A One-Year Placebo-Controlled Study in Non-Radiographic Axial Spondyloarthritis

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Video Abstract

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Abstract

Results from the C-axSpAnd trial, in which patients with active non-radiographic axial spondyloarthritis and inadequate response to at least two NSAIDs showed significant improvements in signs and symptoms after one year of certolizumab pegol treatment, have highlighted the limitations of non-biologic background medication alone in these patients. Axial spondyloarthritis, or axSpA, is a chronic inflammatory disease predominantly affecting the axial skeleton. The main symptoms include back pain, morning stiffness and fatigue. Anti-TNF biologics such as certolizumab pegol are widely approved for treatment of radiographic axSpA, also known as ankylosing spondylitis, in which patients have definitive structural damage to the sacroiliac joints on x-ray. However, they are not approved in some countries for non-radiographic axSpA; axSpA without definitive structural damage on x-ray. Part of the reason for this is the belief that non-radiographic axSpA is a milder form of axSpA that may resolve spontaneously. The C-axSpAnd trial aimed to evaluate the efficaciousness of certolizumab pegol in addition to non-biologic treatment in active non-radiographic axSpA over 52 weeks of treatment, and at the same time investigate the clinical impact of continuing on non-biologic medication alone. To do this, 317 patients with active disease who had failed to respond to treatment with at least two non-biologic NSAID medications were enrolled into the study. Active disease was indicated by the presence of objective signs of inflammation (inflammation of the sacroiliac joint on MRI and/or elevated CRP levels). Patients were randomized to either certolizumab pegol or placebo, which they received on top of their current non-biologic background medication. The trial was conducted over a relatively long period of one year to investigate longterm variations in disease symptoms. The primary outcome was major improvement in ASDAS, a validated scale for assessing disease activity in axSpA patients. After a year, nearly half of all certolizumab pegol-treated patients achieved a major improvement in ASDAS, in contrast to only 7% of placebo-treated patients continuing on non-biologic treatment. There were similar improvements with certolizumab pegol across other disease activity measures, including inflammation on MRI, assessed during the study. Furthermore, 61% of patients assigned to placebo switched to open-label certolizumab pegol during the trial period, indicating the lack of effectiveness of their non-biologic treatment and persistence of symptoms. Conversely, only 13% of certolizumab pegol-treated patients switched to open-label treatment. In summary, results from this trial suggest that in patients with active disease and initial failure to respond to non-biologic treatment, continuation of non-biologic medication alone is inadequate for controlling the signs and symptoms of nonradiographic axSpA. The length of the study indicates that spontaneous remission of non-radiographic axSpA is unlikely.