Exotic European Therapies May Not Reach U.S.

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VIENNA — Americans attending the annual European Congress of Rheumatology are often impressed by the discussion of unfamiliar, even exotic therapies not available in the United States. The most intriguing of these are supported by encouraging clinical trials data. Yet many of these therapies will never reach the U.S. marketplace because they are the property of small companies that find the Food and Drug Administration approval process too fiscally daunting.

Here is a sample of novel therapies, currently unavailable in the United States, that were the subject of research presentations at the meeting, sponsored by the European League Against Rheumatism.

► Diacerein. This plant-derived arthralginaone derivative blocks the downstream proinflammatory effects associated with stimulation of the interleukin-1 receptors located on chondrocytes and inflammatory cells. It does not affect prostaglandin synthesis.

EULAR guidelines categorize diacerein as a symptomatic slow-acting drug for both knee and hip osteoarthritis (OA). It is widely used for this purpose in much of Europe, where it has been the subject of more than 20 randomized controlled trials. At the EULAR meeting, Worowit Louthrenoo, M.D., presented the first randomized double-blind controlled trial of diacerein in an Asian population.

The Thai study involved 161 OA patients randomized to 50 mg b.i.d. of diacerein or 10 mg b.i.d. of piroxicam for 16 weeks, with an additional 8 weeks of follow-up post discontinuation. The primary endpoint in the TRB Chemedica-sponsored trial was pain relief as reflected in WOMAC scores. At week 24, the diacerein group showed a mean improvement of 70% in WOMAC scores, compared with baseline—not significantly different from the 74% improvement in the piroxicam group. However, at week 29—which was 4 weeks following discontinuation—the mean improvement in the diacerein group remained at 67%, compared with 47% for piroxicam. Also at week 24, the diacerein group showed significantly less deterioration in the WOMAC scores, compared with baseline—in contrast, only 37% of controls rated their personal care capability as improved, while 11% said it had deteriorated.

Walking, sitting, standing, and lifting were areas where both groups showed significant improvement. At 3 months, with greater gains recorded in the MBST group, said Dr. Kullich of the Ludwig Boltzmann Institute for Rehabilitation of Internal Diseases in Salfeld, Austria.

► Topical diclofenac for knee OA. A metaanalysis of four randomized, controlled 4- to 12-week trials totaling 1,412 patients with symptomatic knee OA showed the topical agent’s efficacy was equal to oral diclofenac and significantly better than placebo for the endpoints of stiffness, physical function, and pain on walking, according to Michael Doherty, M.D., professor of rheumatology at the University of Nottingham (England).

The number of patients needed to be treated with topical diclofenac for one patient to achieve greater than 50% pain reduction was six. The chief advantage of topical as compared with oral diclofenac was that GI side effects were 41% less common with the topical agent and no more frequent than with placebo.

Topical diclofenac is contained in a dimethylsulfoxide vehicle. The main adverse event associated with the topical therapy was local skin reactions, mainly dry skin and itching, which were 3.6-fold more frequent than with placebo.

‘We have probably 50 papers of [pentosan polysulfate’s] effect in animals and in vitro. The rationale for its use in arthritis is solid as a rock.’

Pentosan polysulfate for OA. A non-commercially funded, randomized, double-blind, and placebo-controlled trial involving 114 patients with knee OA demonstrated that 4-week 5 mg/kg IV injections of pentosan polysulfate resulted in significantly greater improvements in pain at rest and walking, stiffness, and physical functioning involved in activities of daily living out to 24 weeks follow-up post treatment, reported Peter Ghosh, Ph.D., of the Institute of Bone and Joint Research at Royal North Shore Hospital, Sydney, Australia.

Pentosan polysulfate (approved in the United States only for interstitial cystitis) has been used in Europe for nearly 50 years as a postsurgery thromboprophylaxis agent. It promotes fibrinolysis and has antiinflammatory activity. Dr. Ghosh saw its potential as a chondroprotective agent. “We have probably 50 papers of its effect in animals and in vitro. The rationale for its use in arthritis is solid as a rock,” he told this newspaper.

“They’re looking for partners in Japan,” he said. In Europe, Canada, and Australia, pentosan polysulfate is the leading drug for the prevention of progressive OA in dogs and horses. “In fact, we’ve been able to move much faster in the veterinary field than we have in humans,” Dr. Ghosh added.

► Emu oil. Daily oral or topical use of oil rendered from the emu, a large flightless bird, resulted in a 2.34-fold greater reduction in pain than a canola oil placebo in a randomized double-blind trial involving 101 patients with OA hand pain. The observed treatment effect was medium to large, and it was apparent from week 4 onward in the 8-week trial, reported Melanie Cameron, Ph.D., of Victoria University, Melbourne, Australia.

As early as 1860, naturalists reported that Australian aborigines and early Anglo settlers used emu oil to treat wounds and relieve musculoskeletal pain, she added.

DATA WATCH

Adulst Diagnosed With Arthritis

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<th>Men</th>
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Notes: Definition of arthritis includes rheumatoid arthritis, gout, lupus, and fibromyalgia. Percentages are age adjusted.
Source: 2002 data, Centers for Disease Control and Prevention

*Emu oil is contained in a dimethylsulfoxide vehicle. The main adverse event associated with the topical therapy was local skin reactions, mainly dry skin and itching, which were 3.6-fold more frequent than with placebo. The topical diclofenac solution, called Pennsaid, is approved for treatment of knee OA in Canada and seven European countries. A spokesman for Dimension Health Care Ltd., of Markham, Canada, told this newspaper the company hopes to gain U.S. marketing approval for Pennsaid in early 2007. The FDA has asked for two additional long-term safety studies, both of which are nearly completed.