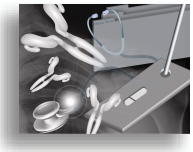


US FDA urge healthcare professionals to follow recommendations regarding mitoxantrone therapy and cardiac events

The US FDA is warning multiple sclerosis (MS) patients who are being treated with mitoxantrone about possible effects on cardiac function. The US FDA have been offering information and informing healthcare professional about additional recommendations for the monitoring of cardiac function in patients with MS.

Previous recommendations has changed labeling on the drug, recommending that MS patients suffering form left ventricular ejection fraction (LVEF) and congestive heart failure (CHF) should be evaluated by their doctor before starting treatment, and evaluated before each dose is administered.

These previous recommendations arose due to postmarketing case reports detailing that a decrease in LVEF was seen in patients with MS receiving cumulative doses lower than 100 mg/m^2. Since then the US FDA has also received information form another postmarkting study that highlights poor adherence to the previous recommendations.

This study used insurance claims data and medical record review to examine cardiac monitoring patterns in clinical practice. In this study it was noted that four patients developed CHF 4–17 months after completing therapy with mitoxantrone. These findings have encouraged the FDA to work with the manufacturers of the drug in educating healthcare providers to become more strict in adhering to the cardiac monitoring recommendations already in place for MS patients. This includes patients who have finished treatment with mitoxantrone, it is recommended that they received yearly quantitative LVEF evaluation to detect late-occurring cardiac toxicity.

Congestive heart failure or LVEF can not only occur during therapy with mitoxantrone, but also at an undefined amount of time subsequent to the therapy. This can be months to years and the risk will keep increasing with an increasing cumulative dose. Researchers have also established that the likelihood of a CHF event in patients taking mitoxantrone increases with cumulative dose regardless of the presence of other cardiac risk factors.

The guidelines recommend that MS patients with a baseline LVEF below the lower limit of normal should not be treated with mitoxantrone; patients should be assessed for cardiac signs and symptoms by using history, physical examination and ECG prior to each dose. Additional doses of mitoxantrone should not be administered to patients who have experienced a drop in LVEF to below normal limits or those who have demonstrated a clinically significant reduction in LVEF during mitoxantrone therapy. Further recommendations suggest that patients should not receive a cumulative mitoxantrone dose over 140 mg/m^2, and as previously mentioned, should undergo yearly quantitative LVEF evaluation after stopping mitoxantrone to monitor for late-occurring cardiotoxicity.

Source: US FDA www.fda.gov/cder/drug/InfoSheets/HCP/mitroxantroneHCP.htm

New trial to investigate if cannabis compounds can slow the progression of multiple sclerosis

of 492 patients with multiple sclerosis, which completes the recruitment stage of the trial.

The CUPID trial aims to evaluate the activity of THC, one of many compounds found in the in the cannabis plant and the main active ingredient, to demonstrate if the compound is able to slow the progression of MS.

The double blind randomized trial follows an earlier study (CAM study) linking THC and the disabling symptoms of MS. Where the previous trial only required patients to take the THC for 1 year, the current study will last for longer. The CUPID trial also aims to asses the effect of THC on progressive MS and not just the slowing of MS symptoms, compared with placebo.

The importance of this trial is reiterated by the fact that current treatments for the disease fall short. Treatments already in use target the immune system in the early stages of the disease or are able to only treat specific symptoms of the disease spectrum, such as muscle spasms or bladder disability. It is hoped that THC treatment may be successful in slowing the progression of MS.

It has taken 2 years to recruit the full cohort and the patients will take part for 3 to 3 and a half years. It is estimated that results could be available by early summer 2012.

The head of the study, Professor John Zajicek from the Peninsula Medical School commented, "We are delighted to have achieved the correct number of patient participants for this trial. Patients have been recruited from 27 sites across the UK. If we are able to prove beyond reasonable doubt the link between THC and the slowing down of progressive MS, we will be able to develop an effective therapy for the many thousands of MS sufferers around the world."

Laura Bell, a research communications officer for the MS Society, added, "People affected by MS are keen to know whether there's any truth in the suggestion that elements of the cannabis plant can help ease the symptoms and slow down progression of the condition."

"The MS Society is supportive of safe clinical trials investigating the medicinal properties of cannabis and it is great news that this trial is going ahead. We look forward to the results of this exciting study."

www.pms.ac.uk/cnrg/files/CUPID%20end%20of%20recruitment%20press%20release.pdf for more information: http://www.pms.ac.uk/cnrg/cupid.php?section=news

'Normal' MRI scans in patients with optic neuritis may demonstrate a lower likelihood of developing MS

25%. The results of a 15-year prospective follow-up suggest that prophylactic treatment can safely be withheld in the absence of other neurologic symptoms.

