of European Cancer Institutes (OECI) has no problem thinking of things that it could do for the European Community. OECI president Marco Pierotti sees the organisation as a prototype platform of comprehensive cancer centres that could be linked to centres of basic research excellence. "We have the idea that by putting these fragmented resources in one single platform, we can succeed in having very strong and competitive answers," he said.

OECI is developing accreditation criteria for cancer centres that could be picked up by the EU as a benchmark for competencies; Pierotti also thinks that the strongest centres could be given a role training others, raising the quality of cancer care across Europe.

'THE EU COULD DEVOLVE SOME RESPONSIBILITY TO OECI OR ECCO'

More radically, he suggests that the EU could devolve responsibility for achieving some goals to organisations such as OECI or the European Cancer Organisation (ECCO). "Give them a clear goal, support them with money and then monitor the results," Pierotti explained. "In this way these organisations would be forced to select from their associates or members the ones that best contribute to achieving the goals, and in principle we should see added value."

For example, OECI could tackle the large number of unvalidated cancer innovations produced by EU research programmes. "We have a short memory in science," Pierotti explained. "We are producing a lot of innovation, but nobody has the patience to then try to apply and validate it."

Meanwhile, ECCO president Alexander Eggermont backs the four priorities identified in a recent paper (*EJC* 2008;**44**:1451–6): primary prevention and health promotion; secondary prevention with proven screening programmes; more equitable access to optimal treatment and integration of cancer care services; and sustained and consistent support of independent research. "ECCO agrees whole-heartedly with this analysis, and I would like to see the cancer action plan promoting these four interventions," he said.

Ian Mundell
Brussels

What colour is my cancer?

A novel way of communicating with teenagers and young adults (TYA) with cancer may change their attitude to the disease, say researchers in Leeds, UK. They found that showing young patients slides of their own tumours helped dispel some of their negative images (*see EJC 2008;***44**:1483–4).

The exploratory study involved only 31 patients and was unable to highlight measurable changes in patients' satisfaction with their sense of control and choice over treatment decision, possibly because baseline scores were already high.

However, patient's descriptions of their cancers changed from 'big, black, evil, destructive, painful, alien' before seeing the slides, to the less formidable 'jelly beans', 'tiny sausages' and 'pepperoni' after viewing them.

The study included 31 patients aged between 13 and 24 years, who were invited to look at tissue samples from their own tumours under a microscope. Most – 27 – accepted. They were shown the samples by a consultant histopathologist, haematologist or cytogeneticist, as appropriate.

The young patients were given an explanation of how the tissue had been processed and were encouraged to discuss what they saw with the specialist.

Lead author Sue Morgan, Macmillan nurse (St. James' University Hospital, Leeds, UK) said that many of the young patients had imagined their tumours as being vile. 'When they see it under the microscope and it looks pretty, even beautiful,' it makes them feel better about what's going on inside them.

Pathologist and patient view the tumour together

'There was a quest for knowledge, they wanted to know absolutely everything and valued the time of the professionals showing them the slides.'

The project also 'had an enormous effect on the professionals who don't ever see the young people whose samples they study.'

'They said that that meeting the young people, knowing they make a difference and seeing who they make a difference to was powerful. It gave them a different view on what they do.'

The project was prompted by a 14 year old who had a large pharyngeal tumour removed, and wanted to know what colour it was. In order to continue with the project – which involves at least an hour of a consultant's time per patient – Mrs. Morgan said that a measurable difference in outcome must be demonstrated. She is planning a 2 centre study, in which some TYAs get to see their tumour slides and some don't.

Obesity and pancreatic cancer risk in women

Obese women, who carry most of their excess weight around the stomach, are 70 percent more likely to develop pancreatic cancer, according to analysis of data from the US' Women's Health Initiative (*BJC 2008. doi: 10.1038/sj.bjc.6604487*).

The researchers followed more than 138,000 postmenopausal women, and during the 7 years of the study, 251 developed pancreatic cancer. Of these, 78 had the highest waist-to-hip ratios, which is 70% more than the 34 women with the lowest waist-to-hip ratios, after adjusting for other potential risk factors including age and smoking status.

'We know that carrying a high proportion of abdominal fat is associated with increased levels of insulin, so we think this may cause the link between obesity and pancreatic cancer', said lead author Dr. Juhua Luo (Karolinska Institute, Sweden). 'Obesity is a growing and largely preventable problem, so it's important that women are aware of this major increase in risk.'

