

Second chance of cure for hepatitis C patients

New data show that re-treatment with Pegasys (peginterferon alfa-2a) plus Copegus (ribavirin) provides previously-treated hepatitis C patients a second chance for a cure (Jensen et al, 2009). The study results demonstrated that patients most likely to respond to re-treatment could be identified after only 12 weeks, allowing patients and their doctors to be confident early on about the likelihood of success.

'While tremendous advances in hepatitis C treatment have cured many hepatitis C patients, a significant proportion of patients do not achieve success with their first treatment course. This is leading to a large and growing population of patients who are in urgent need of alternative treatment options,' said Donald Jensen, US principal investigator for

Donald Jensen, Professor of Medicine and Director of the Center for Liver Diseases, University of Chicago Hospital, Chicago



REPEAT, and Professor of Medicine and Director of the Center for Liver Diseases at the University of Chicago Hospital in Chicago.

'With 72 weeks of Pegasys and ribavirin combination treatment as a new solution for those with the most difficult-to-treat form of the virus, patients can now feel more hopeful that they have the possibility to achieve a cure when previous therapy has failed,' Professor Jensen continued.

Patients with genotype 1 virus who were initially treated with pegylated interferon and ribavirin can be retreated with peginterferon alfa-2a for an extended period of 72 weeks. Peginterferon alfa-2a is now the first and only pegylated interferon to be approved anywhere for treatment of up to 72 weeks. For all other previously treated patients, the recommended treatment period is 48 weeks.

Enrolling 950 patients from Europe, North America and Latin America, the REPEAT (REtreatment with PEGasys in pATients Not Responding to Peg-Intron Therapy) study was designed to explore whether intensified treatment with a higher initial dose of Pegasys (peginterferon alfa-2a) in combination with ribavirin, and/or longer treatment duration, may increase treatment success rates in patients who did not respond

to at least 12 weeks of PegIntron (peginterferon alfa-2b) plus ribavirin and who did not discontinue treatment as a result of haematological adverse events.

The results demonstrated that while a fixed-dose induction did not contribute to treatment success, patients receiving 72 weeks of re-treatment with peginterferon alfa-2a doubled the chance of achieving a cure compared with the previous standard of 48 weeks (16% vs 8%). Furthermore, the study showed that for the 17% of patients who responded by week 12 (defined as HCV RNA levels of less than 50 IU/ml), 57% went on to achieve a cure after a 72-week treatment course, compared with only 35% of patients who were re-treated for 48 weeks.

'It is a significant step forward that we now know patients who have undetectable levels of hepatitis C at week 12 have a good likelihood of achieving a cure with Pegasys and ribavirin. This ability to predict success after just 3 months will give both doctors and hepatitis C patients additional confidence when considering whether to re-treat,' said Professor Jensen.

Jensen DM, Marcellin P, Freilich B et al (2009) Re-treatment of patients with chronic hepatitis C who do not respond to peginterferon-alpha2b: a randomized trial. *Ann Intern Med* 150(8): 528-40

Single cell may cause multifocal lung cancer

Multiple, anatomically distinct lung cancer tumours may often arise from a single cancer cell, according to a retrospective analysis of patient tumour samples (Wang et al, 2009).

Some lung cancer patients have multiple anatomically distinct tumours at diagnosis. Although such tumours usually share a common appearance, it has not been clear whether they arise from a single tumour or are independent primary cancers.

Dr Liang Cheng, of the Indiana University School of Medicine in Indianapolis, and colleagues examined 70 lung cancer tumours from 23 female and seven male patients to see whether multiple tumours from an individual patient shared a common genetic pattern.

The investigators concluded that the multiple tumours in 23 of the 30 patients (77%) arose from a single cancer clone.

Wang X, Wang M, MacLennan GT et al (2009) Evidence for common clonal origin of multifocal lung cancers. *J Natl Cancer Inst* 101: 560-70

Preventing cytomegalovirus infection in transplant patients

A new formulation of valganciclovir (Valcyte) will give doctors greater flexibility in how they tailor the dose of preventative cytomegalovirus (CMV) treatment to better meet the needs of transplant patients, in particular those at high risk of possible infection.

After receiving a transplanted organ, some patients need treatment not only to retain their new organ, but also to prevent CMV disease, which can cause the loss of a new organ and even death.

The current gold standard preventative treatment for

CMV disease is oral valganciclovir tablets. However, some transplant patients need ongoing intermittent dialysis and may need their dosage adjusted depending on how well their kidneys are working. Previously, the only approved adjustable-dose treatment relied on an

intravenous ganciclovir infusion, a less practical treatment for some transplant patients.

