Long term IL-17 A Inhibition by Secukinumab leads to reduced spinal inflammation and unchanged fatty lesions in Patients with Ankylosing Spondylitis

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Background: Secukinumab (fully human IgG1k anti-IL17A monoclonal antibody) significantly improved clinical signs and symptoms of active ankylosing spondylitis (AS) patients enrolled in a recent proof-of-concept (PoC) study. Magnetic resonance images (MRI) of these patients (pts) showed reduction of spinal inflammation at week (W) 6 and W28 after initiation of treatment.

Objectives: To evaluate a subgroup of pts (N=13) in the open label extension study, who had MRI assessments at baseline (BL), W28 and W94.

Methods: In the 28W PoC study, 27/30 pts had sequential MRI studies, 22 had received secukinumab (2x10 mg/kg intravenously; 3 Ws apart), and 5 pts had been randomised to placebo. 20 patients entered the open-label extension study with lower maintenance dose (14x3 mg/kg ;4 Ws apart), 13 having MRI data at W94. Of these 13, ten were treated with secukinumab and 3 with placebo in the core study. MRIs were rescoring for this study. ASspiMRI-a scores and the occurrence of vertebral edges (VE) inflammatory and fatty lesions were evaluated by an independent blinded reader.

Results: All 13 pts completed this exploratory MRI substudy. In pts receiving 2x10 mg/kg secukinumab followed by 14x3mg/kg (n=10) secukinumab, spinal inflammation was reduced compared to BL at W28 – similar to the results of the core study– and this reduction was sustained up to W94 (Fig 1). Also in 3 pts who had initially received placebo switching to secukinumab at W28, MRI inflammation at W94 was reduced. Of the 920 VEs evaluated, the proportion of VEs with inflammatory lesions was reduced from 9.9% (n=91) at BL to 3.7% (n=34) at W28 and 3.6% (n=33) at W94. In contrast, the proportion of fatty lesions at BL (13.5%, n=124) remained largely unchanged at W28 (14.3%, n=132) and W94 (13.7%, n=126). Secukinumab reduced MRI inflammation at W28 and W94.

Conclusions: MRI analysis suggests that the IL-17 inhibitor secukinumab may reduce spinal inflammation and this effect may be sustained for up to 2 years. Unlike reports with TNF-blockers, secukinumab appeared to leave the proportion of fatty lesions unchanged. The potential impact of these preliminary findings on radiographic progression under secukinumab therapy will be studied in larger trials.