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European Approval for HPV Vaccine

The European Commission has approved the quadrivalent human papillomavirus (HPV) recombinant vaccine (Gardasil) for use in young people aged 9 to 15 years, and in women aged 16 to 26 years. It is licensed for the prevention of cervical cancer, high-grade cervical dysplasias/precancers (cervical intraepithelial neoplasia CIN 2/3), high-grade/precancerous vulvar dysplastic lesions (VIN2/3) and external genital warts (condyloma acuminate) caused by HPV types 6, 11, 16 and 18.

The approval, granted to manufacturer Merck, applies to the 25 countries in the European Union. It follows the US Food and Drug Administration (FDA)'s decision in June , 2006, to approve the vaccine to prevent cervical cancer and vaginal and vulvar pre-cancers caused by HPV types 16 and 18, and to prevent low-grade and precancerous lesions and genital warts caused by HPV types 6, 11, 16 and 18. In the US, Gardasil is approved for 9 to 26-year old women and girls.

The vaccine will be marketed by the joint venture Sanofi Pasteur Merck Sharp Dohme (SPMSD) in 19 European countries including 15 in the EU. In the remaining Central and Eastern European countries, it will be marketed by Merck, Sharp & Dohme as either Gardasil or Silgard. The vaccine is already available in countries outside of the US and Europe, and the company has pledged to make its new vaccines, including Gardasil "available at dramatically lower prices to developing world countries."

> ''VACCINATION SHOULD BE MANDATORY FOR ALL GIRLS AGED 11–12''

The vaccine is a suspension for injection that contains purified L1 proteins for 4 types of HPV, assembled in virus-like particles. It is given as an intramuscular injection in three doses (with 2 months between the first and second dose, and 4 months between the second and third).

According to the European Medicines Agency (EMEA), 4 main studies of the vaccine, involving 20,000 16–26 year-old women, have compared the active vaccine with placebo. Among women who had not been previously infected by the 4 types of HPV, and who received the full course of vaccination (8,487 women), none developed high grade dysplastic cervical lesions due to HPV 16 or 18. Of the 8,460 women who received the placebo, 53 had such lesions.

Pooled results of 3 studies found that one woman who received the active vaccine had genital warts due to the 4 types of HPV, compared with 91 in the placebo group.

A *Lancet* editorial (2006;**368**:1212) noted that, following the FDA's decision, the Michigan Senate passed a bill in September, 2006, requiring all girls entering the 6th grade (11–12 years old) to be immunised. "This is the first legislation of its kind in the USA, and a decision from which the EU member states should take heed."

There is growing support for the vaccination of both boys and girls. "For effective and long term eradication of HPV, all adolescents must be immunised. Data from the vaccine trials in boys are urgently needed; in the mean time, EU member states should lead by making the vaccinations mandatory for all girls aged 11–12 years," the editorial concludes.

Suicide Risk in Cancer Patients

A diagnosis of cancer more than doubles the risk of suicide, a Canadian oncologist found. He urged healthcare professionals to offer extra support to the most vulnerable and their families.

Men were 5 times more likely to kill themselves than women, reflecting the male-female ratio for suicide in the general population.

Dr Wayne Kendal (Ottawa Hospital Regional Cancer Centre, Canada) looked at data on 1.3 million cancer cases in the USA (*Annals of Oncology doi: 10.1093/annonc/mdl385*). The risk of suicide varied according to a number of factors, including gender, prognosis, the stage of disease, the type of cancer, ethnicity and family situation.

"If we were to draw a composite picture of the patient most at risk, this would be a widowed white male, with a new diagnosis of possibly head and neck cancer or multiple myeloma, with widespread and perhaps high-grade disease or maybe a history of other cancers," he said.

Both sexes were more likely to commit suicide if their cancer had already spread from its primary site to distant organs by the time it was diagnosed.

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Childhood survivors “need lifelong monitoring”

Long term survivors of paediatric cancers have high rates of chronic and life-threatening conditions which increase with time. These adults require lifelong monitoring, say US researchers (*N Engl J Med* 2006;**355**:1572–82).

The Childhood Cancer Survivor Study (CCSS) included 10,000 adult survivors who were treated for childhood cancer in the 1970s and 1980s. The retrospective cohort study compared their health status with that of their siblings.