However, according to a UK-based study, increasing numbers of people are failing to recognise they have a weight problem (*BMJ 2008. doi: 10.1136/bmj.a494*).

Researchers from University College London compared data taken from 2 household surveys carried out in 1999 and 2007. In each, participants were asked to give their height and weight and categorise themselves as either: very underweight, underweight, about right, overweight or very overweight. The 2007 survey also included 'obese' as a category.

In 1999, 43% of the population had a body mass index (BMI) that put them in the overweight or obese range, of whom 81% correctly identified themselves as overweight. But in 2007, 53% had a BMI in the overweight or obese range but only 75% of these correctly classed themselves as overweight.

The researchers suggest that the growing division between actual and perceived weight may be due to overweight becoming more widespread in the population and the appearance of mild overweight being increasingly accepted as normal.

PODIUM

Social inequalities and cancer

*Susanne Oksbjerg Dalton Ph.D. (Senior Researcher, Danish Institute for Cancer Epidemiology, Danish Cancer Society) is the guest editor of a forthcoming EJC Special Issue on social inequality in incidence of and survival from cancer in Denmark (EJC 2008;**44**:(14)). The data in the CANULI study (covering 1990–2006) is taken from near-complete national registries and provides a snapshot of the impact of social factors on cancer.*

Denmark seems to be extremely well set up for such a study

All Danish residents are issued a PIN number at birth or when they arrive in the country and it is used extensively throughout all our administrative systems. So information from the cancer registry can be linked to information on social and economic circumstances, education, and comorbid somatic and psychiatric disorders. We use encrypted data and can't identify individuals but we have good legislation and can use the data in research.

You found a steep gradient according to social factors?

We found inequalities in cancer risk and survival for almost every cancer. Some cancers showed a steep socioeconomic gradient; with each step up in educational level, the population fared better in terms of cancer incidence and outcome. The data also allowed us to pinpoint vulnerable groups. In almost every cancer, those on disability pensions and those with psychiatric disorders did worse than the rest of the population.

Wasn't this expected?

Our data didn't unearth any major surprises and our findings are mostly in line with what has been found previously in Denmark and in other countries. But there hasn't been such a comprehensive analysis of all cancer sites with such recent data including survival. In many cancers, particularly those with a large lifestyle component, there is a gradient, with the risk of cancer decreasing as the level of education increases. Other studies have pointed to an inequality in smoking habits across educational groups.

Can the gradient be explained by smoking alone?

No; alcohol intake, obesity and exercise are all risk factors for cancer and they vary with socio-economic group. But across all cancers there is inequality in outcome – even once you have cancer, your social standing influences your prognosis, and this part is not related to lifestyle habits.

How do you define social standing?

Educational level and income are both important, but once these are taken into account, the quality of housing – the size of house, whether rented or owned and so on – has an independent effect. The way people are affiliated to the working market matters. If you are unemployed or more loosely connected to the working market, you fare worse.

Do you expect your study to affect policymaking?

I hope so. This snapshot of the current situation in cancer shows that cancer is increasingly a social disease. We have known that there is social inequality in lifestyle, which impacts cancer risk, but it is shocking that in Denmark, where there is free and equal access to health care, there is a difference in outcome according to social factors, after diagnosis. We are not saying that the health care system doesn't work, there could be other explanations associated with compliance, and so on. But it is really important for people in health care to be aware of the different requirements people may have according to their social circumstances.

You suggested that screening can make health inequalities worse?

Yes, and this was also found by a study in Eindhoven. In screening programmes, the group that doesn't attend is probably more socially disadvantaged than those who participate. We need to think about how we communicate. We may be speaking to the broad middle class but not reaching the most vulnerable groups.

What other measures should be taken?

At the population level, a good way to start is by making it easier to obtain a healthy lifestyle. Stratified taxation – by which healthy food is taxed at a lower level than unhealthy food – makes it more easily accessible for those with less money. Legislation in regard to smoking and alcohol also has a part to play.

How relevant is this study to other European countries?

It applies directly to those with welfare systems – e.g., Scandinavian countries, UK, Netherlands, and Germany – but also to the newer members of the EU, where smoking and alcohol use is high and health inequalities across social groups are increasing. We were able to show the size of the problem in straight numbers. If Danish adults in the group with least education adopted the smoking habits of those who are highly educated, we could reduce smoking-related cancers by 25–50%. For many cancers, whatever the pattern of risk factors is, if they could be evened out across groups, there's a potential reduction of between 10 and 30%. That is worth striving for.

Helen Saul