

Patients Dropping Efalizumab Face Rebound

BY BRUCE JANCIN

MAUI, HAWAII — Some psoriasis patients have discontinued efalizumab in response to the recently reported third case of progressive multifocal leukoencephalopathy in users of the drug.

"I've had many patients who have decided to come off therapy. It's unfortunate because a lot of these patients have been on the drug for quite a long time and have been well served," Dr. Craig L. Leonardi said during a panel discussion at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation.

Dr. Leonardi of the department of dermatology at Saint Louis University and his fellow panelists agreed that all patients on efalizumab (Raptiva) need to be informed of their increased risk of progressive multifocal leukoencephalopathy (PML), a uniformly fatal brain disease. The panelists also addressed the daunting challenge in switching patients from efalizumab to another medication without triggering a serious rebound effect.

The latest case of PML, discovered in late January, involved a 47-year-old German who had been on efalizumab for 3.2 years. In contrast, the first two cases occurred in elderly patients, aged 70 and 73 years. They too had been on efalizumab for longer than 3 years, noted Dr. M. Shane Chapman of Dartmouth-Hitchcock Medical Center, Lebanon, N.H.

The first two cases led last October to a Food and Drug Administration-ordered black box warning.

PML is a demyelinating disease of CNS white matter caused by polyomavirus JC. Roughly 80% of all adults carry the virus, having been infected in childhood. In normal individuals, the virus remains latent throughout life and is present in the kidneys, lymphoid tissue, and sometimes the bone marrow.

The virus can be reactivated by immunosuppression. "HIV and organ transplant patients have a lot of issues with PML. So do immunocompromised cancer patients," Dr. Chapman noted.

A negative PCR test for polyomavirus JC DNA in the cerebrospinal fluid indicates a psoriasis patient should not be at increased risk for PML with efalizumab. But not many patients will get a lumbar puncture as a precondition for starting efalizumab when there are a range of effective alternative biologic therapies. An estimated 45,000-50,000 patients are now on efalizumab.

Dr. Leonardi said that because the strongest risk factor for PML in psoriasis patients appears to be duration of therapy, he's telling patients they can take efalizumab for 2 years or possibly 3, but no longer.

Rather than calling in his patients specifically to discuss PML, Dr. Chapman said that he is bringing it up when they come in for their routine quarterly visit. Of the seven patients thus far with whom he has had the discussion, all have opted to stay on the drug for now.

For patients who elect to stay on efalizumab, the emergence of PML-like symptoms—such as ataxia, dementia, visual field changes, limb weakness—require a prompt neurology referral.

Survival following a diagnosis of PML averages just 6 months.

Dr. John Y.M. Koo said he's heard from many physicians in the San Francisco Bay area who have run into tremendous difficulty with severe psoriasis re-

bound in attempting to transition patients from efalizumab to various other therapies. It has been a problem even in trying to switch to adalimumab (Humira), a particularly fast-onset biologic.