Survivors were 3 times more likely than their siblings to have a chronic condition and 8 times more likely to have a severe or life-threatening condition. 30 years after diagnosis, three-quarters (73.4%) had a chronic health condition.

The risk was particularly high for second cancers, cardiovascular disease, renal dysfunction, severe musculoskeletal problems and endocrinopathies. “These findings underscore the necessity of continued follow-up of survivors of childhood cancer,” the authors wrote.

“The incidence of health conditions reported by this population increases with time and does not appear to plateau. The monitoring of survivors is an important part of their overall healthcare,” they said.

The report pointed out that less than 20% of adult survivors are followed at a cancer centre or by an oncologist, and that the likelihood of follow-up in this setting decreases further with time. “For this reason, it is important for general physicians and internists to be aware of the risks facing this population.”

An accompanying editorial (*N Engl J Med* 2006;**355**:1522–3) states that even more problems may cloud the future as this population ages: “One can only speculate about how the combination of pre-existing myocardial damage from anthracycline exposure or heart irradiation for Hodgkin’s disease would affect cardiac risk factors, when combined with the high incidence of hyperlipidaemia, hypertension, diabetes, and kidney disease in the US population at large.”

The editorial describes the CCSS as “a remarkable long-term study” but notes that all patients were treated before 1986. Considerable changes in therapy for most childhood cancers have been introduced during the succeeding 20 years, often with an escalating intensity of treatment, paralleling an improvement in survival rates. At the same time, awareness of the potential for late effects has grown.

“It would be expected that patients who were treated more recently might have an analogous but different array of long-term complications. This historical effect argues for establishing another cohort for future study.”

Complications in survivors can demand a level of knowledge that is beyond the range of the general internist or family doctor, or even of medical oncologists, the editorial says. Specific training could be incorporated into internal medicine, paediatrics and family medicine; alternatively, a postgraduate fellowship could be developed within an adult subspecialty, similar to existing fellowships in adult congenital heart disease.

Patients themselves could be empowered by being given a portable document describing their treatment, its potential late complications, and any types of behaviour that could diminish their risk of late effects. Whatever the eventual approach, the editorial concludes, it is clear that the effects of childhood cancer do not end at 18 or 21 years: “Although the child with cancer may be cured, the effects of treatment are lifelong, and we need to study and treat these late effects.”

Vitamin D “may curb breast cancer progression”

Low levels of vitamin D may promote progression to advanced breast cancer, suggest UK authors. They found that women with early stage disease had significantly higher levels of vitamin D than the women with advanced disease.

The study (*J Clin Pathol* 2006; *doi.10.1136/jcp.2006.042747*) included 279 women with invasive breast cancer, of whom 204 had early-stage disease. The remainder had locally advanced or metastatic cancer.

There was little difference in calcium levels between the 2 groups, but the women with early stage disease had significantly higher levels of vitamin D and significantly lower levels of parathyroid hormone.

However, the authors acknowledge that the exact reasons for the disparity are unclear. The study was observational and did not establish whether the low levels of vitamin D among those with advanced disease are a cause or consequence of the cancer itself.

They note that vitamin D boosts the activity of genes such as p21, which has an important role in controlling the cell cycle. Laboratory studies have shown that vitamin D stops cancer cells from dividing and enhances cell death. Epidemiological evidence has found a link between rates of, and deaths from, breast cancer and exposure to sunlight, they say.

Several questions remain unanswered, but they conclude: “These findings lend support to the hypothesis that vitamin D has a role in the pathogenesis and progression of breast cancer.”

Bread Consumption linked to RCC

Diets which include a lot of bread may raise the risk of renal cell carcinoma (RCC), say Italian researchers. They found a significant association between high consumption of bread and risk of RCC.

The study included 767 adults diagnosed with RCC between 1992 and 2004, each matched with 2 controls by gender, age range and location. Researchers collected sociodemographic information, anthropomorphic measures, lifestyle habits, personal and family medical history from each participant. All answered a food questionnaire.

Those in the highest quintile for bread consumption were almost twice as likely to have RCC (odds ratio = 1.94) as those in the lowest quintile. A modest but non-significant increase was seen for pasta and rice (*International Journal of Cancer 2006 doi: 10.1002/ijc.22225*).

