Sprifermin moves FORWARD with sustained effects in OA

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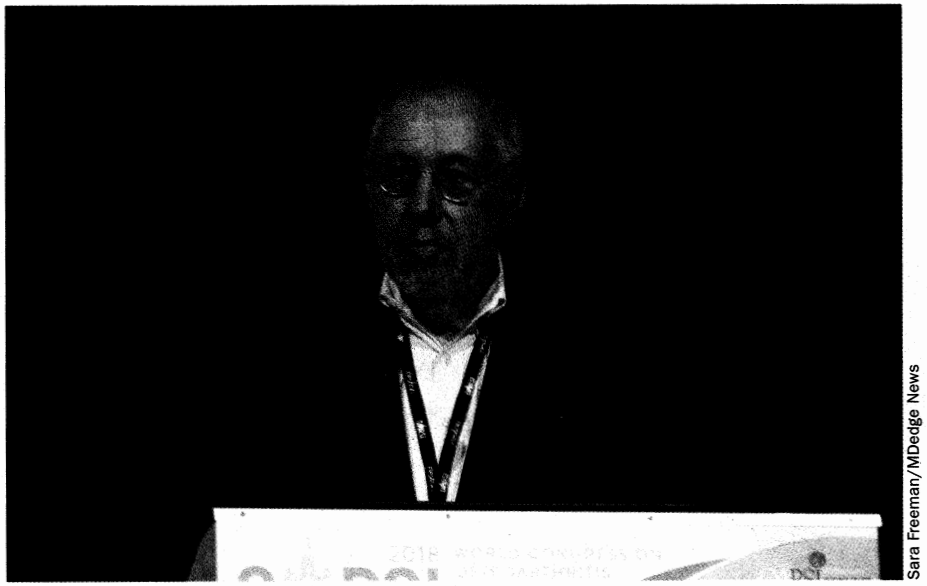
LIVERPOOL, ENGLAND – At 3 years of follow-up, the cartilage-building effects of sprifermin appear to be sustained, according to further data to be released from the phase 2 FORWARD trial.

The difference from placebo in mean cartilage thickness at the tibiofemoral joint (TFJ) at 3 years was 0.05 mm for a 100-mcg dose of sprifermin given every 6 months (*P* less than .0001), 0.02 mm for a 100-mcg dose given every 12 months (*P* = .193), 0.01 mm for a 50-mcg dose given every 6 months (*P* = .530), and –0.02 mm for a 50-mcg dose given every 12 months (*P* = .160).

"These data, 18 months after the last active injection, extend the results which we previously presented and assessed," study investigator Marc Hochberg, MD, said at the World Congress on Osteoarthritis.

The prior 2-year findings, which were reported at the annual meeting of the American College of Rheumatology in November 2017, showed statistically significant dose-dependent structural modification in TFJ cartilage. Furthermore, the increase in cartilage thickness was seen in both medial and lateral compartments of the TFJ, and in the central medial subregion of the TFJ.

Sprifermin is one of several drugs currently being investigated as a potential disease-modifying osteoarthritis drug, none of which are currently licensed for use. It is a novel human recombinant version of fibroblast growth factor 18 that has been shown to increase chondrocyte proliferation that results in overall extracellular matrix production and subsequent hyaline-line cartilage formation.



Sara Freeman/MDedge News

Dr. Marc Hochberg: "The difference in cartilage thickness observed in year 2 with sprifermin at the highest dose [100 mcg every 6 months] versus placebo persisted through year 3."

The study comprised 549 patients with symptomatic radiographic primary femorotibial knee OA who were aged 40-85 years. For inclusion, patients had to have Kellgren-Lawrence grade 2 or 3, with a medial minimum joint space width of 2.5 mm or more. In addition, patients had to have a history of OA pain for at least 6 months and either symptoms requiring pain medication or a pain score of 4-9 on the 10-point question 1 of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

Dr. Hochberg, professor of medicine, epidemiology, and public health and head of the division of rheumatology and clinical immunology at the University of Maryland, Baltimore, noted that the current analysis at 3 years' follow-up had been prespecified and that the plan was to continue follow-up out to 5 years.

There was a statistically significant treatment effect and dose-response effect seen in TFJ cartilage thickness.

"Although cartilage thickness declined in all treatment groups between years 2 and 3, the difference in cartilage thickness observed in year 2 with sprifermin at the highest dose [100 mcg every 6 months] versus placebo persisted through year 3," Dr. Hochberg said at the congress, which was sponsored by the Osteoarthritis Research Society International.

As for secondary endpoints of thickness in the medial and lateral tibiofemoral cartilage, "there are significant differences between the higher-dose sprifermin group and the placebo group," he said.

"Based on imaging, sprifermin appears to be effective at modifying structural changes in articular cartilage in a dose-dependent manner in patients with knee osteoarthritis, with an acceptable safety profile."

Dr. Hochberg added that there was "marked symptomatic improvement" as shown by changes in WOMAC scores in all treatment groups including placebo. The improvement in total WOMAC scores by approximately 50% in all treatment groups by the second year was continued to the third.

Adverse effects occurred with a similar frequency in the active-treatment groups and the placebo group. They were also of a similar nature. The most commonly reported side effects involved the musculoskeletal system or were connective tissue disorders (e.g., arthralgia). Importantly, there was no difference in the frequency, severity, or nature of serious adverse events, treatment-related adverse events, or discontinuation due to adverse events with active versus placebo therapy, Dr. Hochberg said.

Merck KGaA and EMD Serono Research Institute funded the study. Dr. Hochberg has received consulting fees from EMD Serono and other companies developing treatments for OA.

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SOURCE: Hochberg M et al. Osteoarthritis Cartilage. 2018:26(1):S26-7. Abstract 32.