A total of 389 patients with acute unilateral optic neuritis between 1988 and 1991 were observed by members of the Optic Neuritis Study Group. The study used MRI scans to determine the number of lesions present in the white matter of the brain that are at least 3mm in diameter.

Overall the cumulative probability of developing MS after the onset of optic neuritis was 15% over the 15 years of study. The study also demonstrated that patients with at least one brain lesion had a higher chance of developing MS (72% of patients) compared with patients who presented no brain lesions (25%). Those patients who appeared MS free at 10-year follow up with brain lesions present at baseline had a 32% likelihood of developing MS over the next 5 years. Only one patient without evidence of lesion at baseline went on to develop MS after 10-year follow up.

The lead author of the study, Robin Gal explained, "Patients with abnormal brain MRI findings already have morphologic evidence of disseminated disease and could be considered to have MS at the time of the optic neuritis episode."

Risk factors that should be taken into account for MS include, female sex and retrobulbar neuritis, in patients without brain lesions. The study also notes that both sexes had a low risk when atypical features of the optic neuritis were present, namely, no light perception in the affected eye, absence of periocular pain, and ophthalmoscopic findings of severe optic disc swelling, peripapillary hemorrhages or retinal exudates.

The authors recommend additional ancillary testing to determine if prophylactic treatment for these patients is appropriate. The results are said to justify withholding treatment in some patients as they may never develop MS.

Arch. Neurol. *65, 727-732 (2008).*

Correlation found between restless legs syndrome and multiple sclerosis

and was found to be 14.6%. A total of 212 healthy control subjects were matched for age and sex and again the prevalence of RLS was calculated. The prevalence in the healthy control group was 2.8%, which indicates a significantly increased risk for patients with MS. This data confirms previous trials and links made between MS and RLS.

The lead author of the study, Giovanni Cossu, from the General Hospital S. Michele AOB G. Brotzu, Cagliari, Italy, explained, "RLS [is] a phenomenon frequently observed in MS. Future studies, already in progress and oriented to establish a more accurate correlation between RLS phenomena and neurophysiological and [magnetic resonance imaging] MRI data of MS patients, may allow [us] to definitively include RLS as an integral symptom of MS."

The symptoms of RLS can include; an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs. Sometimes the urge to move is present without the uncomfortable sensations. Sometimes the arms or other body parts are involved in addition to the legs; the urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity, such as lying down or sitting; the urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.

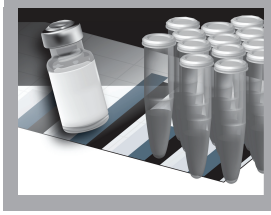
The urge to move or unpleasant sensations are worse in the evening or night than during the day or occur only in the evening or night. RLS can also be associated with sleep disturbances, daytime fatigue and involuntary muscle spasms.

The study required all the patients to complete a questionnaire according to criteria of the International Restless Legs Syndrome Study Group (IRLSSG). A total of 45% of the patients answered that they had symptoms of RLS. Patients who fulfilled 4 of the criteria for RLS were referred to neurologists to verify the diagnosis. Only 6 of the healthy volunteers were verified as having RLS.

Although interesting, the results may have selection bias as highlighted by the authors, "This is interesting, but the result needs to be confirmed before I say anything to my patients with MS," explained Serge Przedborski, professor of neurology and pathology at Columbia University, in New York, USA.

Source: 12th International Congress of Parkinson's Disease and Movement Disorders: Abstract LB6. Presented June 25, 2008.

Trial Watch



Drug: *Laquinimod and Avonex*
Indication: *Relapsing–remitting MS*
Patients: *Recruiting up to 1200 with RRMS*
Trial: *Phase III comparative efficacy trial*

Source: NEUROLOGY 2005;64:987-991Treatment with laquinimod reduces development of active MRI lesions in relapsing MS. C. Polman, MD, PhD, F. Barkhof, MD, PhD, M. Sandberg-Wollheim, MD et al.: www.tevaclinicaltrials.com

Drug Watch

'We know the reports of two new cases of PML will be of some concern to people who are taking the drug, however we would reassure people that the risk of developing these serious side effects remains very small. As with all treatments, the benefits must be weighed with the risks of side effects and these issues should be discussed fully between you and your doctor.' Insists Lee Dunster, Head of Research at the MS Society, based in London, UK.
Source: