Platelet stimulation to treat adults with chronic immune thrombocytopenic purpura

Nplate (romiplostim) is the first platelet producer approved by the European Medicines Agency for the long-term treatment of adult patients with chronic immune thrombocytopenic purpura, a rare but serious bleeding disorder.

Romiplostim works similarly to thrombopoietin. It contains an active peptide component that stimulates the thrombopoietin receptor, which is necessary for growth and maturation of megakaryocytes and therefore stimulates platelet production.

Romiplostim increases platelet production at a rate that outpaces their destruction by the immune system, bringing a new approach to the long-term treatment of immune thrombocytopenic purpura by raising and sustaining platelet levels.

Romiplostim is a peptibody is a novel platform developed by scientists at Amgen. A peptibody is an engineered protein, made with recombinant DNA technology, that has attributes of both peptides and antibodies but is distinct from each. Amgen Inc. received the Prix Galien USA 2009 award for best biotechnology product for Romiplostim.

Romiplostim is licensed for the treatment of adult splenectomized immune thrombocytopenic purpura patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins), and may be considered as second-line treatment for adult non-splenectomized immune thrombocytopenic purpura patients where surgery is contraindicated.

Dr Drew Provan, Consultant Haematologist, Barts and the London School of Medicine

Dr Drew Provan, Consultant Haematologist, Barts and the London School of Medicine, commented: 'Nplate is a welcome option for this group of seriously affected adults. Results of the trials have been very encouraging.'

'Nplate is well tolerated and increases and maintains platelet counts both in patients who have undergone a splenectomy and in those who have not. There is a durable increase in platelet counts and a response is seen within approximately 1 week. This is an important step forward in the treatment of immune thrombocytopenic purpura', he concluded.

New class of treatment for rheumatoid arthritis

A new interleukin-6 antagonist tocilizumab (RoActemra) achieves clinical remission rates for rheumatoid arthritis almost six times higher than the current standard of care, the disease-modifying antirheumatic drug methotrexate (47% *vs* 8%).

Tocilizumab, the first licensed interleukin-6 receptor antagonist, used in combination with methotrexate also halts joint damage in 85% of people with rheumatoid arthritis compared to just 67% of patients treated with methotrexate alone.

This is the first time in a decade that rheumatoid arthritis patients who cease to respond to the current standard of care (disease-modifying antirheumatic drugs) have a new option to help control their disease. Until now, patients' only option after disease-modifying antirheumatic drug failure was to be given tumour necrosis factor antagonists. Interleukin-6 inhibition offers a wholly different approach for doctors treating rheumatoid arthritis.

Professor Paul Emery, Professor of Rheumatology at University of Leeds, and one of the investigators involved in the study of tocilizumab, commented: 'This is certainly one of the most exciting therapies to have emerged in the last decade. Interleukin-6 receptor inhibition is an innovative approach to the treatment of rheumatoid arthritis and RoActemra is a much anticipated addition to the armoury of treatments needed to combat the condition.'

Professor Emery continued: 'Rheumatoid arthritis is an unrelenting disease and it is vital that patients have options available to them when they are no longer responding to, or can no longer tolerate, their current treatment.'

Tocilizumab has been studied in one of the largest phase III clinical trial programmes for any biologic drug in rheumatoid arthritis to date, with 4200 patients in five clinical trials, and open-label clinical studies in 38 centres across the UK.

NHS Early Warning Scoring system

The Society for Acute Medicine 3rd International Conference provided an opportunity to review further initiatives with which the society is trying to improve the management of acute medical illness.

Professor Derek Bell, professor of acute medicine, Imperial College, London outlined the new NHS Early Warning Scoring (NEWS) system for identifying patients at risk for deterioration. 'There are several scoring systems used around the country, but we need a common system that we can use to follow an individual throughout the patient journey,' he explained.

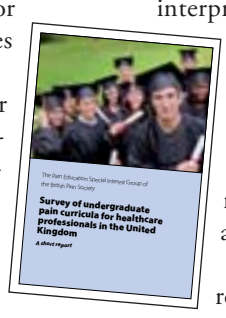
NEWS incorporates best practice and current evidence, and the patient's age and use of supplemental oxygen have been added to give a better indicator. 'Initiatives such as NEWS are part of making improvements in standardization and promoting the quality agenda,' said Professor Bell.

