FEDERATION OF EUROPEAN CANCER SOCIETIES

PARIS
30 October - 3 November 2005

ECCO 13
the European Cancer Conference

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New options for prostate cancer

Clinical data from trials presented at the 13th European Cancer Conference (ECCO 13, 30 October–3 November, 2005, Paris, France), showed prostate cancer patients benefiting from higher doses of radiotherapy (RT), early anti-androgen intervention, maximal androgen deprivation (MAD) therapy and single agent immunotherapy.

A multi centre phase III study led by Dr J.V. Lebesque (The Netherlands Cancer Institute, Amsterdam) showed that at 5 years, freedom from failure (FFF) in prostate cancer was significantly higher in patients receiving 78 Gy RT than those receiving the standard 68 Gy dose (64% vs. 54%, $P = 0.025$). The study recruited 669 patients with stage T1b-T4N0M0 prostate cancer, who were divided into low, intermediate and high prognostic risk groups (18%, 27% and 55% of participants, respectively) and randomized to receive either 68 Gy or 78 Gy RT. Some patients (143) in the intermediate and high-risk groups also received hormonal therapy (HR).

When the treatment groups were analyzed separately it was only in intermediate-risk patients that the benefits in FFF seen with increased radiation doses were statistically significant (74% vs. 58%, $P = 0.03$). The gain in FFF for the high risk group was smaller (52% vs. 44%, $P = 0.1$), and there was no benefit in the low risk group (84% vs. 66%, $P = 0.7$). No significant differences in overall survival and freedom from clinical failure were seen between both arms.

Professor Harry Bartelink, president of Federation of European Cancer Societies and the organizer of ECCO, commented: "From this first analysis trial the standard treatment for prostate cancer should be changed to a higher radiation dose."

The Early Prostate Cancer (EPC) programme presented its third analysis data at 7.4 year follow-up on the largest ever randomized double-blind trial of patients with non-metastatic prostate cancer, investigating the efficacy of the anti-androgen drug bicalutamide.

In the EPC trial, 8113 men with localized (T1-T2, N0/Nx) or locally advanced (T3-4, any N; or any T, N+) were treated with either 150 mg bicalutamide or placebo plus standard care (RT, radical prostatectomy or watchful waiting [WW]). Results showed that in men with locally advanced prostate cancer bicalutamide improved their chance of survival by 35% ($P = 0.003$) compared to radiotherapy alone, and reduced their risk of disease progression by 31% ($P < 0.001$). No significant progression-free survival (PFS) or OS benefit was demonstrated by the addition of the drug in patients with localized disease.

Professor Peter Iversen (Rigshospitalet, Denmark), who headed the study commented: "The results provide a significant step forward and show that men with localized disease gain no significant benefit while men with locally advanced disease derive significant benefit from the addition of bicalutamide. There was minimal impact on quality of life, allowing men to remain active and retain sexual function and interest."

Dr Heather Payne, a clinical oncologist (London, UK) added that prior to this data survival advantages had only been shown for medical castration treatments. "This study gives men with locally advanced disease a welcome choice of treatment," she said.

In a separate study, effects of HT in the form of MAD, administered 3 or 6 months prior to and during RT on locally advanced non-metastatic prostate cancer (T2bc, T3 and T4; N0, M0) in 802 patients was reported by Dr James Denham and colleagues (University of Newcastle, Australia). Results showed that in comparison to RT alone, 3 months MAD significantly improved various clinical indicators including clinical disease-free survival (HR 0.66; $P < 0.001$) and freedom from salvage therapy (HR 0.71; $P = 0.024$). Greater advantages were seen with 6 months MAD, but the authors concluded further follow-up was required to better estimate survival benefits.

