

IMPACT OF NEUTROPENIA IN CHEMOTHERAPY EUROPEAN STUDY GROUP

Major Prospective Neutropenia Study Close to Initiation

The *Impact of Neutropenia in Chemotherapy European (INC-EU) Study Group's* landmark Prospective Observational European Neutropenia Study has received widespread interest from oncology centres across Europe and is close to being initiated. Over 80 centres from Belgium, Germany, the UK, Spain and France have expressed an interest in participating in the audit, and these centres are being evaluated for their eligibility to enrol. The study protocol has been developed and approved by all members of the INC-EU Study Group, and is already undergoing ethical review in the UK.

Speaking recently at the third meeting of the INC-EU Study Group in Frankfurt, Germany, Principal Investigator Dr Ruth Pettengell from St George's Hospital in London, UK, said she has received a favourable response to the study from potential investigators who have reviewed the protocol.

'Everyone knows that this is an extremely ambitious project, but our initial contacts with investigators have been very encouraging,' she told the Study Group. 'I think one of the main reasons why we have had so much interest in our study is that clinical practice audits are very topical, and everyone is keen to understand and monitor how their hospitals are performing in terms of chemotherapy dose delivery.'

Unique European study

One of the unique aspects of this audit is that a large cohort of lymphoma patients (300) will be recruited, in addition to a substantial population of breast cancer patients (450). This will provide unequivocal data on the

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incidence and impact of neutropenia in these potentially curable patients, but, says Dr Pettengell, it will also add an extra level of complexity to patient recruitment.

'We are anticipating that we will recruit our target number of breast cancer patients relatively quickly,' she told the meeting, 'but it may take longer to recruit the target number of patients in the lymphoma arm of the study.'

'For this reason, we are planning to initiate more lymphoma centres than breast cancer centres in order to ensure that we have a good representation of all of the malignancies in which we are interested.'

In this issue of *INSIGHT*, we present an overview of the protocol for the *Prospective European Neutropenia Audit* see pages 2-3. If you are an academic or community oncology treatment centre in France, the UK, Belgium, Spain or Germany, and are interested in participating in this audit, please contact the INC-EU Co-ordinating Centre (t: +44 (0) 1256 884000, e: info@inceu.org).

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The INC-EU Prospective European Neutropenia Audit

Major milestones

| | |
|--------------------------------|--|
| Target recruitment: | 750 patients (450 breast cancer, 200 NHL, 100 HL) 80 study centres 5 countries (Belgium, Germany, UK, Spain, France) |
| Protocol finalised: | July 2003 |
| First centre initiated: | October/November 2003 |
| Last patient completed: | June 2005 |
| Results available: | December 2005 |

'This study will give us a true picture of the moment, clarifying issues relating to today's chemotherapy regimens, with better-quality supporting data.'

Dr Manuel Constenla, Spain

It is well known that neutropenia is a common and potentially dangerous complication of many widely used chemotherapy regimens, but the true incidence and clinical consequences of neutropenia in everyday practice is unknown. Retrospective clinical practice audits in Europe^{1,2,3} have suggested that up to 40% of patients being treated with chemotherapy for breast cancer experience a neutropenic event, and approximately 5–10% suffer febrile neutropenia during the course of their chemotherapy. Less is known about the incidence and consequences of neutropenia associated with lymphoma chemotherapy in clinical practice, but there are indications in the literature that neutropenia is likely to be even more of a problem than in breast cancer.

Why a prospective study?

Retrospective clinical practice audits provide a valuable insight into the incidence and consequences of neutropenia in clinical practice, but missing data and the inability to control for confounding factors weakens the evidence base and does not allow a robust assessment of factors potentially predictive of neutropenia or chemotherapy dose reductions/delays.