The researchers suggest that the link with elevated cereal intake “may be due to the high glycaemic index of these foods and their possible involvement in insulin-like growth factors.”

EUROFILE

Cancer United: A Strategy for Europe

When cancer survival rates across Europe vary so much from country to country, why is there no pan-European strategic approach to improving cancer services? This was the question asked at the launch in Brussels of Cancer United, a new campaign aiming to improve access to quality care for patients across Europe, on October 19, 2006.

National cancer plans are needed in all EU Member States, said campaign chair Professor John Smyth. "We know that from countries where cancer care has been given resources and given the priority it deserves. Best practices should be shared across Europe. A patient's chance of survival should not be determined by geography. We must change that."

"ALL EU MEMBER STATES SHOULD HAVE A NATIONAL CANCER PLAN"

The campaign centres around a report produced by Rifat Atun, Professor of International Health Management at Imperial College London, which found that the chance of surviving cancer depended on where patients live in the European Union. Patients from lower socio-economic groups and rural areas had more limited access to quality care than those from higher socio-economic groups, and access to comprehensive quality care varies for different types of cancer, he said. "More Europeans are developing cancer. Projections show that by 2020 the number of new cancer cases will increase by 25% to reach 3.4 million". The report found that survival rates fall well below what could potentially be achieved. "If we don't improve cancer services across Europe, more people will die because they have not had the best treatment", said Professor Atun.

"Europe needs to adopt a more strategic approach to managing cancer. A concerted effort by Member States and the European Union is well overdue," he said.

The Cancer United campaign brings together for the first time under one banner all groups involved in cancer care – patients, patient groups, doctors, nurses, researchers, industry, policy makers and major institutions in cancer care. It aims to gather one million signatures from citizens to pressure the European Union to introduce a cancer strategy.

The Executive Board has invited key opinion leaders in each country to become national presidents and lead the campaign in their country. They will push their own governments to develop a national cancer plan; the plans, once developed, may vary greatly in both objectives and resources (as is the case where cancer plans exist already). The overall aim is to help each country make the best use of its resources and ensure that a fair system is in place.

The campaign aims to roll-out in all Member States – including accession countries Bulgaria and Romania – over the next 18 months and will report back to Brussels in 2008. "Such a comprehensive, grassroots campaign just hasn't happened before", states the Cancer United website (*www.cancer-united.org*).

A worthy cause and nothing to get too upset about, you might think. But the day before the launch an article in the UK newspaper *The Guardian* criticised the campaign for being too closely linked to a single pharmaceutical company. The Swiss giant, Roche, is the sole funder of Cancer United and has a senior executive on its board. The Guardian said that the scale of Roche's involvement had caused some supporters to withdraw before the launch and raised questions about Cancer United's objectivity and real aims. The article also criticised the study on which it said formed the platform for the campaign. "The report, from the Karolinska Institute in Stockholm, links patient survival to the amount their government spends on drugs," it said.

This last point seems to be a misunderstanding, since all the material produced to support the campaign links it to Professor Atun's report. Anyhow, cancer plans are about far more than drugs, which come at the end of the line, says Professor Smyth. "Prevention and screening are far more important, and drugs alone are of little use – they need to be used in conjunction with surgery and radiotherapy, as appropriate to the patient."

"CANCER PLANS ARE ABOUT FAR MORE THAN DRUGS"

But what about allegations of undue industry influence? Running a campaign with just one source of funding was surely asking for trouble. "I just didn't think about it that way", says Smyth. "When I apply for a grant I go to one organisation at a time; I don't apply for the same thing to several bodies at once. I looked at this in the same way. I am sorry if it has meant that people have questioned the real purpose of the campaign. Leading cancer specialists from all over Europe are donating their time to this campaign for free; the idea that this is a front for a pharmaceutical company is ridiculous. We will be using our relationship with Roche to try to persuade them to reduce prices for their cancer drugs, and if other companies want to come on board, we will do the same with them."

He hopes that none of this will detract from an understanding of the real need for an integrated European cancer strategy. "We will know we have succeeded if, by 2008, we have helped establish comprehensive national cancer plans in several more European countries. The great thing at the launch was how many people, especially from Eastern Europe, stood up and said 'This is exactly what we need; please help us.' That was hugely gratifying, and we will do our best not to let them down."