Lastly, Dr Celestia Higano (University of Washington, USA) presented survival data from a second phase III trial on the use of the immunotherapy agent APC8015 in patients with asymptomatic metastatic androgen-independent prostate cancer (AIPC). Similar to the results of the first trial communicated at ASCO, 2005, APC8015 showed that at 36 months, 32% of men in the APC8015 arm were alive, compared to 12% in the placebo group ($P = 0.023$). "The combined data from these trials suggest that immunotherapy might impact survival in men with AIPC. APC8015 has a favorable safety profile and future studies in patients with earlier stage disease or in combination with other agents will be of great interest," said Dr Higano.

Lekshmy Balakrishnan
Paris, France

EJC News is compiled by:
Janet Fricker
Tel: +44(0)1442 216902
E-mail: janet.fricker@tesco.net

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Combined treatments improve pancreatic cancer survival

The addition of capecitabine to gemcitabine, over gemcitabine alone, produced significant improvements in overall survival in patients with advanced pancreatic cancer and should be considered one of the new standards of care, concludes a phase III study presented in the ECCO Presidential Symposium (PS11).

Between May 2003 and January 2005, 533 patients with previously untreated or cytological proven locally advanced/metastatic carcinoma of the pancreas were randomised to receive either gemcitabine alone (GEM), or gemcitabine and capecitabine (GEM-CAP). Treatment was continued until either disease progression was seen or intolerable toxicities occurred. The primary outcome measure was survival. At the time of an interim analysis performed in May of 2005, 70% of the patients had died.

Investigators found the GEM-CAP combination significantly improved overall survival compared to GEM alone (hazard ratio 0.80; 95% CI 0.65–0.98; $P = 0.026$). The median survival for GEM alone was 6 months, compared with 7.4 months for the combination. The one-year survival rates were 19% for GEM alone and 26% for GEM-CAP.

Grade 3 or 4 toxicities for the GEM alone and GEM-CAP arms, respectively, were as follows: anaemia (2%, 1%), neutropenia (11%, 17%), thrombocytopenia (2%, 3%), fever (1%, 0%), diarrhea (1%, 1%), hand-foot syndrome (0%, 2%) and vomiting (2%, 1%). There were no reported cases of stomatitis in either group.

The trial represents the second to show an advantage for combination treatments. In May this year at the American Society of Clinical Oncology meeting (Orlando, Florida) Malcolm Moore from the Princess Margaret Hospital (Toronto, Canada) presented a study in 569 patients showing that at 1 year, 24% of those receiving erlotinib in addition to GEM were alive, compared to 17% treated with GEM and placebo.

However, at ASCO 2005 a study by the Swiss Group for Clinical Cancer Research (SAKK) in 320 patients with locally advanced/metastatic disease showed GEM plus CAP had no effect on survival compared to GEM alone.

Dr Ian Chau, one of the investigators of the current study (Royal Marsden Hospital, UK), commented: "The explanation for these differences is probably that the positive studies were better powered to show small, but clinically relevant survival advantages. In addition, the dose schedule we used was higher than the SAKK study."

He added that the combination of GEM CAP could provide a new treatment platform on which other biological and cytotoxic drugs could be added.

Herceptin shows benefits after adjuvant chemo

Results from the first and only interim analysis of the Breast International Study (BIG) show Herceptin (trastuzumab) given to HER-2 positive breast cancer patients after adjuvant chemotherapy produced significant improvements in disease free survival.

In the study , presented in the presidential symposium (abstract PS4), 5090 early breast cancer patients with HER-2 positive breast cancer, who had completed at least four cycles of neoadjuvant chemotherapy, were randomised to receive 1 year of Herceptin infusions every 3 weeks, 2 years of Herceptin infusions every three weeks or one year of observation. For women with hormone receptor positive disease, adjuvant endocrine therapy (most commonly tamoxifen) followed chemotherapy.

Results released at ECCO on the recommendation of the Independent Data Monitoring Committee, focussing solely on the 1 year Herceptin ($n = 1694$) and observation groups ($n = 1693$), showed a significant difference in disease-free survival (DFS) after a median follow-up of 12 months in favor of herceptin – 85.8% of women on herceptin were disease-free at 2 years vs. 77.4% of the observation group (hazard ratio = 0.54, $P < 0.001$).

A more detailed analysis of the site of recurrences showed herceptin reduced the risk of distant, locoregional, contralateral, and non-breast malignancies. In addition, an exploratory subgroup analysis suggested Herceptin extended DFS irrespective of age, menopausal status, nodal involvement, tumor size, and other variables.

In terms of safety, however, Herceptin-treated women were more likely to develop heart failure or a reduction in left ventricular ejection fractions. Dr Michael Untch, the principle investigator, said that all cardiac events had been manageable and reversible, with no cardiac deaths in the Herceptin group, compared to one in the observation group.

"Long-term follow-up will provide clarification of the survival gain, further safety data, and information on the optimum duration of Herceptin therapy," he concluded.

• A new monoclonal antibody, bevacizumab, for the treatment of locally advanced metastatic breast cancer had Phase III data presented. Bevacizumab is a monoclonal antibody to vascular endothelial growth factor and acts to inhibit tumour angiogenesis. In the E2100 randomized trial, the efficacy and safety of paclitaxel with or without bevacizumab was assessed as first-line therapy in 722 patients with locally advanced or metastatic breast cancer. Combination therapy increased response in all patients (28.2% vs. 14.2%; $P < 0.0001$) and in those with measurable disease (34.3% vs. 16.4%; $P < 0.0001$). Progression-free survival (PFS) was also improved in the bevacizumab arm relative to paclitaxel alone (10.97 vs. 6.11 months; HR 0.498; $P < 0.001$).

Dr Kathy Miller (Indiana University Cancer Centre, USA), lead author, said: "Importantly, the improvements in response rate and PFS were obtained with minimal increase in side effects. Given the benefit of bevacizumab in patients with metastatic disease, we look forward to initiating trials in the adjuvant setting".

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Venous thromboembolism toll in cancer

A modeling study, presented at ECCO, shows venous thromboembolism (VTE), to be a major public health problem among EU cancer patients that needs to be urgently addressed. In the study the VTE Impact Assessment Group in Europe (VITAE) estimate VTE to responsible for over 140,000 deaths each year.

"The study reveals for the first time the true burden of unrecognized deaths from VTE in cancer patients," said Dr Alexander Cohen, principal investigator and a vascular physician at King's College, (London, UK); adding that due to the often silent nature of VTE, difficulty of diagnosis and follow up, and lack of routine post-mortems the morbidity and mortality have been difficult to assess. Death certificates under diagnose VTE deaths by 70–85%.

Cancer patients are particularly vulnerable to VTE due to their hypercoagulable state, and additional factors such as their relative immobility, vascular damage from the cancer itself and the effect of treatments such as chemotherapy, radiotherapy and central venous lines.

Therefore the group undertook a modified incidence-based epidemiological model to estimate the true number of VTE events and deaths. Community events were derived from a large European epidemiological study (EPI-GETBO), while hospital events came from a hospital statistics databases. The study looked at populations from 6 EU countries UK, Spain, France, Germany, Italy and Sweden (with populations of 300 plus million) and then extrapolated the figures to 25 EU member countries.

Results reveal that the total annual burden of VTE in the EU exceeds 1.5 million events. Of the 641,275 symptomatic DVT events, 181,449 (28%) could be attributed to cancer, of the 382,550 non-fatal PE, 103,289 (27%) could be attributed to cancer, and of the 78,500 VTE related deaths, 143,550 (30%) could be attributed to cancer.

"The clinical message from this study is that oncologists should be taking thrombosis more seriously as a major complication of cancer, and should be adopting prevention more widely," said Dr Cohen.

Next, the team plan to estimate the impact that realistic thromboprophylaxis uptakes would have on the incidence of VTE in cancer patients.