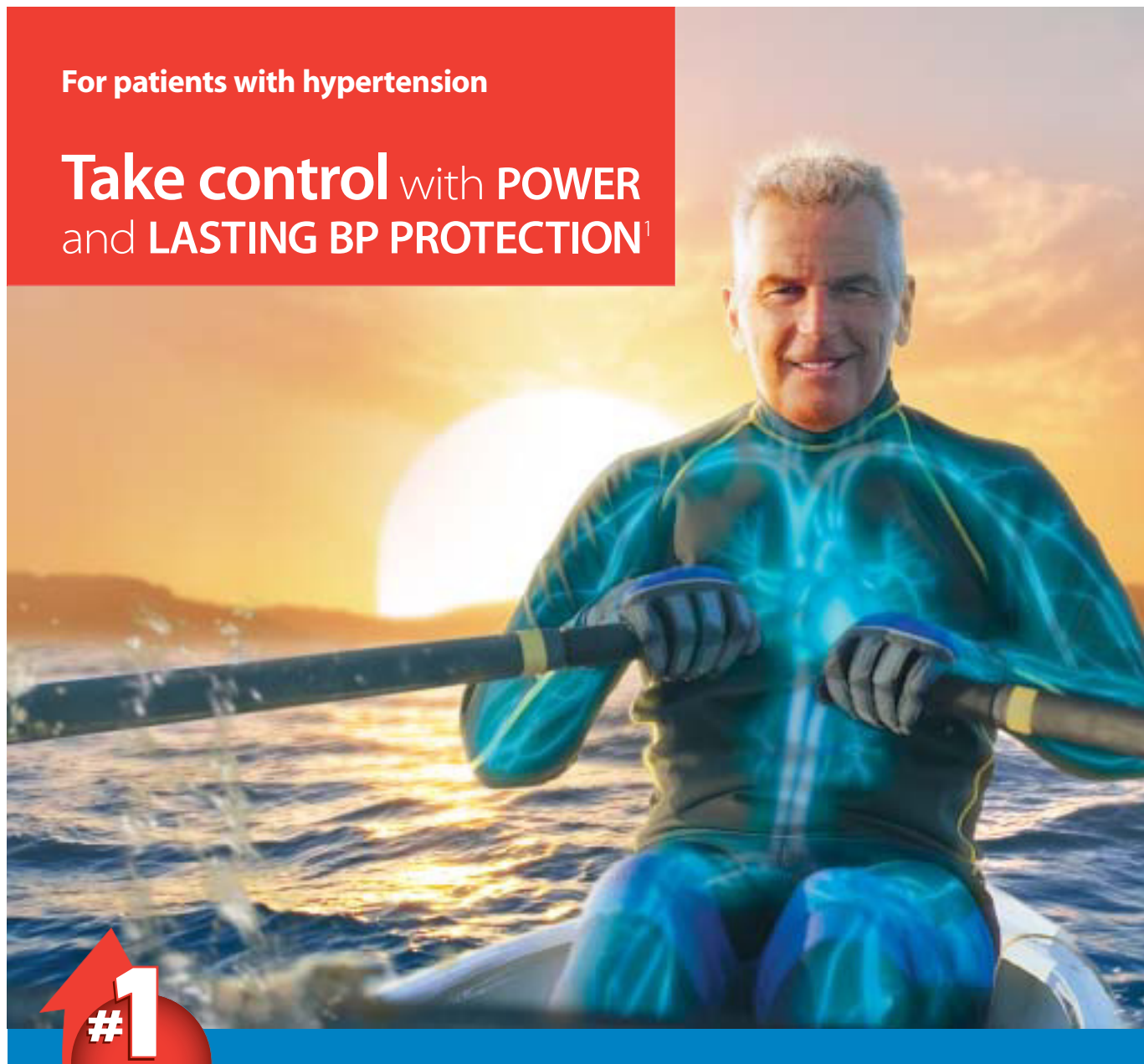
"In my personal experience, by far the most effective treatment to minimize rebound with [efalizumab] is cyclosporine," he said. "A non-wimpy dose—5 mg/kg—is the best choice. But if someone has been on [efalizumab] for

many years, even cyclosporine doesn't guarantee that the patient won't end up with a horrendous rebound," according to Dr. Koo, professor and vice chairman of the department of dermatology at University of California, San Francisco.

All three panelists disclosed that they have received research grants from and serve as consultants to and/or on the speakers bureaus for multiple manufacturers of biologic agents for psoriasis. ■

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*Source: IMS Health. Year-to-year comparison of NRxs and TRxs for MICARDIS across all specialties.

References: 1. Freytag F, Holwerda NJ, Karberg BE, Meinicke TW, Schumacher H. Long-term exposure to telmisartan as monotherapy or combination therapy: efficacy and safety. *Blood Press.* 2002;11:173-181. 2. IMS HEALTH, IMS National Prescription Audit™, January 2007 to December 2008.

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