Merck & Co.'s investigational drug, Zostavax®, shows promise in the Phase III Shingles Prevention Study by significantly reducing the incidence of persistent nerve pain and shingles. It is hoped that the drug could potentially be used as a vaccine against shingles, a disease that has the potential to affect approximately 90% of the population of the USA alone.

Zostavax® shows promise as a potential shingles vaccine

Results from a new study carried out by the Department of Veterans Affairs (VA) Healthcare System in collaboration with the national Institute of Allergy and Infectious Diseases (NIAID), the National Institutes of Health (NIH) and Merck & Co., which compared the company's investigational drug Zostavax with placebo in a group of 35,000 men and women, has demonstrated that the drug reduced the incidence of persistent nerve pain (PNP) by 67% and the incidence of shingles by 51%.

Results from the trial, which was carried out as part of the Phase III Shingles Prevention Study, have been published in the June 2 issue of the *N. Engl. J. Med.* and it is now hoped that the drug could potentially be used as a vaccine against shingles, a disease that has the potential to affect anyone who has suffered from chickenpox in the past. It is estimated that between 800,000 and 1 million cases of the disease appear annually in the USA and this figure is expected to increase as the population ages.

PNP, one of the most frequent complications associated with shingles, is known as postherpetic neuralgia (PHN) and is estimated to develop and persist in 25 to 50% of shingles patients over the age of 50 years.

> Shingles is a common, frequently painful disease that can occur without warning in anyone who has had chickenpox.

Speaking of the success of the trial and the results obtained to date, Michael Oxman of the San Diego VA Healthcare System and the University of California (CA, USA) commented "we are delighted that the results from this study published in The *New England Journal of Medicine* met or exceeded the predefined criteria for success." Commenting further on the disease, he noted that "Shingles is a common, frequently painful disease that can occur without warning in anyone who has had chickenpox. For those people who develop the most common complication of shingles, PHN, pain can last for weeks, months or even years. Even the touch of one's own shirt against the affected area can be very painful for someone suffering from PHN."

Jeffrey Silber, Senior Director for Biologics and Vaccines Clinical Research with Merck Research Laboratories speaking on the design of the study pointed out that "In this study, the investigational vaccine, zostavax, significantly reduced the shingles pain burden of illness and led to a significant reduction in the incidence of PHN. The investigational vaccine also reduced the incidence of shingles itself." He continued that "The investigational vaccine showed efficacy on these end points, regardless of participants' gender, age and other demographic factors."

The Shingles Prevention Study enrolled patients with a history of varicella or who had been resident in the continental USA for at least 30 years, over a 5-year period between November 1998 and September 2001. The study excluded immunocompromized patients or those unable to adhere to the assessments specified in the study protocol, and follow up was completed in April 2004. Results showed that zostavax significantly reduced the incidence, severity and duration of pain and discomfort associated with the disease by 61.1%, as well as significantly reducing the incidence of PHN by two thirds (66.5%). Zostavax significantly reduced the overall incidence of shingles by 51.3%.

Rituximab shows potential for use in the treatment of lupus

Reports from the Annual European Congress of Rheumatology (Vienna, Austria) have suggested that rituximab, traditionally used for the treatment of non-Hodgkins lymphoma, may prove useful in the treatment of patients with the immune disorder, lupus. Results from a trial of 22 patients taking place over a 6-month period were presented at the conference by Michael Neuwelt of the University of California (SF, USA) where he revealed "I spent considerable time with oncologists and saw how the drug works in patients with non-Hodgkins lymphoma. Patients with blood disorders of lupus and severe complications of the CNS also surprisingly improved."

However, whilst he praised the drug and the results of the studies carried out to date, he noted that further trials were warranted "It is the first drug in my 26 years of treating patients with severe CNS lupus, used alone or in combination with other therapies that has not only significantly boosted the quality of life for patients with this dreadful disease, but also reduced the burden of side effects of standard treatment with steroids and cyclophosphamide. However, we desperately need randomized, controlled trials."