This phase IV study has therefore been designed to assess prospectively the frequency of neutropenia with common myelosuppressive chemotherapy regimens used in the treatment of both breast cancer and lymphoma, and to estimate the frequency of chemotherapy dose delays and dose reductions in these patients. Secondary objectives of the study include:

- Quantifying and defining the relationship between neutropenic complications and chemotherapy dose delays and reductions
- Identifying the relationship between patient treatment variables, patient comorbidities and the frequency and severity of neutropenic events

INC-EU Prospective European Neutropenia Audit: Protocol Overview

Study design

This is an observational study, which aims to recruit 750 patients receiving myelosuppressive chemotherapy for the treatment of breast cancer, Hodgkin Lymphoma or non-Hodgkin Lymphoma. The dose and administration of chemotherapy will be as clinically indicated, and treatments will be selected and delivered as per usual clinical practice.

Each study centre will be expected to enrol a minimum of five patients into the study and assessments will be made at baseline and during each treatment cycle. It is anticipated that the duration of involvement for each study site will be 16 months from receipt of ethics

committee approval: 10 months to recruit patients and up to 6 months to complete the treatment and study assessments.

The inclusion and exclusion criteria for this study are shown in Table 1.

Study endpoints

The **primary endpoint** of this study is to assess the incidence of neutropenia:

- Grade III (ANC <1.0 x 10⁹/L)
- Grade IV (ANC <0.5 x 10⁹/L)

Collection of data relating to the ANC nadir will be mandatory for the first chemotherapy cycle, and optional for subsequent cycles.

Table 1. Inclusion and exclusion criteria for INC-EU Prospective European Neutropenia Audit

| Inclusion criteria | | | | | |
|---|--|---------------|----------|---|--|
| <ul style="list-style-type: none"> ■ Histologically-confirmed diagnosis of breast cancer (Stage I–IIIb), Hodgkin's disease (Stage Ib–IIb) or non-Hodgkin's lymphoma (International Prognostic Index 0–3) ■ Permitted chemotherapy regimens: <table border="0" style="width: 100%;"> <thead> <tr> <th style="text-align: left;">Breast cancer</th> <th style="text-align: left;">Lymphoma</th> </tr> </thead> <tbody> <tr> <td> <ul style="list-style-type: none"> • CMF • Anthracycline-containing regimens, e.g. FEC, AC, FAC • Taxane-containing or sequential regimens, e.g. AT, FEC→T </td> <td> <ul style="list-style-type: none"> • ABVD • BEACOPP • Stanford V • Alternating hybrid regimen • 14- or 21-day CHOP or R-CHOP • Weekly regimens </td> </tr> </tbody> </table> ■ Adequate organ function, as determined by investigator, to receive myelosuppressive chemotherapy regimen ■ Subjects starting new myelosuppressive chemotherapy regimens ■ Patients receiving prior or concurrent radiation therapy eligible ■ Age ≥18 years ■ Life expectancy with treatment of at least 3 months ■ At least four chemotherapy cycles planned ■ Written informed consent | | Breast cancer | Lymphoma | <ul style="list-style-type: none"> • CMF • Anthracycline-containing regimens, e.g. FEC, AC, FAC • Taxane-containing or sequential regimens, e.g. AT, FEC→T | <ul style="list-style-type: none"> • ABVD • BEACOPP • Stanford V • Alternating hybrid regimen • 14- or 21-day CHOP or R-CHOP • Weekly regimens |
| Breast cancer | Lymphoma | | | | |
| <ul style="list-style-type: none"> • CMF • Anthracycline-containing regimens, e.g. FEC, AC, FAC • Taxane-containing or sequential regimens, e.g. AT, FEC→T | <ul style="list-style-type: none"> • ABVD • BEACOPP • Stanford V • Alternating hybrid regimen • 14- or 21-day CHOP or R-CHOP • Weekly regimens | | | | |
| Exclusion criteria | | | | | |
| <ul style="list-style-type: none"> ■ Active infection or administration of systemic antibiotics or anti-infective within 72 hours before start of chemotherapy ■ Patients receiving antibody – or cell-based immunotherapies ■ Continuous single-agent chemotherapy ■ Medical diagnoses known to cause neutropenia, e.g. HIV ■ Female subjects who are pregnant or lactating ■ Patients with active infections requiring treatment ■ Concurrent participation in phase I or II clinical trials ■ History of stem cell or bone marrow transplantation ■ Any premalignant myeloid conditions or any other conditions with myeloid characteristics ■ Any disorder that compromises the ability of the patient to give informed consent ■ Patients in studies receiving blinded administration of growth factor support (G-CSF, GM-CSF or erythropoietic agents). | | | | | |

Secondary endpoints include:

- The incidence of:
 - Febrile neutropenia
 - Chemotherapy cycle delays and dose reductions due to a neutropenic event
 - Transfusions
- Relative dose intensity (RDI)
- The incidence and duration of:
 - Adverse events
 - Concomitant medication use
 - Radiotherapy
 - Hospitalisation
 - IV anti-infective use
 - Growth factor use
- Healthcare resource utilisation.

Investigators will be required to record details of planned chemotherapy dosing data at baseline, and actual chemotherapy delivered at each cycle, in addition to a range of physical and laboratory parameters.

Data entry and evaluation

Case record data will be submitted using a secure, simple-to-use, on-line data entry system. The system requires no remote software and needs only basic technical skills. The advantages for investigators in using this system is that it saves time by reducing the duplicated data entry associated with paper-based systems; edit checks are integrated into the software, and there are facilities for rapid and easy query handling.

The data will be analysed by the European Data Collection and Evaluation Centre – an independent research unit at the University Hospital in Basel, Switzerland.

Study outcomes

According to Principal Investigator, Dr Ruth Pettengell, the most important outcome of the study from her point of view is that the data should be of such good quality that it may be possible to develop risk models for neutropenia that can be broadly applied in clinical practice.

‘We urgently need to identify those patients who will benefit most from pre-emptive use of growth factors or antibiotic prophylaxis,’ she says.

‘Most neutropenic events happen in the first chemotherapy cycle⁴, so growth factor support needs to be given from the outset in those patients at greatest risk.’

Introducing the European Oncology Nursing Group...

The *European Oncology Nursing Group* was established in April 2003 in recognition of the important role played by specialist nurses across Europe in educating patients about cancer treatments and managing the side effects of these treatments. Thirteen leading oncology nurses from 10 different countries (Belgium, Denmark, France, Germany, Italy, The Netherlands, Spain, Switzerland, UK and the US) attended the first meeting. The Group will be working closely with the *European Oncology Nursing Society* (EONS) to help improve the way anaemia and neutropenia are managed, through a range of educational activities, and by providing tools to help nurses implement best-practice management strategies.

Two of the Group’s top priorities are to develop simple triage tools for patients who may require more in-depth assessment and to develop a core curriculum on cancer in the elderly.

The INC-EU Study Group wishes the Nursing Group every success and looks forward to working as partners with its members in the future.

Outcomes Research for Oncologists: New Book Available

Written with oncologists in mind, this new book has recently been published with the aim of familiarising healthcare professionals with the ideas and principles of outcomes research and economic evaluation in medicine. Increasing accountability for the outcomes of healthcare interventions means that all physicians now require a basic understanding of the cost-effectiveness of their treatment choices, and on how effective research is influencing policy making in every country.

This easy-to-read paperback book provides a succinct summary of the basic types of economic evaluation that are increasingly being included in clinical trials of new interventions, and should help physicians to understand and interpret clinical papers that include health economic or quality of life assessments. The book includes a review of popular

research tools, such as the Health Utilities Index (HUI) and the EuroQoL (EQ-5D), and it shows a useful example of an economic evaluation of a specific chemotherapy (paclitaxel) in ovarian cancer.

‘This book is designed to inform oncologists in this expanding field of outcomes research,’ says Professor Thomas Szucs from the European Center of Pharmaceutical Medicine in Basel, Switzerland. ‘The book is concise enough not to leave readers feeling overwhelmed with the subject matter, but thorough enough to give readers a working understanding of the principles of health economics.’

Silvia M Ess. *Outcomes Research and Economic Evaluation*.

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Controversies in Adjuvant Chemotherapy for Primary Breast Cancer: Workshop Slides Now Available

A CD-ROM containing all the slides shown at this well-attended workshop, held during the 25th Annual San Antonio Breast Cancer Symposium in December 2002 is now available. The slides are highly illustrated and contain fully-referenced notes for use in lectures or other educational activities.

The content of the slide kit includes:

- An overview by **Professor Gary Lyman** of current issues relating to dose intensity and the impact of neutropenia on the treatment of primary breast cancer, on evidence for the benefits of G-CSF in preventing febrile neutropenia and maintaining chemotherapy dose intensity in breast cancer, and on the ongoing development of clinical prediction models for neutropenia
- A presentation by **Professor Robert Leonard** of the individual results of three European clinical practice audits (Belgium, UK, Spain) showing the incidence of neutropenia and febrile neutropenia with common chemotherapy regimens, the frequency of dose delays and dose reductions and their impact on relative chemotherapy dose intensity, and current trends in the use of CSF in these countries
- A summary by **Dr Jeffrey Crawford** of the clinical development programme for pegfilgrastim – a new, fixed-dose, long-acting G-CSF that can be used once per chemotherapy cycle to protect patients against neutropenic complications, including febrile neutropenia
- The goals, objectives and membership of the INC-EU.

Proceedings submitted to the EJC

The proceedings of this workshop have now been submitted to the European Journal of Cancer, where they are currently undergoing peer review. First author, Professor Robert Paridaens from the University Hospital Gasthuisberg, in Leuven, Belgium, is hopeful that the proceedings will be published in 2003.

IN THE LITERATURE...

In-line with its educational remit, the INC-EU will be highlighting key papers and offering comments on recently published studies. In this issue of *INSIGHT* we review two major studies that have recently been published showing the value of time-intensive chemotherapy administration strategies in the treatment of breast cancer and NHL. We also review a breast cancer study in which G-CSF (filgrastim) support was targeted according to a risk stratification model based on first-cycle ANC nadir.

Citron ML, Berry DA, Cirrincione C *et al.* Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as post-operative adjuvant treatment of node-positive primary breast cancer: first report of Intergroup Trial C9741/ Cancer and Leukemia Group B Trial 9741. *JCO* 2003; **21**: 1431–1439.

PD Dr Christian Jackisch, Germany comments:

This paper was presented, with massive worldwide interest, at the San Antonio Breast Cancer meeting last year, and the fact that it has been published so quickly reflects the view that these findings could change the way we treat primary breast cancer in the future. CALGB 9741 has proved the concept that giving chemotherapy (in this case,

ACT) every 2 weeks instead of every 3 weeks significantly improves survival outcomes. It has also illustrated the importance of using growth factors (in this case, filgrastim) to prevent neutropenia and to sustain, or allow an increase in chemotherapy dose intensity. This paper probably represents one of the most exciting developments in breast cancer chemotherapy for many years. It would be my recommendation that every oncologist who treats breast cancer should read this paper and consider the implications of the findings in their own practices.



PD Dr Christian Jackisch, Deputy Director, Department of Gynaecology, University of Marburg, Marburg, Germany.



Prof André Bosly, Head of the Department of Haematology Cliniques, Universitaires UCL, Godinne, Belgium.

Wunderlich A, Kloess M, Reiser M *et al.* Practicability and acute haematological toxicity of 2- and 3-weekly CHOP and CHOEP chemotherapy for aggressive non-Hodgkin's lymphoma: results from the NHL-B trial of the German High-Grade Non-Hodgkin's Lymphoma Study Group (DSHNHL). *Ann Oncol* 2003; **14**: 881–893.

Professor André Bosly, Belgium comments:

CHOP-21 has been the standard therapy for NHL since it was introduced in the 1970s and despite various attempts to improve on the outcome of the CHOP-21 regimen, it has not been bettered in clinical trials outside of the addition of Rituximab. The interim results from the German NHL-B study were first presented in 2001 and clearly demonstrated an advantage of reducing the interval between chemotherapy cycles from 3 weeks to 2 weeks in terms of response rates, time to treatment failure, and overall survival in elderly patients with aggressive NHL. Despite the fact that these results have never been reported in full in the literature, many centres now use CHOP-14 as their preferred regimen in aggressive forms of NHL.

This paper is important in that it reviews the safety and tolerability of CHOP-14 in a patient population that includes elderly individuals up to the age of 75 years. It shows that CHOP-14, when given with G-CSF support for six cycles, is not associated with increased toxicity compared with the 3-weekly CHOP standard regimen. Indeed, the incidence

of grade 4 leucocytopenia was almost halved in patients >60 years of age with the 2-weekly regimen compared with the 3-weekly regimen (24% vs 44%; $P < 0.001$), which was attributed to the use of G-CSF to support fortnightly administration.

This paper has confirms what we have begun to see in clinical practice. CHOP-14 is a feasible chemotherapy regimen for NHL patients of all ages, and it can be delivered without additional toxicity as long as growth factor support is given.

Rivera E, Haim Erder M, Moore TD *et al.* Targeted filgrastim support in patients with early-stage breast cancer: toward the implementation of a risk model. *Cancer* 2003; **98**: 222–228.

Professor Robert Paridaens, Belgium comments:

This is an interesting paper because the study reported is the first to implement a very practical approach to neutropenia risk stratification in a prospective manner. Rivera and co-workers have used a risk assessment model, originally developed by Jeffrey Silber in Pennsylvania, which uses the first-cycle ANC nadir as a predictor of neutropenic complications in patients receiving adjuvant chemotherapy for early-stage breast carcinoma.

In the Rivera study, the first-cycle ANC nadir was used to guide risk-related prophylactic filgrastim treatment to the neediest patients (i.e. those whose first-cycle ANC nadir $\leq 0.5 \times 10^9$ cells/L), the



Prof Robert Paridaens, Head of Clinic - Department of Oncology, University Hospital, Gasthuisberg, Leuven, Belgium.

hypothesis being that targeted use of filgrastim in this high-risk group would enable delivery of a full dose of chemotherapy on time to both high and low-risk groups and that the low-risk group would have minimal neutropenic complications in the absence of filgrastim support.

Overall, Rivera's hypothesis proved to be correct in this study, since a similar proportion of both groups of patients received >85% of their planned chemotherapy dose intensity. This indicates that prophylactic use of filgrastim in patients who experience severe neutropenia in their first cycle may help more at-risk patients to receive their planned chemotherapy dose on time.

Ideally, of course, we would like to predict those patients at risk of first-cycle neutropenia and apply pre-emptive strategies from the outset. However, until we have identified those risk factors, Rivera's proposal to stratify patients according to their first-cycle ANC and to use prophylactic growth factors from the second cycle in high-risk patients appears to be a reasonable next-best option.

Join the Neutropenia Forum at www.inceu.org

Healthcare professionals with an interest in oncology and neutropenia can now access the resources of the INC-EU at its recently launched web site, www.inceu.org. The website is managed by the INC-EU Co-ordinating Centre, with all content being written or reviewed by members of the INC-EU Study Group.

Highlights of the INC-EU website include:

- Oncology/neutropenia case studies
- INC-EU publications
- Slide library
- Journal highlights
- Conference reports
- Updates on the *Prospective European Neutropenia Audit*
- Patient information.

The INC-EU would be pleased to hear from healthcare professionals interested in publishing articles on the website. You can register your interest by contacting the INC-EU Co-ordinating Centre. e: info@inceu.org

Patient Information on Neutropenia: How Effective Are We Being?

