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PHARMA DESK

Sprifermin Is Under Investigation as A Disease-Modifying Osteoarthritis Drug

May this New Year 2020 be the most amazing and jubilant year of your life!

Osteoarthritis is the most common form of arthritis but unfortunately has got the least number of effective disease-modifying drugs. There is immense scope for development of newer molecules. Sprifermin is a recombinant form of human fibroblast growth factor 18 (FGF18) which is under development for the treatment of osteoarthritis.

Sprifermin is a potent agonist of the FGF receptor 2 and FGF receptor 3. FORWARD (FGF-18 Osteoarthritis Randomized Trial with Administration of Repeated Doses) was a five-year, dose-finding, multicenter randomized clinical trial1. Participants aged 40 to 85 years with symptomatic, radiographic knee osteoarthritis and Kellgren-Lawrence grade 2 or 3 were enrolled and randomized to 1 of 5 groups: intra-articular injections of 100 μg sprifermin were administered Q6 monthly (n=110) or Q12 monthly (n=110), 30 μg sprifermin Q6 monthly (n=111) or Q12 monthly (n=110), or placebo Q6 monthly (n=108). Each treatment consisted of weekly injections over three weeks.

The primary end point was change in total femorotibial joint cartilage thickness measured by quantitative magnetic resonance imaging at two years. The secondary end points (of 15 total) included two-year change from baseline in total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores. The minimal clinically important difference (MCID) is unknown for the primary outcome; for total WOMAC score in patients with hip and knee osteoarthritis, the absolute MCID is 7 U (95% CI, 4 to 10 U) and the percentage MCID is 14% (95% CI, 9% to 18%).

Among 549 participants, median age was 65.0 years; 69% were females, 474 (86.3%) completed two-year follow-up. Compared with placebo, the changes from baseline to two years in total femorotibial joint cartilage thickness were 0.05 mm (95% CI, 0.03 to 0.07 mm) for 100 μg sprifermin Q6 monthly; 0.04 mm (95% CI, 0.02 to 0.06 mm) for 100 μg sprifermin Q12 monthly; 0.02 mm (95% CI, -0.01 to 0.04 mm) for 30 μg sprifermin Q6 monthly; and 0.01 mm (95% CI, -0.01 to 0.03 mm) for 30 μg sprifermin Q12 monthly. Compared with placebo, there were no statistically significant differences in mean absolute change from baseline in total WOMAC scores for any of the sprifermin groups. The most frequently reported treatment-emergent adverse event was arthralgia (placebo: 43.0%; 100 μg sprifermin Q6 monthly: 41.3%; 100 μg Q12 monthly: 45.0%; 30 μg sprifermin Q6 monthly 36.0%; and 30 μg sprifermin Q12 monthly 44.0%).

The authors concluded that among participants with symptomatic radiographic knee osteoarthritis, the intra-articular administration of 100 μg sprifermin Q6 or 12 monthly vs. placebo resulted in an improvement in total femorotibial joint cartilage thickness after two years that was statistically significant, but of uncertain clinical importance. Durability of response also was uncertain.

The three-year results of this study2 are consistent with the two-year results: although cartilage thickness declined in all treatment groups between Year 2 and 3, the difference at Year 2 with sprifermin 100 μg vs. PBO was maintained up to Year 3. So, this new molecule is slightly encouraging with its effects on the disease process, but it seems we still have a long way to go on this path in developing molecules, which can modify the disease as well as improve patient's clinical symptoms and signs.

References:

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