Priority Paper Alerts

Treatment of hidradenitis suppurativa with infliximab in a patient with Crohn's disease.
Rosi YL, Lowe L, Kang S. *J. Dermatolog. Treat.* 16(1), 58–61 (2005).
Hidradenitis suppurativa is a chronic, relapsing, scarring suppurative cicatricial disease occurring in the apocrine follicles and characterized by recurrent flares. This paper examines the use of infliximab for the treatment of hidradenitis suppurativa in a patient with a history of inactive Chron's disease. Following treatment with infliximab, a subsequent improvement in the patient's skin disease was observed, suggesting a possible role for the drug in the treatment of hidradenitis suppurativa in association with Crohn's disease.

Comparison of two recombinant erythropoietin formulations in patients with anemia due to end-stage renal disease on hemodialysis: a parallel, randomized, double blind study.
Perez-Oliva JF, Casanova-Gonzalez M, Garcia-Garcia I *et al. BMC Nephrol.* 23, 6(1), 5 (2005) (Epub ahead of print).
The aim of this study was to compare the pharmacokinetic, pharmacodynamic and safety properties of two, recombinant human erythropoietin (EPO) formulations, that are used in the treatment of end-stage renal anemia, in patients with anemia occurring as a result of end-stage renal disease (ESRD) on hemodialysis. A total of 34 patients with anemia due to ESRD on hemodialysis were examined in a parallel, randomized, double-blind study that determined that both formulations were comparable, indicating that the newer formulation should be considered for acceptance in order to make this treatment widely available.

Improvement of glycemic control in subjects with poorly controlled Type 2 diabetes: comparison of two treatment algorithms using insulin glargine.
Davies M, Storms F, Shutler S, Bianchi-Biscay M, Gomis R. *Diabetes Care* 28(6), 1282–1288 (2005).
The aim of this study was to compare two treatment algorithms, one investigor-led and the other carried out by study subjects, for insulin glargine initiation and titration. Results demonstrated that glargine is safe and effective in improving glycemic control in a large, diverse population with longstanding Type 2 diabetes. In addition, the subject-administered titration algorithm conferred significantly improved glycemic control with a low incidence of severe hypoglycemia compared with that of the physician-managed titration.

Extended-release Glumetza™ is approved by the FDA for use in Type II diabetes

It has been announced that Glumetza™, a once-daily, extended-release formulation of metformin hydrochloride (HCl), has received approval by the US Food and Drug Administration (FDA) for use in the treatment of Type II diabetes. The news has been welcomed by the drugs manufacturers, Biovail Corporation and Depomed, Inc., as the drug has the potential to offer distinct advantages, including a less frequent dosing regime and proven effectiveness in combination with other diabetes drugs.

Sherwyn Schwartz, endocrinologist and a principal investigator in the Phase III clinical trials of Glumetza commented that "Glumetza has excellent tolerability, which is important because side effects, such as nausea and diarrhea, are thought to be a primary reason that 60% of patients prescribed metformin are no longer taking their medication as prescribed after the first year." He continued that "a Phase III clinical trial confirmed Glumetza's effectiveness in combination with the sulfonylurea glyburide, another diabetes drug that is frequently prescribed with metformin. Glumetza's effectiveness in combination with other diabetes drugs is key because the American College of Endocrinology and American Association of Clinical Endocrinologists recently recommended that physicians aggressively treat diabetes early, often with two or more drugs."

Douglas Squires, Chief Executive Officer of Biovail Corporation added that "Type II diabetes currently affects more than 17.5 million Americans" and that "Hyperglycemia is a major cause of many of the complications that happen to people who have diabetes, so keeping your blood sugar as close to normal as possible not only helps you to feel better, but will help to reduce the risk of long-term complications."

Biovail currently hold the commercialization rights for Glumetza for the USA and Canada and they are currently looking into marketing opportunities to enter the drug into the lucrative diabetes drug market in the USA. Metformin products were responsible for taking the highest share of the market of new prescriptions over the 12-month period ending March 2005.

