NEWSROUND

Selected press reports compiled by the ESO Cancer Media Centre

Chromosome alterations in neuroblastomas may help predict survival

➔ New England Journal of Medicine

New tumour biomarkers may help to identify outcomes for patients with neuroblastoma, a form of childhood cancer, according to a study published in the *New England Journal of Medicine*. Neuroblastoma is one of the most common cancers found in babies or young children, with two-thirds of cases diagnosed in children younger than five years of age.

The disease originates in the adrenal medulla or other sites where sympathetic nervous system tissue is present. There are different types of neuroblastoma tumours. Some are highly aggressive and require assertive treatment, others will remain slow-growing and can spontaneously regress.

Treatment for neuroblastoma varies greatly, depending on the stage of the disease and its ferocity. It is important that doctors can identify the strain of neuroblastoma so that patients can be given the appropriate treatment.

Scientists in the latest published study examined over 900 different samples of neuroblastoma, and looked at the abnormalities of chromosomes 1p and 11q. The results suggested that abnormalities in patients with the disease are associated with worse outcomes. Three-year event-free and overall survival rates were worse for those with the chromosome abnormalities. In the future, scientists will be able to screen tumours for the presence of abnormalities, to determine the appropriate form of treatment for the cancer patient. In some cases more aggressive chemotherapy and immediate bone marrow transplant may be appropriate to improve chances of survival.

■ Chromosome 1p and 11q deletions and outcome in neuroblastoma. EF Attiyeh, WB London, YP Mossé, et al. *NEJM* 24 November 2005, 353:2243-2253

Diabetics have a higher risk of colorectal cancer

➔ Journal of the National Cancer Institute

Diabetes is associated with an increased risk of colorectal cancer according to a meta-analysis published in the *Journal of the National Cancer Institute*. Previous studies have been inconclusive about the link between the two conditions.

Colorectal cancer is the most common form of cancer in the European Union, but it is one of the most curable cancers if caught early enough. Diabetes currently affects 5% of the world's population and occurs when the body cannot break down sugar in the normal way. Obesity is a risk factor for both conditions and may provide evidence for the link.

Scientists examined 15 published studies including just over 2.5 million participants. The meta-analysis found that people with diabetes were at a higher risk of colorectal cancer than those without diabetes. Previous studies have indicated that men with diabetes may be more at risk; however, the study proved that the link between colorectal cancer and diabetes did not differ significantly by sex or by cancer sub-site.

The study also revealed that people with diabetes are more likely to die from colorectal cancer. Scientists are unsure what causes the relationship between diabetes and the increased risk of colorectal cancer. It seems that the high sugar levels found in diabetics may hold the key; or alternatively hormonal changes associated with diabetes could promote tumour risk. Further research is needed to fully understand the link.

■ Diabetes mellitus and risk of colorectal cancer: a meta-analysis. SC Larsson, N Orsini, A Wolk. *JNCI* 16 November 2005, 97:1679-1687

Chemotherapy improves survival for patients with endometrial cancer

➔ Journal of Clinical Oncology

A new study published in the *Journal of Clinical Oncology* has found that chemotherapy improved survival for patients with advanced endometrial cancer when compared to radiation therapy.

Women who take tamoxifen for breast cancer are at increased risk of endometrial cancer, as are women taking oestrogen (without progesterone) as a type of birth control or to treat menopausal symptoms.

The US study compared the two types of treatments currently given to endometrial

cancer patients – irradiation of the abdomen versus chemotherapy with doxorubicin-cisplatin. Nearly 400 women (average age 63) with advanced endometrial cancer (stage 3 or 4) took part in the study. Approximately half of the study population was given radiation and the other half chemotherapy. The patients were then monitored and followed up for a number of years.

The study found that, at five years, after adjusting the results to take into account the different stages of the disease, 50% of the patients receiving chemotherapy were predicted to be alive and disease free compared to just 38% of patients receiving radiation therapy. Moreover, 55% of women treated with chemotherapy were predicted to be alive compared to 42% of patients treated with radiation therapy.

