MIV-711 not associated with pain reduction, but may reduce disease progression in osteoarthritis

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MIV-711, a novel selective cathepsin K inhibitor, was not more effective than placebo for reducing pain related to knee osteoarthritis. However, MIV-711 significantly reduced bone and cartilage progression. Findings from a randomized, placebo-controlled study are published in *Annals of Internal Medicine*.

Osteoarthritis of the knee is a painful, disabling condition affecting more than 14 million people in the United States and hundreds of millions worldwide. The pain of knee OA arises from a series of pathologic processes involving articular cartilage, subchondral bone, synovium, meniscus, and other joint structures, ultimately leading to joint failure and pain-related functional limitations. Researchers sought to test the hypothesis that cathepsin K inhibitor could alleviate osteoarthritis symptoms by reducing degeneration of bone and cartilage.

In a multicenter study led by the University of Leeds, 244 patients with primary knee osteoarthritis were randomly assigned to receive either 100 or 200 mg daily of MIV-711 or matched placebo for 26 weeks to evaluate the efficacy, safety, and tolerability of MIV-711. The primary endpoint of the study was change in pain score, but changes in disease progression were also assessed using quantitative MRI outcomes. The researchers found that compared with placebo, MIV-711 was associated with less bone remodeling, less cartilage volume loss, and lower levels of bone resorption and collagen loss. However, it showed no beneficial

effects on osteoarthritic knee pain. According to the authors, further evaluation is needed to confirm the structural benefits of MIV-711 and to determine whether these translate to more tangible benefits on disease symptoms.

The authors of an accompanying editorial from Brigham and Women's Hospital say that while the work is promising, they agree that more research is needed to determine the longer term benefits of MIV-711. They point out the study findings do not contradict that there is a foundational link between modification of structure and improvement in osteoarthritis pain, but rather clarify that changes in structure do not beget immediate changes in symptoms.

More information: *Annals of Internal Medicine* (2019). Abstract: annals.org/aim/article/doi/10.7326/M19-0675
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