

New research from the John Hopkins University School of Medicine (MD, USA) reveals the benefits of screening for osteoporosis in the prevention of hip fractures in the elderly population.

## Osteoporosis screening can prevent the development of hip fractures in the elderly

Results from a study carried out at the John Hopkins University School of Medicine (MD, USA) has revealed that screening for osteoporosis in men and women aged 65 years or older, can help to prevent a significant number of hip fractures, which are believed to affect 340,000 elderly people each year.

The study examined 3107 patients from the Cardiovascular Health Study (CHS), which was set up in an attempt to determine the risk factors for cardiovascular disease in older adults living in a community setting.

Lead investigator of the study and Robert Wood Johnson Clinical Scholar at The Johns Hopkins University School of Medicine at the time of the study, Lisa Kern, commented on the findings "Although some groups recommend screening for osteoporosis, no study had proven that screening prevents fractures. This study provides new evidence for the effectiveness of osteoporosis screening."

"Our hope is that our study can provide a foundation on which physicians can base their medical practices regarding screening for osteoporosis, and that it can also be relevant to groups that are drafting clinical guidelines on screening for osteoporosis," added co-investigator, Neil Powe, Director of Hopkins'

Welch Center for Prevention, Epidemiology and Clinical Research.

As part of the study, the group examined a total of 3107 men and women aged 65 years or older, not previously diagnosed with osteoporosis or a previous hip fracture, or those taking bisphosphonate drugs, who were taking part in the CHS between 1994 and 1995.

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Patients' bone density measurements were recorded locally and then sent to their primary care doctors, with all subsequent treatment strategies left to the decision of the participants in conjunction with their doctors. The patients were then followed for 6 years and data concerning hip fractures recorded.

It was found that a total of 33 screened and 69 unscreened patients developed hip fractures. Dr Kern commented that "This difference is statistically significant, but there were some other differences between the groups that can partially explain the variance in the incidence of hip fracture." "Surprisingly, differences in prescription of

vitamin D, calcium, estrogen and bisphosphonates did not account for the entire difference in hip fractures" she continued.

The study, which was not a randomized trial, did not collect any information pertaining to changes in life-style and behaviour, such as increased physical activity or use of fall-prevention strategies. However, it was believed to be the most accurate method of examination. "It is hard to randomize persons into screened and nonscreened groups today because Medicare now reimburses for screening," noted senior investigator Linda Fried, Director of Hopkins' Center on Aging and Health. "Use of medication to enhance bone density has increased over the last 11 years, too, further making a randomized evaluation difficult. Our study has several strengths but should be useful to National Institute of Health [NIH] consensus development panels and groups drafting clinical guidelines on screening for osteoporosis," added Fried.

It is currently estimated that 18% of women and 6% of men aged 50 years or older suffers from osteoporosis in the USA alone.

For further information on treatment strategies for osteoporosis, see this month's Ibandronate Drug Profile pp179-189.

### New patient information brochure to aid patients with gynecologic cancers in understanding the treatment options available

A new patient information brochure entitled *Radiation Therapy for Gynecologic Cancers: Facts to Help People Understand Their Treatment Options* has been published by the American Society for Therapeutic Radiology and Oncology (ASTRO) in an attempt to educate both patients and their families on the treatment options available for gynecologic cancers.

Louis Harrison, MD, Chair of the ASTRO Communications Committee, commented on the publication "Being diagnosed with a gynecologic cancer can be an overwhelming experience and making sense of the different treatments available isn't an easy task." He continued that the ASTRO hopes that "This brochure will help patients better understand the different types of treatments available and allow them to make the best, most informed decision about which treatment to receive."

It is hoped that the brochure will help to inform the 83,000 women who are diagnosed with some form of gynecologic cancer each year of the treatment options available to them, and enable these women to talk with their healthcare providers if radiation therapy is being considered as part of their treatment, as well as providing patients with help on finding support groups and information on clinical trials.

## Priority Paper Alerts

### Increase in airway neutrophils after oral but not inhaled corticosteroid therapy in mild asthma.

Nguyen LT, Lim S, Oates T, Chung KF. *Respir. Med.* 99(2), 200–207 (2005).