The results clearly showed that chemotherapy with doxorubicin-cisplatin significantly improved progression-free and overall survival compared with radiation therapy. However, scientists did find that there was greater acute toxicity seen with chemotherapy, and further advances are needed in reducing the levels of toxicity.

■ Randomized phase III trial of whole-abdominal irradiation versus doxorubicin and cisplatin chemotherapy in advanced endometrial carcinoma: A Gynecologic Oncology Group Study. ME Randall, VL Filiaci, H Muss, et al. *JCO*, published online 5 December 2005, doi: 10.1200/JCO.2004.00.7617

Fentanyl patch is a safe and effective alternative to oral opioids for children

➔ Cancer

A new study has found that using a transdermal patch to deliver the opioid fentanyl is an effective way to control pain in children. Results from an international study published in *Cancer* indicate that the fentanyl patch is safe for children aged 2–16 years.

Opioids, such as morphine, have been shown to clearly reduce pain and improve quality of life in adults. However, little is known about the safety and efficacy of this class of analgesics in children. Until recently, children were thought to feel pain to a lesser degree and have a higher risk of addiction than adults. Newer information indicates that children experience severe pain and have the same addiction risk as adults.

They are also at greater risk for psychological disturbances that have an immediate and long-term developmental impact. However, children often have difficulty taking opioids; they may not like swallowing pills and get distressed at injections.

Julia Finkel, of the Children's National Medical Center in Washington DC, and international colleagues, examined 173 children from between the ages of 2 and 16 years, many of whom were cancer patients and had a history of chronic severe pain and previous oral opioid use.

They were given the fentanyl patch that equalled the amount of oral analgesics they had received, and were followed for 15 days. The researchers found that subjective pain and quality of life improved significantly. By day 16, the average daily pain intensity score had decreased. Many patients elected to continue in the study for three months. After one month, quality of life scores improved. At the end of three months, average play performance scores also showed significant improvement.

There were no more adverse experiences than reported in adults, and no adverse experiences specific for the paediatric population. The authors conclude: "Results from global measurements of pain treatment, safety and quality of life indicate that transdermal fentanyl is an acceptable alternative to oral opioid therapy in children."

■ Transdermal fentanyl in the management of children with chronic severe pain: results from an international study. JC Finkel, A Finley, C Greco, et al. *Cancer*, published online 14 November 2005, doi: 10.1002/cncr.21497

Discovery of molecular signature will help treat patients with brain cancer

➔ New England Journal of Medicine

Researchers at the University of California at Los Angeles Jonsson Cancer Centre have identified key characteristics in certain fatal brain tumours that make those tumours more likely to respond to a specific class of drugs than tumours where the specific molecular signature is absent.

The discovery of this molecular signature (the expression of a mutant protein and a tumour suppressor protein called PTEN) will allow researchers to identify patients who are likely to respond to the drug treatment, before they embark on therapies that might not work.

According to Paul Mischel, an associate professor of pathology and laboratory medicine and a Jonsson Cancer Center researcher, the discovery of this treatment could change the way doctors treat glioblastoma, which is the most common type of malignant brain tumour and one of the most lethal forms of cancer. "In a biologically aggressive disease like glioblastoma, it's vital to be able to stratify patients up front so we can treat them with drugs that they are more likely to respond to...this will help prevent patients from having needless therapies that are toxic and not beneficial. With the short survival times associated with glioblastoma, this is critical."

Quality of life is an important factor, as patient survival is on average less than one year. Although treatment may prolong life, most malignant brain tumours are not curable, making the search for better treatments even more urgent. Epidermal growth factor receptor (EGFR) is commonly over-produced in glioblastoma, making it the focus for therapies.

Mischel and his team studied a group

of 26 glioblastoma patients who either responded very well or very poorly to EGFR-blocking drugs, and developed a way to test their brain tumours for the presence of both mutant and PTEN proteins. Mischel's team found that patients with both genetic variations were 51 times more likely to respond to EGFR blockers. They also lived five times longer after having the therapy than those without the variation, surviving for 253 days instead of 50.

