OA Treatment Options Remain Disappointing

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EXPERT OPINION FROM A SEMINAR ON RHEUMATOLOGY

SANTA MONICA, CALIF. – Advances in biomarker research and imaging may eventually make earlier diagnosis of osteoarthritis a reality. Unfortunately, such technologies remain prohibitively expensive for routine use.

And there's another problem: nothing to offer patients by way of an effective early therapy for knee OA.

"So at the present time, when such treatments are not available, the benefit of early diagnosis is really to identify individuals at an early stage when an investigational therapy might be of use, and such individuals can be enrolled in clinical trials," Dr. Amanda E. Nelson noted.

"In the absence of specific disease-modifying treatments, the extra expense of an MRI for diagnosis is not warranted in daily practice at this time," advised Dr. Nelson of the University of North Carolina at Chapel Hill.

What has stymied the development of effective drugs for altering the course of knee OA?

The progress is slow for a few reasons, according to Dr. Nelson. Among them are lack of sensitive, cost-effective early diagnostics to best identify candidates for treatment, medicine's as-yet poor understanding of the causes of progression in OA, and its inability to identify which patients will progress to knee OA. This disease has a very long natural history: An injury in one's 20s may not lead to OA until after age 40 years. These things make trials difficult to conduct and to fund.

Current treatment is directed toward late-stage disease, and by and large these therapies focus on easing pain, not on modifying the course of the disease, Dr. Nelson said at a meeting sponsored by Skin Disease Education Foundation and the University of Louisville.

Corticosteroids have no effect on function, but they do relieve pain for 1-3 weeks. The administration of intra-articular hyaluronans eases pain and preserves or improves function for 5-13 weeks, judging from a systematic review (Cochrane Database Syst. Rev. 2006 [doi:10.1002/14651858.CD005328.pub2]).

On the investigational front, at least one phase III trial of the cyclooxygenase/lipoxygenase (COX/LOX) agent licofelone has been completed.

This investigational agent is an anti-inflammatory agent without the adverse effects of COX inhibition. Findings from a trial of 355 patients with knee OA showed that licofelone given in a 200-mg dose twice daily preserved the volume of knee cartilage as well as did naproxen given in a 500-mg dose twice daily, with less GI toxicity (Ann. Rheum. Dis. 2009;68:938-47).

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A video interview with Dr. Amanda E. Nelson is available at http://www.rheumatologynews.com/.

Another category of symptomatic treatment that has gone through a phase III trial is COX-inhibiting nitric oxide donators (CINODs). These agents have anti-inflammatory properties similar to those of NSAIDs, but – unlike NSAIDs – CINODS protect the gastric mucosa and act as both a vasodilator and an inhibitor of platelet aggregation, thereby preventing vascular damage (J. Pharm. Pharm. Sci. 2008; Sep 20;11:81s-110s).

Findings from research using intra-articular injection of the cytokine inhibitor IL-1Ra in humans has been disappointing. The drug did not ease pain at 12 weeks but did provide more short-term pain relief.

Some investigators were keeping a close eye on trials of tanezumab, a monoclonal antibody against nerve growth factor that showed early efficacy in OA pain.

Although Pfizer Inc. has halted the trials because of increased progression and higher numbers of joint replacement, it is unclear whether that was related to the drug or to increased activity by the study subjects who experienced pain relief.

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