Less toxic therapy for lung cancer

The STELLAR 2 trial, presented in the presidential symposium, showed in second-line treatment of non-small cell lung cancer (NSCLC), paclitaxel poliglumex (PPX) demonstrated similar efficacy to docetaxel, but with significant reductions in toxicities. More over, it could be delivered as convenient infusions without the need for premedication.

The phase III study randomised 849 NSCLC patients with disease progression on or after a single platinum-based regimen to either PPX 210 mg/m^2 (PS0/1 patients) or 175 mg/m^2 (PS2 patients); or docetaxel 75 mg/m^2. Treatment resulted in a median survival of 6.9 months in both arms, with no significant differences in complete response, partial response or stable disease.

However, patients treated with PPX had significantly fewer hematologic side effects than patients in the docetaxel arm, including grade 3/4 neutropenia ($P < 0.001$), febrile neutropenia ($P = 0.002$), anaemia ($P = 0.002$), and infections ($P = 0.03$). PPX therapy also resulted in a significant reduction in alopecia ($P < 0.001$), fatigue ($P = 0.01$), asthenia ($P = 0.015$), respiratory adverse events ($P = 0.02$), mucositis ($P < 0.001$), and gastrointestinal toxicity ($P = 0.012$). As expected, neuropathy with PPX was higher than in the docetaxel arm ($P < 0.001$).

"While PPX had comparable efficacy, it resulted in a significant reduction in many side effects attributable to docetaxel therapy in relapsed lung cancer and can be delivered in a patient-convenient, 10 min infusion, without hair loss or the need for premedications," said Dr Philip. Bonomi (Rush Cancer Institute, Chicago, USA), one of the study's investigators.

Lekshmy Balakrishnan

Speak UP! Campaign

The European Oncology Nursing Society (ENOS) launched the "Speak UP!" campaign at ECCO to encourage cancer patients to talk about their chemotherapy induced nausea and vomiting (CINV). The program, developed by the European Oncology Nursing Society, includes an educational brochure about CINV for cancer patients receiving chemotherapy, a nurse discussion guide to assist nurses in talking to patients about CINV and a poster for use in medical centres to remind cancer patients to mention their symptoms.

Jan Foubert, EONS President, said: "CINV no longer has to be an accepted part of receiving chemotherapy, now there are medications that can help patients overcome these side effects. However, if cancer patients do not speak up, we will not be able to help them."

The Speak Up! Campaign will be run in several European countries, including Italy, the Netherlands, Portugal, Spain and the UK. For further information telephone 32 2 779 9923.

Inspiring Cancer Journeys

The 2006 Lilly Oncology on Canvas International Art Competition and Exhibition invites people who have been diagnosed with cancer, oncologists, nurses, family members, and carers as well as professional artists and art student to express their feelings about cancer journeys through art. Contributions can be in watercolour, oil, pastel, acrylic or other mediums. Entries should be submitted by 31 July 2006 and must be accompanied by a narrative explaining what inspired you on the journey. Prizes will consist of contributions to the artist's cancer charity of choice.

Entry forms and further information are available from *Jeremy Parsons. Tel. 44 1491 410 471; E-mail:* parsons_consulting@tiscali.co.uk

FECS/EJC Award

The Federation of European Cancer Societies/European Journal of Cancer (*FECS/EJC*) Award for 2005 was presented to Dr Dimitry Nuyten from the Netherlands Cancer Institute, Amsterdam. The award was in recognition of Dr Dimitry's work on combining two biological gene expression signatures in predicting outcome in breast cancer as an alternative to supervised classification.

Presenting the Award, Professor John Smyth, editor of *EJC* said: "We received several excellent submissions for this prize, and therefore on behalf of the selection committee I congratulate Dr Nuyten for his outstanding work."

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Chlamydia clue in lymphoma

Infection with the bacteria *Chlamydia psittaci* may be linked to the development of ocular adnexal lymphoma (OAL), suggests a study presented at ECCO.