Mischel and his team also took 33 tissue samples from brain cancer patients treated at another facility. They were able to replicate their results, confirming that those with both genetic variations were more likely to respond to EGFR blocking drugs. The study shows that glioblastoma patients can respond to targeted agents, and suggests that patients likely to benefit from treatment can be identified by molecular testing.

The study also raised the possibility that patients whose tumours lacked the genetic variations in the molecular signature could possibly be treated with drugs to make them more sensitive to EGFR blockers. "Many cancers have a similar combination of a mutant cancer-causing protein and either the expression or loss of the PTEN protein…The interactions of the two may be important in determining response to targeted agents."

About 10%–20% of patients have the combination of the mutant and PTEN proteins.

Mischel and his team are also working to uncover the molecular signatures in the tumours of non-responders, so they can determine which therapies might be most effective for those patients.

"Glioblastoma is still a difficult disease, but the idea that it may be possible to induce long-term disease suppression gives reason for hope."

■ Molecular determinants of the response of glioblastomas to EGFR kinase inhibitors. IK Mellinghoff et al. *NEJM* 10 November 2005, 353:2012–2024

Survival rates for colon cancer patients improve

➜ JAMA

More patients with stage 3 colon cancer are receiving chemotherapy after surgery, improving their five-year survival rates, according to a study in the December 7 issue of JAMA.

However, women, black patients and the elderly, are less likely to receive adjuvant treatment.

The National Institutes of Health Consensus Conference recommended in 1990 that adjuvant chemotherapy (5-fluorouracil-based regimen) should be given to all patients with stage 3 colon cancer. Researchers looked at information from almost 86,000 patients entered into the National Cancer Data Base between 1990 and 2002 to see whether the Conferences' recommendations had been followed.

The researchers found an increase in the use of adjuvant chemotherapy for all patients with stage 3 colon cancers, from 39% of patients in 1990 to 64% in 2002. Between 1991 and 1997, the five-year survival rate almost doubled in patients who had adjuvant chemotherapy compared to those who had surgery alone.

The study also revealed that the use of adjuvant chemotherapy was lower in female and elderly patients. Significantly, 3% fewer women than men received adjuvant chemotherapy after surgery, even though the treatment is equally beneficial in both.

Elderly patients were also given adjuvant chemotherapy less frequently, despite the fact that they benefit as much as young patients.

■ Adjuvant chemotherapy for stage III colon cancer. Implications of race/ethnicity, age and differentiation. JM Jessup, A Stewart, FL Greene, et al. *JAMA* 7 December 2005, 294:2703-2711

Breast cancer treatment may be affected by altered gene

➜ Journal of Clinical Oncology

A new study has found that Tamoxifen may be less effective in treating women with breast cancer if they have a relatively common genetic variation, according to research published in the *Journal of Clinical Oncology*.

Tamoxifen usually reduces the risk of breast cancer recurrence by almost 50% in women with oestrogen-receptor positive breast cancer. However, this study indicates that women whose CYP2D6 gene is altered have a higher risk of relapse when treated with tamoxifen for five years compared to women who do not have the altered gene.

The genetic alteration, which occurs in about one in ten women, affects the level of CYP2D6, a liver enzyme that is involved in metabolising the drug. Researchers found that normally the enzyme CYP2D6 converts tamoxifen to a metabolite called endoxifen – an anti-oestrogen that is nearly one hundred times stronger than tamoxifen itself. However in women with the altered gene, the process does not work as well, and the tamoxifen may be less effective at preventing relapse.

The study looked at 223 tumour and tissue samples from tamoxifen-treated women who took part in the American Phase III North Central Cancer Treatment Group adjuvant breast cancer trial.

The results showed that women with the altered gene tend to have a higher risk of disease relapse and a lower incidence of hot flashes.

A larger study is needed in order to corroborate the findings.

■ Pharmacogenetics of tamoxifen biotransformation is associated with clinical outcomes of efficacy and hot flashes. MP Goetz et al. *JCO* 20 December 2005, 23:9312-9318