Susan Mayor

Professor Derek Bell, Professor of Acute Medicine, Imperial College, London

Medical student education in pain management

A descriptive, exploratory survey has been carried out by the Pain Education Special Interest Group of the British Pain Society to assess the level of teaching about pain management. Pain-specific curricula have been published by the International Association for the Study of Pain, but it is not clear whether these curricula are used with current programmes for health-care professionals. This survey involved 11 major university cities across the UK.



Nineteen higher education institutions were included which offered 108 undergraduate programmes from: dentistry, medicine, midwifery, nursing, occupational therapy, pharmacy, physiotherapy and veterinary science.

The UK Pain Education Questionnaire was adapted from previous work and designed to elicit the quantity and nature of the pain teaching, learning strategies used, assessment techniques, International Association for the Study of Pain curricula implementation and extent of interprofessional education. Data collection took place in spring 2009.

Seventy four questionnaires were returned (68.5%), 10 of which related to undergraduate medicine (83.3%).

Medical students received a median of 13 hours of teaching on pain management in their curricula, from a minimum of 6 to a maximum of 50 hours. Lectures and case studies dominated as learning strategies used in pain teaching although student-led approaches such as enquiry or problem-based learning were a feature of some courses. The most frequently taught topics were neurophysiology and analgesics.

Interprofessional education around pain was rare. Predominantly medicine, occupational therapy and physiotherapy shared an average of 5.5 hours but this was typically lectures, suggesting a multi-professional approach of learning alongside one another rather than with, from and about each other.

Hospital at Night improves patient outcomes

Research reported at the Society for Acute Medicine 3rd International Conference, Birmingham (1–2 October) demonstrated that the coordinated care provided by specialists in acute internal medicine and acute medicine teams significantly improves patient outcomes. Implementing a Hospital at Night scheme reduced the number of patients needing transfer to critical care or suffering cardiac arrest by two-thirds, according to a new study.

The Hospital at Night scheme is based on having a multiprofessional team with the full range of skills and experience required to meet patients' immediate needs providing overnight cover across a hospital, rather than junior staff working on individual wards having to contact senior doctors who are on-call at home.

The observational study compared a period of 14 consecutive nights before the scheme was implemented at the Royal Infirmary of Edinburgh with a 14-night period afterwards, matched for time of year.

The researchers found similar numbers of episodes of clinical concern, where patients became unwell and needed additional review – 209 before the implementation of Hospital at Home and 216 afterwards. However, the number of patients with adverse outcomes – defined as unplanned transfer to critical care or suffering cardiac arrest – fell from 17% to 6% of those reviewed overnight ($P<0.01$).

Further results showed that the Hospital at Night scheme eradicated previous variations in the time for response when wards asked for patients to be reviewed. In addition, patients were more likely to be reviewed by senior medical staff in the high dependency units (50% *vs* 22%, $P<0.001$) and in the combined surgical and medical assessment unit (28% *vs* 4%, $P<0.05$). Standardized early warning scores were used more frequently and recorded more accurately under the scheme.

Reporting the findings, Daniel Beckett, now a consultant in acute medicine, NHS Forth Valley, Stirling, said: 'This is the first study directly comparing out-of-hours performance before and after the implementation of Hospital at Night. It showed significant improvements in both patient and system outcomes, with no adverse effects.'

Dr Beckett noted that most hospitals now have Hospital at Night schemes, many of which are led by acute medicine physicians.

Susan Mayor

Once-daily dosing for treatment-naive HIV patients

Lopinavir/ritonavir (Kaletra) has been approved for once-daily as well as twice-daily use in adult patients new to human immunodeficiency virus (HIV) therapy in combination with other antiretroviral agents, giving physicians another option when deciding on the most appropriate HIV dosing regimen.

Taskforce launches: Experts in Severe and Complex Obesity

A taskforce, Experts in Severe and Complex Obesity, has been set up to promote equitable access and viable funding for the treatment of people with severe or complex obesity on the NHS. The group has called for action to tackle the current situation.

Improving therapy adherence in Parkinson's disease

Boehringer-Ingelheim has launched a once-a-day formulation of pramipexole (Mirapexin) for the treatment of the signs and symptoms of idiopathic Parkinson's disease, to be used either alone or in combination with levodopa.

One of the key benefits of prolonged release formulations is improved adherence.

ECCO/ESMO CONGRESS
BERLIN, GERMANY, 20–24 SEPTEMBER

Daily aspirin protects against colorectal cancer

Taking a daily aspirin can prevent cancer in people at high genetic risk because of Lynch syndrome. This is the conclusion of a study led by Professor John Burn of the Institute of Human Genetics, Newcastle University.