The provision of simple, clear patient information on the risks and symptoms of neutropenia could mean the difference between life and death. Patients who understand that ‘flu-like’ symptoms or an increase in body temperature in the days after their chemotherapy could actually be life-threatening are more likely to seek the medical attention they need, and less likely to develop potentially fatal neutropenic sepsis.

But how many oncology units routinely offer this vital information at the time of chemotherapy treatment initiation? And how do we know that any information that is given to patients at this difficult time actually delivers the right results? According to Professor Robert Leonard, the Director of the South West Wales Cancer Institute in Swansea, UK, no formal studies have been conducted to assess the effectiveness of patient information about neutropenia, and in most instances, he suspects, no information is given at all.

‘One of the major problems in providing information to patients on issues such as neutropenia is that they are often still shocked from their diagnosis, and although they really need to have this information before or at the time their chemotherapy begins, they are usually so worried about losing their hair or feeling sick, that the possibility of infections in the future may seem less important to them.’

Importance of getting it right

Febrile neutropenia is usually defined as a temperature $\geq 38.2^{\circ}\text{C}$ with an ANC $< 0.5 \times 10^9$ cells/L. Fever in the setting of neutropenia is considered to be a medical emergency, with most patients requiring immediate hospitalisation and the administration of empiric broad-spectrum antibiotics. Although the risk of febrile neutropenia may vary according to a number of factors such as the patient’s age, the type of cancer, and the presence of various comorbid conditions, it has been estimated that up to 40% of patients receiving full-dose-intensity CHOP⁶ and between

Risk factors for febrile neutropenia⁵

- Chemotherapy regimen
- Chemotherapy dose intensity
- Patient factors:
 - ↑ Age
 - Female
 - ↓ Performance status
 - Poor nutrition
 - ↓ Pre-treatment blood counts
 - ↓ Haemoglobin
 - ↑ LDH

5–10% of patients receiving adjuvant chemotherapy (e.g. CMF, CAF, AC, ACT) for breast cancer⁷ experience this complication. Even with a comprehensive evaluation, an infectious cause is not isolated in between 60–70% of patients with febrile neutropenia⁸. Fortunately, the introduction of potent broad-spectrum antimicrobial agents and improvements in supportive care in the past few decades have led to a substantial decrease in infection-related mortality. Nevertheless, if febrile neutropenia does develop in a patient receiving chemotherapy, **time is of the essence**. An elegant study conducted in the 1980s clearly showed that delaying the first dose of antibiotic for more than 12 hours after the onset of fever in neutropenic patients with *Pseudomonas* bacteraemia dramatically increased the death rate from 15% to 55–75%⁹.

Today, despite substantial improvements in infection management, approximately 10% of all cancer patients who develop febrile neutropenia still die, and those who survive the complication can expect hospital stays of around 10 days or longer¹⁰.

Empowering patients

Professor Leonard believes that the power to reduce the mortality and morbidity associated with chemotherapy-induced neutropenia lies – at least in part – in the hands of patients.

‘If you provide patients with a clear set of instructions about what to look out for and what to do in the event of symptoms developing, they are equipped with the knowledge to act promptly and to seek urgent medical attention.’

‘Unfortunately, I have seen only too often the consequences of patients delaying seeking treatment, and it frustrates me that loss of life or a protracted hospital stay could easily have been avoided.’

What patients need to know

Patients with potentially serious neutropenia usually develop symptoms within 7–10 days of their chemotherapy – although a low ANC can develop at any time – and all signs of infection should be taken seriously in a patient undergoing chemotherapy. The signs and symptoms of infection are often muted in the neutropenic patient, but fever remains the cardinal sign of early infection, and patients should be encouraged to take their temperature regularly after their chemotherapy and to report any increases above 37.5°C . ‘Flu-like’ symptoms and the sudden onset of diarrhoea are also worthy of

mention to the patient as these may also herald the arrival of a potentially serious opportunistic infection.