New valganciclovir powder for oral solution is licensed for oral protection against CMV disease for transplant patients, including those on haemodialysis.

Preventing atherothrombosis in PCI patients

A new antiplatelet agent Efiel (prasugrel hydrochloride), co-administered with aspirin, has been launched for the prevention of atherothrombotic events in patients with acute coronary syndromes undergoing percutaneous coronary intervention (PCI).

The authorization of prasugrel is based upon data from several clinical trials including TRITON-TIMI 38 (Wiviott et al, 2007), the pivotal head-to-head superiority study that evaluated the safety and efficacy of prasugrel compared to clopidogrel, the current standard of care.

Prasugrel plus aspirin showed a statistically significant 19% reduction in the primary end point of cardiovascular death, non-fatal heart attack and non-fatal stroke compared to clopidogrel plus aspirin (9.9% vs 12.1%, hazard ratio=0.81, 95% confidence interval=0.73–0.90, $P<0.001$, absolute risk

reduction=2.2%) in 13 608 acute coronary syndrome patients undergoing percutaneous coronary intervention.

Prasugrel also significantly reduced all pre-specified secondary end points, including a 52% reduction in the incidence of stent thrombosis over clopidogrel.

A sub-analysis of TRITON-TIMI 38 showed that, compared to clopidogrel, prasugrel significantly reduced the risk of recurrent cardiovascular events in acute coronary syndromes undergoing percutaneous coronary intervention patients by 35% (10.8% vs 15.4%, hazard ratio=0.65, 95% confidence interval=0.46–0.92, $P<0.016$, absolute risk reduction=4.6%).

Prasugrel is the first new oral antiplatelet to be licensed in the UK for more than a decade. It offers a much quicker onset of action and a more consistent and higher level of platelet

inhibition than clopidogrel in healthy subjects. However, any differences in platelet inhibition between antiplatelet agents have not been correlated to clinical outcomes.

Dr Marcus Flather, Consultant Cardiologist at Royal Brompton Hospital, London, said: 'Prasugrel is a welcome breakthrough in protecting acute coronary syndromes undergoing percutaneous coronary intervention patients from potentially life-threatening atherothrombotic events... The UK has one of the highest rates of acute coronary syndromes and this is rising. Prasugrel meets a critical medical need by building on existing antiplatelet treatments. It has the potential to become a routine treatment.'

Wiviott S, Braunwald E, McCabe CH et al (2007) Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 357: 2001–15

Annual infusion treats osteoporosis

A once-yearly infusion of zoledronic acid 5 mg is significantly more effective than oral daily risedronate 5 mg in preventing and treating bone loss caused by glucocorticoid-induced osteoporosis in both men and women, at 12 months of treatment, says a study published in *The Lancet*.

Patients do not know disease activity score

The National Rheumatoid Arthritis Society has found that nearly 90% of people with rheumatoid arthritis do not know about their disease activity score. This is despite the National Institute for Health and Clinical Excellence recommending regular monitoring using the disease activity score and adjusting treatment accordingly.

Bone marrow transplant may offer new HIV treatment

Doctors from Berlin, Germany announced at the 35th Annual Meeting of the European Group for Blood and Marrow Transplantation that they have successfully controlled human immunodeficiency virus (HIV) infection by transplanting bone marrow cells from an HIV-resistant donor. This has important implications for the future treatment of HIV.

Concurrent topical ointment does not add benefit in patients with moderate to severe psoriasis

New data shows that adalimumab (Humira) is as effective in patients with moderate to severe psoriasis at 16 weeks with or without the concurrent use of topical therapy. The data also show that patients who did not have success with other systemic treatments could achieve a high response with adalimumab.

The results were presented at the European Academy of Dermatology and Venereology Spring Symposium in Bucharest, Romania. They come from BELIEVE, the first major clinical trial to compare biological therapy used in combination with a topical ointment to biological therapy alone, in patients with moderate to severe psoriasis.

'Studies have previously demonstrated the safety and efficacy of adalimumab monotherapy in the management of moderate to severe psoriasis, but in clinical practice some dermatologists may choose to supplement adalimumab with a topical therapy,' said Dr Diamant Thaçi, director of clinical research at Goethe University Frankfurt and lead study investigator. '...psoriasis can be effectively managed with adalimumab without the simultaneous use of ointments, which patients often find to be messy and inconvenient.'

Patients in one arm were treated with adalimumab alone, while those in the other arm had a combination of adalimumab

and a topical treatment (calcipotriol and betamethasone). Response rates were reported using the Psoriasis Area and Severity Index (PASI), with PASI 75 defined as a 75% improvement from baseline in a patient's PASI score.

During the first 4 weeks of the study, patients in both arms of the study improved rapidly, but those receiving combination therapy improved more than patients on adalimumab monotherapy. However, after 4 weeks, use of a topical ointment as well as adalimumab did not offer any benefit compared to adalimumab alone, with 71% of patients on monotherapy achieving PASI 75 at week 16.

BRITISH PAIN SOCIETY SANDOWN, SURREY, 31 MARCH–3 APRIL

A new approach to management of chronic cancer pain is needed

A new approach is needed to manage pain in the growing population of patients either living with or cured of cancer, according to Professor Allen Burton, Texas, USA. He was speaking during a plenary session at the British Pain Society.

Professor Burton reminded delegates that cancer pain is frequently difficult-to-treat neuropathic pain, and that it occurs in all tumour types and at all stages of cancer. Furthermore, current approaches that optimize the chance of cure also increase the potential for treatment-related toxicity and chronic pain states.

'Cancer pain is increasingly turning into chronic pain because of oncology colleagues' success in diagnosing and treating cancer more effectively. The cancer care cycle is fraught with

many episodes of acute and repeated painful events, and their treatment can either set up the patient to develop chronic pain or enable them to live with their cancer. There are therefore many opportunities to intervene to improve patient quality of life throughout the cancer care cycle,' he said.

Professor Allen Burton, Professor, Department of Pain Medicine, MD Anderson Cancer Center, Texas, USA



According to Professor Burton, it is time for a critical appraisal of the World Health Organization (WHO) cancer pain ladder. First published over 20 years ago, the ladder aims to achieve freedom from cancer pain through a stepped approach ending with opioids with or without adjuvant drugs.

He explained: 'This advice was based on expert consensus rather than evidence or pathophysiology. In many cases we find a lack of efficacy when using the ladder. For example, opioids are the recommended gold-standard treatment, but they are not the panacea that we hoped for. And we now have better evidence for specific treatment algorithms, for example, in neuropathic pain conditions.'

Instead of the WHO pain ladder, Professor Burton advo-

cated a mechanism-based, customized approach. This uses a combination of therapies and technologies, and may involve interventions by a range of specialist disciplines, such as pain medicine, surgery, palliative care, psychology and other therapies.

The success of this unified theory of pain management depends on rigorous assessment to diagnose the causes of the pain. 'We should then follow a patient-centred approach that aims at reduction of pain using the full range of treatments. We should also aim to rehabilitate and be realistic with patients, explaining that we may not be able to free them from pain, but we can help them live with it and optimize their quality of life,' he concluded.

Sue Lyon

Highlights of poster presentations: from pathways to fibromyalgia

Back pain care pathway

When preparing recommendations for commissioners, a care pathway effectively illustrates the evidence-based changes needed to improve current service provision.

In the lower back pain pathway in this study, the major new recommendations were to reduce physiotherapy waiting times for spinal manipulation and to educate GPs about identifying patients with lower back pain associated with psychosocial needs.

Stanton E, Perks W, Morris T, Coetzer H (2009) Using evidence-based care pathways to improve management of lower back pain. Poster 115. British Pain Society Annual Scientific Meeting, 31 March–3 April 2009

Acute pain guidelines

Most (69%) hospitals have no guidelines for the management of acute pain in opioid-tolerant surgical patients, according to respondents to a UK survey.

Nearly half (45.7%) said that guidelines were under discussion, while in 20.9% management was on an individual patient basis. However, 18.6% of respondents cited lack of clinical need and 12.4% insufficient literature as reasons for not having guidelines.

Emmanuel J, Hetreed M (2009) UK survey. Availability of guidelines for acute pain management in surgical patients with opioid tolerance. Poster 39. British Pain Society Annual Scientific Meeting, 31 March–3 April 2009

Ultrasound in pain management

A UK-wide survey of lead pain clinicians found limited usage of ultrasound in pain management. Only 22% of respondents had formal training in its use, but 76% wished to include the technique in their interventional pain practice.

Of those wishing to use ultrasound, 50% reported lack of training and 55% lack of a suitable machine as the main obstacles.

Ahmad RI, Baloch M, Markham K, Fish A (2009) A nationwide survey of the use of ultrasound for interventional pain procedures. Poster 2. British Pain Society Annual Scientific Meeting, 31 March–3 April 2009

Sleep disturbance in fibromyalgia

Medication is currently the most effective treatment for sleep disturbance in patients with fibromyalgia according to a systematic review which looked at 53 randomized controlled studies.

Despite this, additional research is needed to support findings that exercise and psychological treatments may also benefit these patients.

Deasy M, Fullen BM, Murphy S (2009) Management of sleep disturbance in patients with fibromyalgia: a systematic review. Poster 30. British Pain Society Annual Scientific Meeting, 31 March–3 April 2009

Sue Lyon

BRITISH PAIN SOCIETY SANDOWN, SURREY, 31 MARCH–3 APRIL

Audit shows improving access to new pain treatment is cost-effective

An effective, cost-saving prescription strategy will persuade primary care trusts to take over responsibility for a new pain treatment, according to audit data (Mattheus and Coupe, 2009). The study, by investigators from the Royal United Hospital, Bath, was in response to local primary care trusts' initial reluctance to continue management and funding of topical 5% lidocaine plaster (Versatis).

The first step was to negotiate agreed prescribing criteria for topical 5% lidocaine plaster with the local Drug Policy Group:

- Indication of neuropathic pain with allodynia
- Consultant assessment and treatment only
- Initial 1-month trial
- Use in accordance with manufacturer's guidelines

- Regular review of prescription practice
- Treatment cessation if no relief or undesired side effects
- Telephone follow-up after 2 weeks.

There was 100% compliance with these criteria when practice was audited at 6 months. At the start of the study, initial trial packs of 10 plasters were prescribed to 20 patients. This was based on predicted use of 0.5–2 plasters per patient per day, but actual use was 0.25–1 plaster per patient per day. Eight patients did not continue treatment after their initial trial, but 11 requested repeat prescriptions, and one received a repeat prescription from the GP. Although the sample size was small, topical 5% lidocaine plaster was most effective in

patients with post-herpetic neuralgia, scar pain, phantom pain and intercostal neuralgia.

Following presentation of the data to the Drug Policy Group, the local primary care trust agreed to be responsible for funding and management of 5% topical lidocaine plaster. According to the investigators, the result has been improved access to the treatment for patients, while containing costs for both the acute and primary care trust.

Commenting on the study, Dr Mark Ritchie, GP with a special interest in pain, Swansea, said: 'The agreed prescribing guidelines are certainly appropriate, and if they could be circulated to other primary care trusts, I believe it would help to improve GPs' confidence in using this treatment. Equally,

primary care trusts should remember that there is more to health economics than the cost of a drug. There is also reduction in appointments and the need for other medications if pain is not relieved. No one wants to waste money, but we should also be thinking about patient care and be willing to give a treatment that is easy to use, well tolerated, and effective.'

Topical 5% lidocaine plaster is currently licensed in the UK for the treatment of post-herpetic neuralgia.

Sue Lyon

Mattheus C, Coupe M (2009) 5% lidocaine medicated plaster: audit of use and cost-saving prescription strategy. Poster 79. British Pain Society Annual Scientific Meeting, 31 March–3 April 2009

This report has been reviewed for accuracy by Grünenthal Ltd

Managing side effects is vital when treating pain

GPs have called for new pain treatments better suited to patient needs, according to new survey findings.

The results found that nine out of ten GPs believe there is a need for an opioid treatment which addresses gastrointestinal related side-effects. Gastrointestinal side effects, the most common and debilitating of which is constipation, can affect up to 90% of patients taking an opioid pain medication.

According to the survey of 200 GPs, nearly half (44%) believe that the negative impact of such side effects is the key factor in patient non-compliance with prescribed opioid treatments.

These survey findings are reinforced by patient experience, with a recent study conducted among over 1300 patients who have taken pain medication identifying that nearly 35% of patients would stop taking pain medication and instead put up with the pain just to avoid the side effects.

Despite innovations in pain medicines being few and far between for many years, there have recently been a number of new medications launched which address the most common gastrointestinal side effect of opioid treatment – constipation.

'To those of us involved with pain management, the ability

to provide adequate analgesia for each patient is paramount. With opioids, sadly this can come at the expense of producing significant side effects, particularly constipation', said Dr Steve Allen, Consultant, Pain Relief Unit, Oxford.

The attitudes expressed by GPs and patients suffering from pain echo those of the Chief Medical Officer in his latest report, that more needs to be done in pain management. The latest guidance to the NHS recommends that a new initiative to provide broader access to pain services is required, including chronic pain being included in the curricula for all health-care professionals.

Honorary membership for Dickenson

Professor Anthony Dickenson, of the UCL Research Department of Neuroscience, Physiology and Pharmacology, London has been awarded Honorary Membership of the British Pain Society in recognition of 'an outstanding contribution to the alleviation of pain through personal endeavour and through his work for the Society'.

Professor Dickenson's research interests are pharmacology of the brain, including the mechanisms of pain and pain control.