The worldwide study involved 1071 Lynch syndrome carriers who were randomized to 4 years treatment with aspirin 600 mg/day or Novelose 30 g (a resistant starch not digested in the small intestine). Investigators believe that aspirin may achieve its effect by attacking mutant stem cells in the colon.

Professor Burn commented: 'To date [up to 10 years after randomization] there have been only six colon cancers in the aspirin group as opposed to 16 who took placebo. There is also a reduction in endometrial cancer. This is a statistically significant result and we are delighted – all the more so because we stopped giving aspirin after 4 years, yet the effect is continuing and is directly correlated with the duration of aspirin use in the trial.'

Professor John Burn, Institute of Human Genetics, Newcastle University, Newcastle

Lynch syndrome is an inherited cancer of the digestive tract that causes about 5% of all colon cancers. Patients are also at higher risk of cancers of the stomach, small intestine, liver, gall bladder ducts, upper urinary tract, brain, skin, prostate, endometrium and ovary.

Sue Lyon

Improving survival in advanced colon cancer

A new treatment strategy may improve long-term survival in patients with metastatic colorectal cancer whose liver metastases are initially thought to be unsuitable for upfront resection.

Data from the prospective, single-arm, phase II BOXER study were reported by Dr Rachel Wong, Royal Marsden NHS Foundation Trust, London.

Using a pre-surgical combination of chemotherapy (capecitabine and oxaliplatin, CAPOX) and bevacizumab, Dr Wong and her colleagues successfully converted one-third of patients to a position where complete resection was possible.

Dr Wong said: 'The CAPOX/bevacizumab combination is already a standard first-line treatment option for metastatic colorectal cancer, and in the neoadjuvant setting it has been shown that it can be administered to patients with upfront resectable liver metastases without increasing perioperative complications.'

The hypothesis was that neoadjuvant therapy might allow some patients with initially unresectable liver metastases to be adequately downsized in order to achieve resection.

All patients received CAPOX (oxaliplatin 130 mg/m^2 on day 1, capecitabine 850 mg/m^2 twice daily on days 1–14) and bevacizumab 7.5 mg/kg on day 1 then every 3 weeks. The capecitabine dose was reduced to 650 mg/m^2 in patients ≥75 years. Resectability was reassessed after every four cycles of CAPOX and bevacizumab, with the latter discontinued a minimum of 8 weeks before surgery.

After a median follow up of 11.4 months in all 45 patients (63% male) assessed for efficacy, there was an overall response rate in 35 (78%), with a complete radiological response in 9% (all of whom had additional capecitabine-based chemotherapy to the primary tumour).

Median progression-free survival was 12.0 months (73% at 6 months, 50% at 12 months), and 86% of patients were still alive at 12 months.

Specific grade III/IV bevacizumab-related toxicities included venous thromboembolism, hypertension and gastrointestinal perforation.

Dr Wong concluded that the CAPOX and bevacizumab combination is associated with a high response rate (78%) in patients with initially unresectable or synchronous liver-only colorectal cancer metastases: 'To date, 33% of initially unresectable patients have been downstaged to potentially resectable status – and with no clinically significant perioperative complications, we were able to demonstrate that liver metastatectomy can be performed safely as early as 8 weeks post-bevacizumab.'

Stephen Pinn

This conference report is published online by Doctors.net.uk

Keep taking the tablets in breast cancer

Long-term adherence to adjuvant treatment is worthwhile for women with breast cancer, according to the Tamoxifen Exemestane Adjuvant Multinational (TEAM) trial.

Principal investigator Professor Cornelis van de Velde explained: 'Patients who stopped study treatment [exemestane or tamoxifen] had a significantly higher chance of recurrence.... This underlines the need for good information for patients concerning the side effects of drugs and treatment efficacy.'

Adherence in TEAM was lower than any previous study of adjuvant therapy at 19.8% for tamoxifen and 12.9% for exemestane. A total of 9779 postmenopausal women with hormone-receptor-positive early breast cancer were randomized to tamoxifen 20 mg/day or exemestane 25 mg/day.

After 2.75 years treatment, there were 11% fewer cases of local recurrence, distant metastases, contralateral breast cancer and deaths without disease relapse for patients in the exemestane group. There were no differences in time to contralateral breast cancer and overall survival, and no unexpected safety issues. Outcomes after 5 years treatment are expected shortly.