Mary Rice
Brussels

30 Cents on a Pack of Cigarettes

Hiking the price of a pack of cigarettes by 20 pence (Euro 0.30) is the UK Government's best hope of reaching its smoking targets, a tobacco studies expert said. The aim is to reduce the proportion of adult smokers to 21% by 2010.

Professor Robert West (Cancer Research UK's Health Behaviour Unit) said that the money generated should be used to fund a tobacco control task force. He told delegates at the NCRI Conference that properly resourced evidence-based tobacco control activities could then drive smoking rates down progressively.

Smoking taxes introduced in California, USA, and Victoria, Australia, have reduced smoking rates to 15% and 18% respectively. In the UK, 25% of the population smokes and the number is being reduced by only 0.4% a year.

Professor West said that the UK has been successful in helping smokers quit: "But efforts are stalling and unless new initiatives are introduced, hundreds of thousands of people will develop smoking related diseases and many will die as a result."

"Putting 20 pence on a pack of cigarettes would not only have an immediate effect on smoking, ultimately saving 100,000 lives, through the new task force it has the potential to kick-start the next big decline in UK smoking prevalence."

Concerns that the price rise would drive lower-income smokers further into poverty were addressed. Professor West said that the vast majority of smokers want to quit: "We have a duty to support their motivation to do so and make sure they have ready access to treatment. Evidence from elsewhere indicates that smokers who are less well off are most likely to stop smoking in response to higher prices. And those that do not stop will cut down, reducing their costs."

Risk of Recurrence in Rectal Cancer

A quick course of radiotherapy, followed by surgical removal of rectal cancer, may minimise the risk of local recurrence, an international study found. The best surgery, combined with pre-operative radiotherapy, cut local recurrence rates to as little as 1%.

The Medical Research Council Trial, CR07, included 1350 patients from the UK, Canada, South Africa and New Zealand. In the pre-operative group, patients received 5 daily treatments of radiotherapy, followed within 2 weeks by surgery. In the post-operative group, 10% of patients were selected to receive 25 daily treatments of radiotherapy over a 5-week period, combined with chemotherapy. Patients were selected for chemotherapy if pathological examination revealed cancer cells within 1 mm of the edge of the removed tissue.

The results were presented at the UK's National Cancer Research Institute (NCRI) Cancer Conference (Birmingham, UK, 8–11 October, 2006). Overall, 5% of patients in the pre-operative group had local recurrence after 5 years, compared with 17% of the post-operative group. The pre-operative patients had a higher chance (75%) of being alive at 5 years, than the post-operative patients (67%).

Pre-operative radiotherapy benefited patients irrespective of the position of the cancer or quality of the surgery received. However, the trial confirmed that quality of surgery is directly linked to risk of local recurrence. The combination of pre-operative radiotherapy and the best surgery reduced the risk of local recurrence to 1%.

"This is good news for patients and clinicians alike and could lead to an increase in the use of pre-operative radiotherapy," said Dr David Sebag-Montefiore (Cookridge Hospital, Leeds, UK), principal investigator. "The trial results show that patients should have the opportunity to discuss the benefit of radiotherapy before rectal cancer surgery."

Professor Phil Quirke (Leeds Institute of Molecular Medicine, UK), called for an education programme to train surgeons to change their technique. "It is a very cheap and simple way of making improvements. Getting surgery right in bowel cancer is amazingly important."

Cyber-Patients Predict Response to Treatment

A biomathematical model predicted with 70% accuracy how patients with advanced breast cancer would respond to treatment, scientists told the NCRI Conference. In future, such technology could help doctors tailor treatment for individual patients, they said.

The computer-generated "virtual cancer patient" was developed by teams from Nottingham City Hospital, UK, and the Institute for Medical Biomathematics, Bene Ataroth, Israel. The model was "trained" using clinical data from real patients; researchers programmed it to evaluate how the drugs affected the growth of the cancer, how the drugs behaved in the body, and how the cancer cells responded to the drugs. To test its effectiveness, they then compared the predictions of the virtual patient programme with the actual response of patients.