The purpose of this study was to determine whether oral or inhaled corticosteroid therapy can induce airway neutrophilia in patients with severe asthma. Two separate placebo-controlled studies examined patients with mild asthma treated with prednisolone or placebo for 7 days, or either of inhaled budesonide or inhaled placebo for 4 weeks. Examination of bronchial sections by the use of fiberoptic bronchoscopy revealed that corticosteroid therapy by the oral route, but not by the inhaled, can induce the recruitment of neutrophils into the airways of patients with mild asthma.

### Venlafaxine extended release versus placebo and paroxetine in social anxiety disorder.

Liebowitz MR, Gelenberg AJ, Munjack D. *Arch. Gen. Psychiatry* 62(2), 190–198 (2005).

The main objective of this study was to examine the efficacy, safety, and tolerability of flexible-dose venlafaxine extended release (ER) compared with placebo in the short-term treatment of generalized social anxiety disorder. The trial also compared paroxetine with venlafaxine ER and paroxetine with placebo. A total of 440 adult outpatients with DSM-IV generalized social anxiety disorder for 6 months or longer were examined, and results revealed that venlafaxine ER is effective in the short-term treatment of generalized social anxiety disorder, with demonstrated efficacy and tolerability that is comparable with paroxetine.

### Response to therapy with once-weekly alendronate 70 mg compared to once-weekly risedronate 35 mg in the treatment of postmenopausal osteoporosis.

Sebba AI, Bonnick SL, Kagan R, Thompson DE, Skalky CS, Chen E, de Papp AE; Fosamax Actonel Comparison Trial investigators. *Curr. Med. Res. Opin.* 20(12), 2031–2041 (2004).

The present study examines the Fosamax Actonel Comparison Trial (FACT) to determine the percentage of patients involved in the study who had changes during the study in bone mineral density (BMD) and biochemical markers (BCMs) of bone turnover above or below specific cut-off points.

## Tysabri<sup>®</sup> voluntarily withdrawn from the market following a death caused by the drug

Tysabri<sup>®</sup>, the new Food and Drug Administration (FDA)-approved multiple sclerosis drug from Biogen Idec and Elan Pharmaceuticals (see Bulletin Board, *Therapy* 3–6 2[10], [2005]), has been voluntarily withdrawn from the market following reports of one death and one incident of serious side effects in patients being treated with the drug. In addition, all studies involving the drug have been suspended and notification has been sent to healthcare professionals in a bid to suspend prescribing or use of the drug until further notice.

The move comes following the discovery of one confirmed and one suspected case of the rare but often fatal nervous system disorder, progressive multifocal leukoencephalopathy (PML), which is characterized by demyelination or

destruction of the myelin sheath of nerve cells. Both patients had been taking tysabri in combination with Avonex<sup>®</sup> for over 2 years. Of the 3000 patients who have been treated with tysabri in studies thus far, the only cases of PML reported occurred in patients taking the tysabri/avonex drug combination.

Previous reports indicated that sales of the drug could exceed US\$3 billion and in order to meet the demand, Biogen Idec opened a new manufacturing plant in North Carolina (NC, USA) to cope with demand. However, following the recent announcement, shares of Biogen Idec dropped by 43% and Elan by 70%. A spokesman for Biogen, Jose Juves, commented “It’s premature to gauge the impact on the company.” He continued, “There are a lot of unanswered questions.”

## Atacand<sup>®</sup> approved by the FDA for the treatment of heart failure

It has been announced by AstraZeneca that the angiotensin receptor blocker (ARB) Atacand<sup>®</sup> (candesartan cilexetil) has been approved by the US Food and Drug Administration (FDA) for the treatment of heart failure in New York Heart Association (NYHA) Class II–IV patients, with an ejection fraction less than or equal to 40%.

Approval was granted by the FDA following results from the Candesartan in Heart Failure Assessment of Reduction in Mortality and morbidity Alternative Trial (CHARM-Alternative) which demonstrated that in patients with congestive heart failure (CHF) who were

intolerant to angiotensin-converting (ACE) inhibitors but were receiving other standard heart failure therapy, the use of atacand resulted in a 23% relative risk reduction in cardiovascular death or heart failure hospitalization.

These results were then further supported with results from a second study, CHARM-Added, which examined NYHA Class II–IV heart failure patients with an ejection fraction less than or equal to 40%, in which subjects were mostly on submaximal doses of ACE inhibitors. In combination, it was determined that patients on atacand had a 15% lower risk of cardiovascular mortality.