Sue Lyon

ECCO/ESMO CONGRESS
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Benefit of long-term exemestane

New data from the Intergroup Exemestane Study (IES) of breast cancer adjuvant therapy show the benefits of switching to exemestane after 2–3 years of tamoxifen are maintained over the next 6 years.

Professor Charles Coombes, principal investigator of the IES study and director of the oncology department at Imperial College, London, said: 'These results give us confidence in the switch strategy as used in this trial because the survival advantage is robust and enduring.'

The risk of experiencing a disease-related event over the follow-up period of 91 months among those switched to exemestane was reduced by 18% (hazard ratio=0.82, 95% confidence interval=0.73–0.92, *P*=0.0009) compared to those who had continued on tamoxifen for a full 5 years in women whose tumours were either oestrogen-receptor positive or were of unknown hormone receptor status.

Exemestane also significantly prolonged overall survival in women with hormone-receptor-positive tumours, with a 14% relative reduction in the risk of dying (hazard ratio=0.86, 95% confidence interval=0.75–0.99, *P*=0.04). The intention-to-treat analysis showed a 16% relative reduction in the risk of disease-free survival events. For the secondary endpoint of overall survival, there was an 11% non-significant relative risk reduction of death (*P*=0.09).

The IES trial included 4724 patients, of whom 97% were oestrogen-receptor positive or unknown.

Rhonda Siddall

'Extraordinary' 2-year survival data in metastatic melanoma

Nearly 60% of treatment-naive metastatic melanoma patients treated with ipilimumab are alive at 2 years, reported an updated phase II study presented in Berlin.

A randomized double-blind trial evaluated grade two diarrhoea in 115 patients receiving ipilimumab with or without prophylactic oral budesonide. Results in treatment-naive patients (*n*=32) given ipilimumab plus placebo showed 18-month survival rates of 61% and 2-year survival rates of 56.6%.

A phase II open label single arm study evaluating 155 previously treated patients showed survival rates of 39% at 18 months and 33% at 24 months.

Ipilimumab is an investigational monoclonal antibody which binds to cytotoxic T lymphocyte-associated antigen 4, a molecule which 'switches' off the T cell response. This increases active T cell production, facilitating tumour targeting.

'These results are nothing short of extraordinary since historically most patients die between 12 and 18 months,' commented Professor Alexander Eggermont, President of ECCO.

Janet Fricker

Governments must act now to tackle cervical cancer

Vaccination against human papilloma virus (HPV) plus national screening programmes with HPV testing could eradicate cervical cancer in the next 50 years. But national governments and the European Union need to take the lead, according to Professor Jack Cuzick of the Wolfson Institute, London.

Speaking in Berlin, Professor Cuzick said: 'The European Commission and Parliament, together with national governments, could be doing more to promote HPV testing… There's been a lot of concern, particularly with the vaccine, that dissemination of information about HPV has come mainly from the drug companies, and people are, not surprisingly, a little sceptical about pharmaceutical-based education programmes.'

Current vaccines could eradicate the 70–75% of cervical cancers caused by HPV types 16 and 18, but vaccinated women still need lifelong screening. Citing 'overwhelming evidence' for its effectiveness, Professor Cuzick recommended switching to screening for HPV which could be conducted at longer intervals, e.g. every 5 years starting at 25–39 years of age, increasing to every 8 years at the age of 50 years in HPV-negative women.

Sue Lyon

New option for pancreatic cancer

Treatment with the tyrosine kinase inhibitor sunitinib significantly prolonged progression-free survival with an 'acceptable' safety profile in patients with progressive well-differentiated pancreatic islet cell tumours, data revealed.

Investigators assessed the safety and efficacy of placebo or sunitinib 37.5 mg/day continuous daily dosing, with best supportive care, in 154 patients with well-differentiated pancreatic islet cell tumours not amenable to curative therapy. The trial was stopped early after a planned review by a data monitoring committee recommended all patients should be offered sunitinib as the study had met its primary endpoint and there was acceptable toxicity.

The interim analysis presented at ECCO showed median progression-free survival was 11.1 months with sunitinib *vs* 5.5 months for placebo. The hazard ratio for progression-free survival was 0.397 in favour of sunitinib (*P*<0.001), giving a 60% improvement. Lead investigator Dr Eric Raymond, from Hospital Beaujon, Clichy, France, said: 'We are currently analysing the final data and we expect to see an overall survival benefit [with sunitinib treatment].'

He added: 'There are few medical options for advanced pancreatic islet cell tumours so our trial is important because it opens up the possibility for future treatment.'

Rhonda Siddall