Of paramount importance is the need to stress the urgency of the situation. Patients should be informed that onset of any of the above symptoms or a rise in temperature requires **immediate** contact with the emergency medical services, and since severely neutropenic patients can develop sepsis within a matter of hours, waiting until morning simply is not an option.

Professor Leonard believes that one of the most important pieces of advice a patient should be given is **who** to contact in the event of neutropenic symptoms developing. He is especially concerned that, in some countries, the pathway to emergency care can be arduous, and precious hours can be lost if the patient contacts the wrong services or if the urgency of the situation is unclear to the medical personnel to whom they present.

'In our hospital, patients have direct telephone access to the Chemotherapy Day Unit and, out of hours, to the Medical Registrar on call,' he explains. 'It is an unfortunate fact that, particularly in the UK, it can be very difficult for patients to access other medical services within the short window of time they have, so we have to insist that they contact us directly.'

Getting the message across

Cancer patients receive a burdensome volume of information at or around the time of their diagnosis, and information relating to neutropenia therefore needs to be clear, memorable, and in a form that is readily accessible in an emergency. Printed patient advice leaflets can be very helpful, and Professor Leonard urges all oncology teams to consider developing or using these when discussing the side effects of chemotherapy with their patients.*

* An example of a patient advice leaflet developed by Professor Leonard's team can be found at www.inceu.org.

“One of the most important pieces of advice a patient should be given is who to contact in the event of neutropenic symptoms developing.”

Professor Robert Leonard, Director of the South West Wales Cancer Institute, UK.

'Although we don't know for sure what is the best way of informing our patients about neutropenia, providing *some* information has got to be better than providing none,' he says. 'As well as offering written advice on neutropenia, I also record our discussions on audiotape and I offer the tape to patients at the end of the consultation.'

'I feel very strongly that we need to know more about how to effectively communicate information on neutropenia to our patients. After all, here is a very real opportunity to prevent chemo-

What patients need to know about neutropenia

- ✓ Patient factors:
 - Feeling unwell or tired
 - 'Flu-like' symptoms
 - Sore throat, earache, cough
 - Sudden onset of diarrhoea
- ✓ When to expect them
- ✓ Who to contact
- ✓ How to contact them
- ✓ The urgency of the situation

therapy-induced mortality or, at the very least, to avert lengthy and expensive stays in hospital.'

What information do you give your patients about neutropenia? The INC-EU are interested to hear about how patient information is used in Europe, and would like to invite you to participate in our survey at www.inceu.org

INC-EU Neutropenia Audit Packages Forge Ahead

Neutropenia audit packages for breast cancer and lymphoma treatment are under development by the INC-EU and will be ready for testing from December 2003 onwards. The audit packages have been designed for use by European clinical oncology centres in order to measure the impact of neutropenia on chemotherapy dose delivery, to document haematological complications due to chemotherapy treatment and to assess the use of haematopoietic growth factors and other supportive measures during treatment.

PD Dr Christian Jackisch, Deputy Director of the University Hospital of Marburg in Germany, has been driving the project on behalf of the INC-EU and he told *INSIGHT* that he was very pleased with the way the audit package was shaping up.

'We have made very good progress over the past few months in terms of the structure and content of the audit package,' he says. 'The software is now under development and early indications are that it will be very easy to use.'

The *European Oncology Nursing Group* and INC-EU member organisations will be testing and approving both audit packages before being made available, by request to all European oncology centres.