Already a link has been established between cervical cancer and the Chlamydia strain, *C.trachomatis* , and lung cancer and the respiratory Chlamydia strain, *C. pneumoniae*. The study from the Asian Medical Centre (Seoul, Korea) looked at the chlamydia strain, *C. psittaci,* that can be caught from infected birds and may even be transmitted by household cats carrying the bacteria.

Between 2003 and 2004, DNA was extracted from 33 OAL cases, and compared with DNA extracted from a further 21 cases of a comparable, yet non-cancerous condition, non-neoplastic ocular adnexal disease (NNOAD). The extracted DNA was analyzed using a touchdown enzyme time-released polymerase chain reaction technique to isolate the presence of the three Chlamydia strains – *C. psittaci, C. trachomatis* and *C. pneumoniae*.

Results show *C. psittaci* infection was found in 78% of all OAL cases, yet observed in only 23% of cases of the non-cancerous disease NNOAD. Infection with *C. trachomatis* or *C. pneumoniae* was either non-existent or present at a very low rate in both OAL and NNOAD. Of the *C. psittaci* infections analyzed, a total of six distinct bacterial sequences were identified.

Study author, Dr Chaghoon You, commented: "Certain subtypes of low grade lymphoma are thought to be caused by some antigenic stimuli, for example, *Helicobater pylori* (*H. pylori*) induced gastric low grade MALT lymphoma, Hepatitis C (HCV) related marginal zone B-cell lymphoma, and *C. psittaci* – induced ocular adnexal lymphoma. Other types of low grade lymphoma may be related with some antigenic stimuli that have not been identified so far. In the future, eradication of the antigenic stimuli could be a common treatment method of low grade lymphoma, replacing current cytotoxic chemotherapy or radiation."

Treatment hope for resistant GIST

Updated results from a Phase III trial demonstrate sunitinib (SU11248) increases the average time to progression 4 fold in patients with metastatic gastrointestinal stromal tumours (GIST) who have failed imatinib mesylate (IM) therapy.

The double-blind placebo controlled multi centre trial, presented at ECCO, involved 312 patients with GIST whose cancer had progressed despite previous treatment, randomised 2:1 to receive SU or placebo. The sunitinib treatment was in a repeated 6-week cycle consisting of a 50 mg capsule once daily for 4 weeks, followed by a 2-week break.

It is known that most patients who respond to IM develop secondary resistance after 1–2 years of therapy, and that up to 20% exhibit primary resistance.

Results show the estimated median TTP was 6.3 months with sunitinib, versus 1.5 months for placebo ($P < 0.00001$). Although the average overall survival point has not yet been reached in either arm, sunitinib was associated with a significantly greater estimated overall survival (HR 0.491; $P = 0.00678$).

Treatment with sunitinib was well tolerated with fatigue, diarrhoea, nausea, sore mouth and skin discolouration proving to be the most common non-haematological side effects.

Dr George Demetri, the lead investigator from the Dana-Farber Cancer Institute (Boston, USA), commented : "These results provide important confirmatory evidence that documents the significant efficacy and acceptable tolerability of SU in patients with metastatic GIST whose disease was resistant to IM or those who experienced unacceptable side effects from IM. Before sunitinib there was no therapy of proven value for such patients."

GIST are the most common sarcomas of the GI tract, with around 85% having activating mutations of stem cell factor receptor (KIT), and an additional 5% activating mutations of platelet-derived growth factor receptor-alpha. SU is an oral, multi targeted tyrosine kinase inhibitor of VEGFR, PDGFR, KIT, RET, and FLT-3, with additional anti angiogenic and anti tumour activities.

Nanoparticle drug delivery first

The first ever example of targeted drug delivery to cancer cells using nanoparticle-aptamer biconjugates was presented at ECCO (abstract 804).

Nucleic acid ligands (referred to as aptamers) are short DNA or RNA fragments that can bind to target antigens with high specificity and affinity, and are analogous to monoclonal antibodies. Aptamers have the potential to act as targeting molecules directing the delivery of nanoparticles (encapsulating drugs) to tumour antigens present on the surface of cancer cells.

In proof of concept study, researchers from Harvard Medical School and Massachusetts Institute of Technology (MIT), USA, synthesized nanoparticles for controlled drug release made from a biocompatible and biodegradable PLA polymer system and then encapsulated a fluorescently labeled model drug within them to visualize nanoparticle uptake in target cells. Nanoparticles were conjugated to RNA aptamers that bind to the prostate specific membrane antigen (PSMA) that is over expressed on certain prostate epithelial cells.

The data presented at ECCO showed that the biocongjugates successfully adhered to PSMA-positive prostate cancer cells, and not PSMA-negative cancer cells. Dr Omid Farokhard, the principal investigator from Harvard Medical School, commented: "Through modification of the controlled-release polymer system or tweaks to the aptamer targeting group it may be possible to produce a diverse range of specific and selective bioconjugates. In this way drug delivery vehicles can be made to target a myriad of important human cancers."

CAM use falls after cancer diagnosis

Complementary and alternative medicine (CAM) use falls after a diagnosis of cancer, reveals a study presented at ECCO (Abstract 1584). In the study by J Harewood from the University of Southampton, 304 recently diagnosed cancer patients attending two cancer centres were surveyed over a 30 month period to determine CAM use both before and after diagnosis.

Results showed before diagnosis, 33% of patients surveyed reported using CAM, but this figure dropped to 28% after diagnosis. Interestingly, only 57% of patients who used CAM before diagnosis continued to use the treatments after their cancer was confirmed.

The authors conclude the availability of CAM within the cancer treatment settings, information about CAM and safety considerations are important influences on CAM use.

Call for more drug delivery capacity

The capacity of the NHS in the UK to deliver cancer drugs to patients is at crisis point, warns an expert report published in November. The report '*Optimising Service Capacity to Meet Demand for Cancer Drug Treatment*', by the Cancer Capacity Coalition, calls for urgent action to ensure resources will be available not only to deliver current treatments, but to also allow for emerging treatments.

"Even if the Government fast-tracks certain treatments then we may be in a position where we can't offer them to patients because we do not have the capacity to deliver them," comments the chairman of the Cancer Capacity Coalition working party Professor Jim Cassidy, from Beatson Medical Oncology Centre, Glasgow. "Patients will continue to bear the brunt of inequalities in treatment and care unless the best use is made of current and planned cancer resources. We therefore hope this report provides the practical inspiration for change."

The authors recommend the NHS adopts a number of practical measures, already being implemented in certain units, to provide high quality and equitable care for cancer patients. They add that recommendations can be as easily applied to cancer services across Europe, as they can to the UK. The measures include:

- Regular audits to determine emerging capacity shortfalls.
- Horizon scanning to identify the impact of forthcoming NICE guidance on centre resources.
- Incentives for capacity-saving measures through the Payment by Results tariff.
- Replace i.v. treatment with oral alternatives that have equivalent safety and efficacy data.
- Promote the delivery of both oral and i.v. cancer treatment closer to or in a patient's home.
- Inform all patients about the range of cancer treatment options available to them.
- Develop a national strategy to extend all training of chemotherapy nurses to encompass all aspects of cancer drug therapy.
- Increase patient flow through chemotherapy suites through faster infusion techniques or staggered nursing shifts.

For a copy of '*Optimising Service Capacity to Meet Demand for Cancer Drug Treatment*' phone Victoria West at Ketchum on 44 1 2076 113521 or *E-mail:* Victoria.west@ketchum.com.

Protein helps stratify treatments for medulloblastoma

A protein signalling favourable outcomes for children with medulloblastoma has been identified, offering the potential for stratifying patients with milder disease into therapeutic regimens that produce less long term side-effects, reports the *Journal of Clinical Oncology* (2005: 23:7951–57).

Treatment advances in medulloblastoma, an embryonal neuroepithelial tumour of the cerebellum and the commonest malignant central nervous system tumour among children, have improved 5-year survival rates for standard-risk patients to approximately 70%. "But many surviving children have educational difficulties and need treatment for neuroendocrine problems. The challenge now is to tailor treatments to the sub-type of medulloblastoma maximising cure-rates and minimising side-effects," said the principal author, Professor David Ellison from Newcastle University's Northern Institute for Cancer Research.

Professor Ellison and his team examined β-catenin immunoreactivity in tumours taken from a series of 109 children with medulloblastoma registered on the International Society for Pediatric Oncology/UK Children's Cancer Study Group trial of central nervous system primitive neuroectodermal tumours. Interest focused on nuclear accumulation of β-catenin, because this is associated with activation of the Wnt/Wg signalling pathway, and mutations affecting components of this pathway have been reported in approximately 15% of sporadic medulloblastomas.

Results reveal that the 25% of children with medulloblastomas showing a nucleopositive β-catenin immunophenotype had significantly better overall (OS) and event-free (EFS) survival than children with tumours showing either membranous/cytoplasmic β-catenin immunoreactivity or no immunoreactivity ($P = 0.0015$; $P = 0.0026$, respectively). For β-catenin nucleopositive and nucleonegative medulloblastomas, 5-yr OS was 92.3% vs. 65.3, and 5-yr EFS was 88.9% vs. 59.5%, respectively. Findings were unaltered by the inclusion or exclusion in the analysis of patients presenting with metastatic disease.

Professor Ellison commented: "What was surprising about our results is that nuclear accumulation of β-catenin had previously been shown to be associated with aggressive behaviour in some other cancers. In contrast, we found that it was such a strong marker of positive outcome in medulloblastoma that even two high-risk patients whose cancer had spread to other regions of the central nervous system by the time of diagnosis turned out to have survived for at least 5 years."

He added that if the utility of β-catenin immunoreactivity can be tested prospectively alongside other molecular markers of prognosis, a refined classification of medulloblastoma might be possible.

Preventing Chemotherapy Errors

A study reviewing safety of outpatient chemotherapy at a major US Cancer Institute has identified key strategies for error prevention, reports the journal *Cancer* (2005;104: 000–000).

The study at the Dana-Farber Cancer Institute was initiated in recognition that chemotherapy risks are especially high in tertiary care settings where patients are subject to complex treatment protocols with high dosages, novel agents, or novel combinations of agents. The problem was highlighted by the case of Betsy Lehman at the Institute, who in 1994, as a participant in a clinical trial investigating a non-standard schedule of cyclophosphamide, received a fatal overdose. Multiple system failures allowed the error to propagate over the course of 4 days.

In the prospective cohort study Tejal Candhi and colleagues from Brigham and Women's Hospital (Boston, MA) reviewed 10,112 medication orders for 1606 patients attending two adult and one paediatric outpatient chemotherapy infusion unit at the Dana-Farber Cancer Institute between March and December 2000.

Results show that the medication error rate was 3% (306 of 10,112 orders), and that approximately two thirds of these errors (2% of all orders) had the potential to cause harm. The most frequent potential adverse drug events noted among the pharmacy orders for adult cancer patients were due to the omission of chemotherapy dosages (5.9 per 1000 orders). Fortunately, the majority of errors were intercepted and none actually caused harm.

As a result of the study several strategies for improving the medication process have been introduced. These changes include implementation of a new adult chemotherapy computerized order entry system with templates for standardized chemotherapy regimens, ancillary premedications, and hydration orders. The pediatric infusion unit also changed from handwritten orders to regimen-specific or protocol-specific computerized order templates.

In an accompanying editorial, Jonathan Nebeker (University of Utahm Salt Lake City) and Charles Bennett (Northwestern University, Chicago) write: "The report represents an important step in implementing computerized solutions and other system changes that are designed to improve pharmaceutical safety in the ambulatory oncology setting."