## MediciNova announce the start of Phase II clinical trials of their anti-anxiety drug, MN-305

A Japanese-based speciality pharmaceutical company, MediciNova, have recently announced the commencement of a Phase II clinical trial to evaluate the use of MN-305, a type 1A serotonin receptor agonist, in generalized anxiety disorder, which is estimated by the National Institute of Mental Health to affect over 4 million adults in the USA alone.

MN-305 was licensed from Mitsubishi Pharma Corporation (Osaka, Japan) in 2004 in a deal which saw MediciNova take over exclusive worldwide rights, except for Japan, China, Taiwan, South Korea and other parts of Southeast Asia, to develop and

MediciNova has recently announced the start of Phase II clinical trials of an anti-anxiety drug MN-305, licensed from Mitsubishi Pharma Corp. (Osaka, Japan) in 2004, for the treatment of generalized anxiety disorder.

commercialize MN-305. Richard Gammans, PhD, Executive Vice President of Clinical Research at MediciNova commented on the announcement "This study signals the beginning of a very ambitious clinical development undertaking for MediciNova during 2005."

"We plan to enroll 400 patients at 15 sites in the USA in this study with MN-305, and before the end of this year we hope to initiate four

additional Phase II clinical studies with other compounds in the Company's portfolio, including potential new treatments for asthma, multiple sclerosis, interstitial cystitis, and premature labor" he continued.

MediciNova are currently involved in the development of several compounds in clinical testing, targeting a variety of prevalent medical conditions, including premature labor, cancer, asthma, multiple sclerosis and anxiety disorders.

## Death risk associated with smoking can be cut by ceasing smoking 30 days following a heart attack

The results of a study published in the February issue of the *American Journal of Medicine* have shown that people who quit smoking after a heart attack develop an immediate reduction in their risk of death. The study, which involved over 16,000 smokers recovering from heart attack reports that those who received counselling within the hospital in a bid to stop smoking significantly reduced their risk of death over the first 30 and 60 days, as well as over the first year following the heart attack.

It has been long known that quitting smoking after a heart attack reduces the risks for a second heart attack and death. However, the fact that this effect can be experienced over such a short space of time following cessation – within the first 30 days – is a new finding by the authors. The study, carried out by researchers at Birmingham VA Medical Center (AL, USA), supports previous reports which found evidence for a reduction in the risk of death over the first year following a heart attack. There is however, the risk that not every smoker who develops a heart attack will be motivated to cease smoking. However, Dr Thomas Houston, author of the report noted "In those patients unwilling to quit for good, [the strategy] would be to recommend, at a minimum, to maintain the in-hospital mandated smoking deprivation for a brief period after discharge."

## Enrolment begins for the ASSERT trial evaluating the relationship between atrial high rate episodes and stroke

St Jude Medical Inc. announced recently the commencement of enrolment of the first patients to take part in the ASymptomatic atrial fibrillation (AF) and Stroke Evaluation in pacemaker patients and the AF Reduction atrial pacing Trial (ASSERT) which is due to examine 2500 patients over a period of 3.5 years to determine whether pacemaker-detected Atrial High Rate Events (AHREs) can predict an increased risk of stroke in elderly hypertensive patients without previous AF. The trial will also examine the efficacy of St Jude Medical's own AF Suppression™ algorithm.

Stuart J Connolly, MD, Professor of Medicine at McMaster University (Ontario, Canada) and one of the principal investigators of the study commented on the announcement "We begin the ASSERT study knowing that pacemaker patients commonly experience atrial high rate

episodes, but the clinical significance remains largely unknown." He continued, "We also hope to discover whether AF suppression technology prevents or reduces symptomatic AF episodes, along with reducing the burden of AF."

Also commenting on the announcement, Eric S Fain, MD, Senior Vice President of Development and Clinical/Regulatory Affairs for St. Jude Medical's Cardiac Rhythm Management Division noted "The state-of-the-art diagnostics in the Identity ADx pacemaker detect and track episodes of atrial tachycardia and atrial fibrillation, generating 6-month trend graphs to help physicians better manage atrial high rate events." "When combined with the AF Suppression algorithm, we're optimistic that this approach may help optimize care of elderly hypertensive patients who have a standard bradycardia pacing indication" he concluded.