If you are interested in running the audit package in your own centre, email the INC-EU. info@inceu.org

Retrospective Neutropenia Audits Get International Exposure

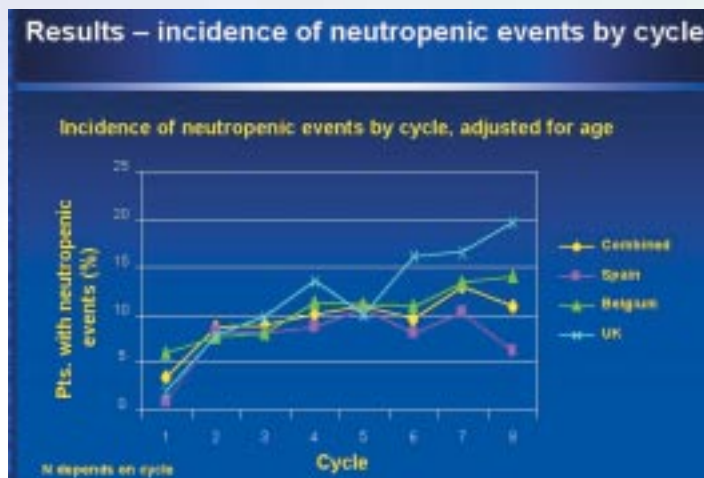


Figure 1: Age-adjusted incidence of neutropenic events by cycle.

A retrospective audit of over 1,000 patients with primary breast cancer receiving adjuvant chemotherapy in Spain has recently been presented as an abstract at the 39th Annual Meeting of the American Society of Clinical Oncology (ASCO), held in Chicago, USA.**

The audit was conducted in 34 Spanish hospitals between 1993 and 2001; the most commonly used chemotherapy regimens were CMF (48%), CEF (18%), CAF (13%) and AC (3%).

A summary of the audit findings:

- Febrile neutropenia was reported in 7.4% of patients
- 25% of patients had a chemotherapy dose-delay
- 7% of patients had a chemotherapy dose reduction
- 81% of patients received less than their planned dose intensity
- 15% of patients received <85% of their planned dose intensity
- 17% of patients received CSFs during treatment.

Principal Investigator, Dr Manuel Constenla from the Complejo Hospitalario de Pontevedra in Spain, said he was not especially

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** Constenla M, Bosly A, Jackisch C *et al.* An audit of primary breast cancer management in Spain: The OSQAR study. *Proc Am Soc Clin Oncol* 2003; **22**: Abstract 312.

surprised at the results from the audit, although he would have preferred to see more patients receiving G-CSF support in order to maintain their optimal chemotherapy dose intensity.

'We have always known that febrile neutropenia was a major cause of chemotherapy dose reductions and delays, but what these data show us is that less severe forms of neutropenia may also be leading to dose modifications in clinical practice,' he said. 'It is disappointing to see that so many of our breast cancer patients are receiving a less-than-ideal chemotherapy dose intensity and I would certainly want to encourage greater G-CSF use in patients who are at most risk of a chemotherapy dose reduction or delay.'

Combined analysis of European audits

A combined analysis by the INC-EU of three large datasets from European retrospective breast cancer audits has also just been completed, and the results were announced in an oral presentation at the 12th European Conference on Clinical Oncology (ECCO12) in Copenhagen, Denmark (21-25 September 2003). The INC-EU is delighted to have been awarded the privilege of an oral presentation at this prestigious European oncology meeting, says Professor Robert Leonard from the South West Wales Cancer Institute in Swansea, UK – who presented the findings at ECCO12 – this probably reflects a growing interest across Europe in the impact of neutropenia on treatment effectiveness and treatment outcomes.

'Our combined analysis of over 2,251 patients with primary breast cancer has revealed that neutropenic events lead to sub-optimal chemotherapy dosing in almost one in five patients,' he explains. 'An apparent reluctance to use growth factors to prevent neutropenia in clinical practice may help to explain why we still have such relatively poor breast cancer treatment outcomes in many parts of Europe.'

Professor Robert Leonard presented full results of this major study at ECCO12 on Monday 22 September 2003. 'Fifty-four percent received CMF-based regimens, 42% anthracycline-based, and 3% other regimens. One or more neutropenic events were observed in 27% of patients. Repeated neutropenic events were observed in 12% of patients.' Said Professor Leonard.

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