So far, researchers have obtained the most clear-cut data when studying drugs that work better alone than those that work in combination. The pilot study included 33 patients with advanced breast cancer that had spread to liver, lymph nodes or lungs. The model compared which of 2 drugs – docetaxel and doxorubicin – would work best on each patient.

In this retrospective study, the model accurately predicted how 70% of patients responded to their treatment. Researcher Dr Stephen Chan (Nottingham City Hospital, UK) said: "This was a pilot study in a small number of patients, so now we want to fine tune the model to improve its accuracy and test it in a larger study. We also want to see how it works when we use combinations of drugs and whether the model can predict if a patient will suffer other side effects in response to treatment."

PODIUM

Patients Need to Know

Dr Yvonne Wengström

Dr Yvonne Wengström (Karolinska Institutet, Stockholm, Sweden) is President of the European Oncology Nursing Society (EONS). She coordinates Care Science Research at the Karolinska Institutet and mentors undergraduate and postgraduate research students in oncology nursing. She is a member of the GAEA (Gathering Information on Adjuvant Endocrine Therapy) Initiative steering committee and recently led a survey which asked more than 500 women in 9 European countries about their experience of receiving adjuvant endocrine therapy for recently diagnosed breast cancer.

What did the GAEA survey find?

The survey found that the patients who were more actively involved in making the treatment decision were much more satisfied with the care they received. In general, they were not sufficiently well informed. Only one-third of the patients taking the endocrine therapy said they were involved in the decision to start this treatment. Almost half (41%) of the women had no involvement at all in the treatment decision and a further 22% were made aware of different treatment options but, again, were not involved in the decision. Less than half received information about how the treatment works and less than one-quarter were informed about potential side effects.

Did the involved women actually receive better care?

We don't have objective evidence to answer this question. But individuals need to be informed in such a way that allows them – with their doctor – to make a judgement which is suitable for them. Patients who are less informed might not get optimal treatment, and they may be less able to handle side effects, which in turn affects their compliance. This is not fair; patients need to be forewarned of potential problems.

Are specific groups of patients disadvantaged?

Older patients, those who were less well educated and those without Internet access were much less likely to be involved in decision-making or to receive the information they need to make informed choices. In healthcare over the last few years, we have become so concerned about future patients that we seem to have forgotten those we are treating now. Most women with breast cancer are more than 60 years old. They want their disease and treatment option explained in simple terms. They want access to the breast care team; they want to be encouraged to have faith in their treatment. Most of our findings were strikingly similar across Europe. It seems the same problems exist everywhere.

Do different patients have different information needs?

I don't think so, we just need to be more savvy in coming up with ways of explaining things to patients. We can't rely on the Internet; we need to supply information in one to one meetings with patients. Our survey found that breast care nurses were not playing an important role and this needs to be addressed.

Do paternalistic attitudes still prevail among professionals?

Healthcare professionals tend to take for granted the level of information women want. Somehow we believe that by not concerning a patient with all the available information we are being careful and caring. We really need to ask patients what they want and not make judgements on their behalf.

What needs to happen?

We need to become more responsive and work more closely with patients. There is, for example, a cognitive difference in the information leaflets produced by professionals alone and those developed with patients. It may be in the language used or in the concerns addressed. Professionals working in cancer care need education to help them use the same language as their patients in consultations. They need to understand how to present information and how to make sure patients understand the information they have been given. At present, we are not doing this correctly.

Professionals and patients see different problems and do not place the same emphasis on symptoms and side effects. We often forget to ask patients what symptom bothers them the most – we're so busy ticking boxes and working out the prevalence of symptoms or side effects that we do not address their main concern. It is the same in information-giving: we need to ask what is important to them.

Were you surprised by the findings of your survey?

Yes. I thought we would have been doing much better than this now. We need to emphasise the importance of informing patients in doctors' and nurses' training. It is still not being taken seriously enough.

How far can things change over the next 5 years?

If we can raise awareness by working locally in each European country – all disciplines in conjunction with the growing number of patient advocacy groups – we can emphasise the importance of informing and involving patients in decision making.

In 5 years' time, patients are gong to have active voices across Europe. We hope the process of change which has already started will be continuing; and that professionals and patients alike will be better informed.