Elderly patients missing out on haematological disorder therapy

Despite evidence that fit, elderly patients respond similarly to younger patients in terms of efficacy and toxicity of chemotherapy treatments, false assumptions about the ability of elderly patients to tolerate aggressive treatment may result in them missing out on optimum treatment and not being included in clinical trials.

Age alone should not be regarded as sufficient criterion to make evidence-based treatment decisions in the management of haematological disorders. These were the key conclusions from an panel of international speakers at a symposium sponsored by Hospira at the 15th Congress of the European Haematology Association, Barcelona.

Haematological disorders and solid tumours mainly affect people over the age of 65 years, but there is often a lack of clear guidance in treatment because this population group is underrepresented in clinical trials.

The management of haematological disorders, such as leukaemia, neutropenia and anaemia present challenges in the elderly. However, if treatment is optimized, older patients can be successfully treated.

Mental health services failing children with autism

Thousands of children with autism in England are needlessly facing a future of mental health problems, because the NHS does not know how to help them. *You Need to Know*, a campaign by the National Autistic Society, aims to tackle an unfit mental health system that fails two thirds of children with autism and often makes their mental health worse.

Over 70% of children with autism have a mental health problem, such as depression, obsessive compulsive disorder or other anxiety disorders, despite many of these problems being preventable.

When mental health problems do develop in children with autism they are much harder to recognize, diagnose and treat without appropriate knowledge. Tragically, they are often dismissed as an unfortunate but unavoidable side effect of having autism.

Mark Lever, chief executive of the National Autistic Society, said: 'Too many children with autism are developing preventable mental health problems.'

Vicious circle results in inadequate chronic pain management

Poor communication between doctors and patients, fear of drug side effects and a failure to individualize therapy to treat different types of pain underlie the current inadequate management of chronic, severe pain, warns a major review from an international group of pain specialists.

Pain is the commonest reason for patients to seek medical attention, and chronic pain affects nearly one in five people according to recent surveys in Europe. Low back pain is the commonest problem but there is evidence that it is often inadequately treated. The literature review revealed major differences in management approaches, despite evidence-based guidelines. Factors determining drug treatment appeared to be based mainly on tradition and personal experience (Varrassi et al, 2010).

The review found that evidence-based guidelines on pain management are often not followed and revealed a vicious circle in which doctors try to balance adequate pain relief and acceptable side effects, particularly with strong opioids.

'Current pain management is often driven by tradition and personal experience, focusing mainly on symptom control,' said Professor Giustino Varrassi, president of the European Federation of the International Association for the Study of Pain and lead author of the review. He was speaking at a meeting of the Change Pain initiative, a programme bringing together pain specialists from throughout Europe to improve chronic pain management, funded by an educational grant from Grünenthal (20–21 June 2010, Rome, Italy).

The report recommends improved education for doctors and patients on the need to accurately assess chronic pain. It also points out that there is a frequently a neuropathic component to chronic pain, which requires appropriate treatment, often with combination therapy.

The Change Pain group has launched an education programme to improve the management of chronic pain. It includes three interactive e-learning modules designed to update health-care professionals on: assessing pain, improving doctor–patient communication, multimodal management of chronic pain, and mechanism-orientated pharmacological pain therapy. The first module is available at www.change-pain.com.

Beverley Collett, Consultant in Pain Medicine, University Hospitals of Leicester NHS Trust

'To improve the treatment of patients with chronic pain, better education of health-care professionals on underlying pain mechanisms and appropriate use of drug treatment and other therapies is important,' said Beverley Collett, consultant in pain medicine, University Hospitals of Leicester NHS Trust, and a member of the Change Pain group. 'Once a patient has had pain for more than 3 months, with no obvious reason, they need to undergo full biopsychosocial assessment and be offered treatment that treats the underlying neuropathology.'

Susan Mayor

Grünenthal provided an unrestricted educational grant to Susan Mayor to attend the Change Pain meeting, but the views expressed are solely those of the author.

Varrassi G, Müller-Schwefe G, Pergolizzi J et al (2010) Pharmacological treatment of chronic pain - the need for CHANGE. *Curr Med Res Opin* **26**(5): 1231–45

Simple injection could save thousands of lives

If recently injured patients with serious bleeding were to receive a cheap, widely available and easily administered drug to help their blood to clot, tens of thousands of lives worldwide could be saved every year, according to research published online by *The Lancet* (CRASH-2 trial collaborators, 2010).

Dr Ian Roberts, Professor of Epidemiology at the London School of Hygiene and Tropical Medicine, revealed results from the CRASH-2 trial showing that early administration of tranexamic acid to patients with recent, severe bleeding injuries saves lives, with no evidence of adverse effects from unwanted clotting.

Dr Ian Roberts, Professor of Epidemiology, London School of Hygiene and Tropical Medicine, London

CRASH-2 was a large, randomized trial involving over 20 000 adult patients in 274 hospitals across 40 countries, funded by England's National Institute for Health Research Health Technology Assessment programme. This is the first trial of tranexamic acid in injured patients, although smaller trials have shown that it reduces bleeding in patients undergoing major surgery.

Severely injured adults were enrolled in the trial if they had significant bleeding or were at risk of significant bleeding and were within a few hours of injury. They were randomly allocated to receive either tranexamic acid 1 g by injection, followed by another 1 g in a drip over the following 8 hours, or a matching placebo.

The researchers studied the numbers of deaths in hospital within 4 weeks of injury in the two groups and found that tranexamic acid reduced the chances of death as a result of massive blood loss by about one sixth.

The researchers estimate that administering tranexamic acid soon after injury could prevent up to 100 000 deaths per year across the world. In India it could save about 13 000 lives each year, with about 12 000 lives saved in China. The drug would also save lives in developed countries, around 2000 each year in the USA and more in Europe.

Tranexamic acid is an off-patent drug, manufactured by a number of different companies, which costs about £3 per gram. For people aged between 5 and 45 years, injury is second only to HIV/AIDS as a cause of death.

CRASH-2 trial collaborators (2010) Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet* (epub before print June 15 DOI:10.1016/S0140-6736(10)60835-5)

'Dramatic' reduction in menstrual blood loss

Data presented at the European Society of Contraception and Reproductive Health meeting in The Hague suggest that the estradiol valerate dienogest (Qlaira) combination pill could be an effective therapy for women suffering from heavy and/or prolonged periods.

Presenting data from the European and Australian trial based on 177 women suffering from heavy periods not caused by underlying disease, Dr Diana Mansour, clinical director for sexual health services at Newcastle and North Tyneside NHS, said this is the first evidence from rigorous randomized trials of an oral contraceptive in the treatment for heavy menstrual bleeding which can have a 'significant impact on quality of life'.

Results showed a 'dramatic reduction in blood loss', with 79.2% of Qlaira users experiencing a significant fall in blood loss compared to 7.4% of those on placebo (P= 0.0001). It also halved the median drop in bleeding days over the 90-day reference period.

Dr Mansour reported a low incidence of adverse and serious adverse events with no unexpected drug reactions. The rate of withdrawal from treatment was 9.7% *vs* 6.2% for Qlaira and placebo respectively. A trial in America showed similar results.

Bayer has applied to extend its licence to include a second indication for Qlaira in the treatment of heavy and/or prolonged menstrual bleeding in women without organic disease.

Rhonda Siddall

End-stage renal failure increasing in patients with diabetes

Data from the National Diabetes Audit Executive Summary 2008–2009 show that the incidence of end-stage renal failure (requiring dialysis or transplantation) is increasing in patients with diabetes. In those with type 1 diabetes it has risen from 0.78% in 2003–4 to 1.27% in 2008–9; the corresponding figures for type 2 diabetes are 0.26% and 0.48%.

New stapler for compression and articulation

Ethicon Endo-Surgery has introduced a new Echelon Flex 45 Endopath stapler, intended to provide surgeons with improved access and compression when deploying a 45 mm staple line. The stapler delivers system-wide compression, natural articulation and optimal staple formation in a variety of tissue thickness.

First cannabinoid drug for multiple sclerosis

Sativex oromucosal spray is available in the UK as a prescription-only medicine for people with multiple sclerosis experiencing spasticity symptoms, such as painful spasms and cramps.

AMERICAN SOCIETY OF CLINICAL ONCOLOGY ANNUAL MEETING
CHICAGO, 4–8 JUNE

Increased survival for heavily pre-treated metastatic breast cancer

A new chemotherapy agent extends overall survival among women with locally recurrent or metastatic breast cancer who have already been heavily treated with conventional therapies.

The finding that eribulin extends median survival by 2.5 months was presented at ASCO by Professor Chris Twelves, professor of clinical cancer pharmacology and oncology, and Head of the Clinical Cancer Research Groups at the Leeds Institute of Molecular Medicine and St. James's Institute of Oncology in Leeds. He said: 'Until now, there hasn't been a standard treatment for women with such advanced breast cancer. For those who have already received all of the recognized treatments, these are promising and clinically meaningful results.'

Professor Chris Twelves, Leeds Institute of Molecular Medicine

Professor Twelves continued: 'These findings may establish eribulin as a new, effective option for women with heavily pre-treated metastatic breast cancer. This is the first single agent phase III clinical trial to show survival benefit in women with heavily pre-treated metastatic breast cancer.'

Eribulin mesylate is a new type of microtubule dynamics inhibitor that affects cell division. The international, multicenter trial, EMBRACE, is the first to compare eribulin mesylate to 'treatment of physician's choice' in women with locally recurrent or metastatic breast cancer who had already received an average of four prior chemotherapy drugs such as anthracyclines or taxanes. This comparison was chosen because no single chemotherapy regimen is currently standard.

Professor Twelves and his colleagues compared overall survival among 762 patients with metastatic breast cancer who were randomized to receive either eribulin (n=508) or their physician's choice of therapy (n=254), which was almost always another chemotherapy. The median survival for the eribulin group was significantly longer: 13.1 months *vs* 10.7 months (P=0.04).

The study's secondary endpoints (progression-free survival and objective response rate) also favoured eribulin, which Professor Twelves said was generally well tolerated. He concluded: 'This trial is significant because the era of targeted biological therapies had led us to assume that advances in patient care were not likely to come from innovations in chemotherapy. Results from EMBRACE prove that this assumption was incorrect.'

Rhonda Siddall

Doublet chemotherapy shows benefit for elderly lung cancer patients

The combination of paclitaxel and carboplatin increases both overall and progression-free survival in older patients with advanced non-small cell lung cancer. This is the finding of a randomized study from 62 international centres conducted by the French Intergroup of Thoracic Oncology.

Presenting the results, Dr Elizabeth Quoix, University Hospital, Strasbourg, commented: 'This is the first study entirely devoted to elderly patients showing superiority of doublet chemotherapy over single-agent treatment. These findings represent a new treatment paradigm for these patients.'

The phase III study included 451 patients aged 70–89 years, who were randomized to the doublet regimen or to single-agent therapy with either gemcitabine or vinorelbine. The original plan was to include 520 patients, but the study was terminated early when interim analysis revealed longer overall survival with doublet therapy (10.4 months *vs* 6.2 months with single-agent therapy). Progression-free survival was also longer at 6.3 months *vs* 3.2 months.

Dr Quoix noted that elderly patients may be given single-agent chemotherapy because of concerns about their ability to tolerate a more intensive doublet treatment. She reported that toxicity with paclitaxel-carboplatin was acceptable, although moderate to severe neutropenia was more frequent than with single-agent therapy (47.8% *vs* 12.2%).

According to Dr Mark Kris, Memorial Sloan-Kettering Cancer Center, New York: 'The average lung cancer patient is aged over 70, so this study tells us exactly what we need to know. Other large clinical trials have felt practice changing with a smaller improvement in survival, and this study supports ASCO's latest guidelines that age alone should not be used to select chemotherapy for patients with advanced non-small cell lung cancer.'

Sue Lyon

Oral treatments compared for Ph+ chronic myeloid leukaemia patients

Results of the first global randomized comparison of two oral therapies – nilotinib and imatinib – in 846 newly diagnosed Philadelphia chromosome-positive (Ph+ CML) chronic myeloid leukaemia patients were presented at ASCO and published in the *New England Journal of Medicine*.

Nilotinib was superior in all key efficacy measures to the current gold standard treatment, imatinib, in adult patients with newly diagnosed Ph+ CML in the chronic phase at 12 months.

Saglio G, Kim DW, Issaragrisil S et al (2010) Nilotinib versus imatinib for newly diagnosed chronic myeloid leukemia. *N Engl J Med* **362**(24): 2251–9

American Society of Clinical Oncology Annual Meeting
Chicago, 4–8 June

Bevacizumab improves progression-free survival in ovarian cancer

Bevacizumab (Avastin) significantly improves progression-free survival in women with ovarian cancer, show results from the first study to look at this treatment option.

The study – GOG-0218 – randomized 1873 patients with ovarian cancer to three treatment groups: standard chemotherapy (paclitaxel plus carboplatin) and placebo followed by placebo maintenance; standard chemotherapy with bevacizumab then placebo maintenance; or standard chemotherapy in combination with bevacizumab, followed by bevacizumab maintenance.

Results showed that women treated with standard chemotherapy plus bevacizumab followed by maintenance bevacizumab had significantly longer progression-free survival (median of 14.1 months) compared to those treated with standard chemotherapy alone (median of 10.3 months; $P<0.0001$). Women treated with chemotherapy plus bevacizumab followed by placebo maintenance had a median profession-free survival of 11.2 months, but this did not reach statistical significance.

The lead investigator, Robert Burger, Professor of Surgical Oncology at the Fox Chase Cancer Center, Philadelphia, USA, said: 'This is the first time a phase III trial has demonstrated that an antiangiogenic agent improves progression-free survival in women with this very hard-to-treat disease. Treatment with chemotherapy plus bevacizumab followed by maintenance bevacizumab achieves a 28% reduction in the risk of cancer progression.'

Ovarian cancer remains one of the most deadly cancers in women, Professor Burger warned, adding that nearly 70% of patients die within 5 years of diagnosis. 'Current treatment options are limited to surgery and chemotherapy, and there is a clear need for improved treatment,' he suggested.

Susan Mayor

Reduced risk of skeletal-related events with zoledronic acid

New data from the Myeloma IX study show that zoledronic acid plus first-line chemotherapy significantly improved overall survival for patients who were newly diagnosed multiple myeloma by 16% ($P=0.0118$) and progression-free survival by 12% ($P=0.0179$) compared to oral clodronate plus first-line chemotherapy.

The 5.5-month survival improvement seen with zoledronic acid in this study of nearly 2000 UK patients was independent of the drug's effect on skeletal-related events.

Zoledronic acid was significantly superior to oral clodronate in the prevention of bone complications associated with multiple myeloma, reducing the relative risk of skeletal-related events 24% more than clodronate ($P=0.0004$).

Zoledronic acid is licensed in the UK for the prevention of skeletal-related events in multiple myeloma and across a broad range of metastatic cancers (breast, prostate, lung and other solid tumours) involving bone, as well as for the treatment of hypocalcaemia of malignancy.

A new standard of care for locally advanced prostate cancer?

Compared with hormone therapy alone, combined radiotherapy and hormone therapy reduces the risk of death by a significant 43% in men with locally advanced or high-risk prostate cancer, according to the PRO7 trial.

Lead investigator Dr Padraig Warde, Princess Margaret Hospital, Toronto, commented: 'These results suggest that adding radiation therapy to the treatment plan for these patients could become part of standard therapy and should be considered.'

After 7 years, disease-specific survival was 90% in men receiving hormone therapy and radiotherapy compared with 79% with hormone therapy alone. Overall survival was also significantly greater in men receiving the combination at 74% *vs* 66% with monotherapy.

'Our results may underestimate the value of radiotherapy because of improvements in technology over the decade since the study was designed,' said Dr Warde.

Between 1995 and 2005, the PRO7 study recruited 1205 men with aggressive, locally advanced prostate cancer from the UK, the USA and Canada. Half (602) received hormone therapy alone and half (603) hormone therapy plus radiotherapy. The study was coordinated in the UK by the Medical Research Council and conducted by the NCIC Clinical Trials Group at Queen's University, Ontario.

The PRO7 radiotherapy regimen consisted of 45 Gy in 25 fractions over 5 weeks to the pelvis, plus 20–24 Gy in 10–12 fractions over 2–2.5 weeks to the prostate. Low-grade rectal bleeding and diarrhoea were more common in the radiotherapy group. Late severe toxicities were rare, however, and those affecting the genitourinary system were seen in 2.3% of men in each study arm.

According to Dr Warde, the results of the PRO7 study do not mean that all men with locally advanced prostate cancer should receive hormone therapy plus radiotherapy. The combination is appropriate in men with a life expectancy of 5–10 years. But he recommended avoiding radiotherapy in men with comorbid disease, especially cardiovascular disease, and those with a short life expectancy.

Sue Lyon