Confirmation of the cardiovascular safety of vardenafil with α-blockers

Results from a study into the use of vardenafil in men on α-blockers, which was presented at the American Urological (AUA) Annual Meeting (TX, USA) have indicated that the drug may be less dangerous than previously thought in this patient population. Vardenafil, a member of the phosphodiesterase type-5 class of drugs, was previously thought to have an additive effect on blood pressure when used in combination with α-blockers. However, the FDA recently reduced the erectile dysfunction drug contraindication for α-blockers to a precaution.

The research was carried out at the University of Muenster (Germany) and produced results which confirmed that vardenafil would appear to be "effective and safe in a real-world environment" for men currently taking α-blockers.

Lower parameters of quality of life observed in patients with obesity, even after bariatric surgery

Findings from a study carried out by a group at the University of Munich (Germany) and presented recently at the European Congress on Obesity indicate that despite the weight loss and improvements in metabolic parameters experienced by patients suffering from obesity following bariatric surgery, lower psychological parameters and quality of life assessment scores were still lower when compared with patients suffering from other, chronic diseases.

Quality-of-life assessments of patients with obesity following bariatric surgery reveal that individuals still possess lower psychological parameters of quality of life compared with patients suffering from other chronic diseases

Kristine Leopold of the University of Munich reported that "Our findings show that managing patients after bariatric surgery is challenging, even if they have had some successes." She continued that "Physicians should remember that in our follow-up period, patients were still obese. It would be interesting to see what the quality-of-life results would be 10 years out or so, when they might have lost further weight and had even further improvement in physical functioning."

Leopold's team assessed the quality of life of patients following laparoscopic gastric banding by use of the Short Form-36 (SF-36) questionnaire for patients who were successful in achieving weight loss following surgery. The questionnaire was presented to patients 22.4 months after surgery and compared with patients with diabetes and hypertension, the patients who had undergone gastric banding had higher SF-36 scores on physical functions.

Lower urinary tract symptoms may be improved with tension-free vaginal tape

Studies carried out by a group at the Department of Urology, New York University School of Medicine (NY, USA) have resulted in the findings that tension-free vaginal tape may have a positive effect on stress incontinence plus other disorders of the lower urinary tract. Results from the group were presented recently by Chap Huckabay (New York University School of Medicine) at the American Urologic Society (AUA) Annual Meeting.

It was noted that the overall absolute change in AUASI total score was 7.2, however, there didn't appear to be any significant difference in pre- and postoperative total scores in patients who presented with mixed urinary incontinence.

Results demonstrated that the postoperative total score and storage symptom scores in patients with stress urinary incontinence were lower that those in patients with mixed urinary incontinence, indicating that the lower urinary tract symptoms evaluated by the AUASI were significantly improved following the tension-free vaginal tape.

New data presented on Neurochem's Fibrillex™ in the treatment of amyloid amyloidosis

Helen Lachmann, Senior Lecturer and Honorary Consultant Nephrologist and co-investigator of Neurochem's Phase II/III clinical study for Fibrillex™, presented promising new results recently at the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) meeting in London (UK). Use of Fibrillex™, an investigational drug candidate for the treatment of amyloid (AA) amyloidosis, a rare disease that often results in end-stage renal failure and death, in the current studies resulted in a reduction in the risk of renal decline or all-cause mortality by 42%.

Speaking at the conference, Lachmann noted that "While Fibrillex did not achieve the study's prespecified p-value of 0.01 on the primary endpoint, the analysis of the data suggest useful clinical effects of Fibrillex." She continued that "This result supports the notion hat Fibrillex may preserve kidney function in patients who face this very serious illness with no specific treatment to turn to."

Safety data suggested that the drug is well tolerated, with the most frequent adverse events being gastrointestinal and infections. In addition, the incidence of treatment-emergent adverse events in patients taking the drug was comparable with placebo.

AA amyloidosis is a potentially fatal disease occurring in a significant proportion of patients with chronic inflammatory diseases, as well as in patients suffering from a number of other conditions such as inherited inflammatory diseases and chronic infections. The main clinical presentation of the disease is renal dysfunction with end-stage renal failure presenting as the main cause of death in 40 to 60% of cases. The median time for survival from diagnosis is currently ranges from between 2 to 10 years and there is no specific treatment modality available. Existing therapies merely attempt to control the underlying chronic inflammatory disease and can be toxic and invasive.