Ixekizumab for patients with non-radiographic axial spondyloarthritis (COAST-X): a randomised, placebo-controlled trial

*Atul Deodhar, Désirée van der Heijde, Lianne S Gensler, Tae-Hwan Kim, Walter P Maksymowych, Mikkel Østergaard, Denis Poddubnyy, Helena Marzo-Ortega, Louis Bessette, Tetsuya Tomita, Ann Leung, Maja Hojnik, Gaia Gallo, Xiaoqi Li, David Adams, Hilde Carlier, Joachim Sieper on behalf of the COAST-X Study Group**

RobotReviewer report

Risk of bias table

trial	design	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
Deodhar A, 2019	RCT	+	+	+	+

Trial summaries

n	Participants	Interventions	Outcomes	punchline	finding
?? ?	patients with non-radiographic axial spondyloarthritis (COAST-X	Ixekizumab, placebo, COAST-X, ixekizumab		The most common treatment-emergent adverse events in the ixekizumab groups were nasopharyngitis and injection site reaction.	‚Äï no diff

Characteristics of studies

Deodhar A, 2019

Population	1. 24 Other key inclusion criteria were active disease at screening and baseline (defined as a Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] 25 score of ‚â•4 and total back pain score of ‚â•4 on a 0-10 scale) and either an inadequate response to two or more NSAIDs or a history of intolerance of NSAIDs. 2. Eligible patients were adults (aged ‚â•18 years) with a physician-established axial Research in context Evidence before this study We searched PubMed for research articles published in English between database inception and Sept 4, 2019, using the terms: "non-radiographic axial spondyloarthritis" AND "biologic". 3. 26 Exclusion criteria included previous treatment with bDMARDs.
Intervention	1. Patients were randomly assigned (1:1:1) to receive sub cutaneous injections of 80 mg ixekizumab Q2W, 80 mg ixekizumab Q4W, or matching placebo Q2W. Patients assigned to ixekizumab treatment regimens were randomly assigned (1:1) to receive a starting dose of either 80 mg ixekizumab or 160 mg ixekizumab (two 80 mg injections) at week 0 to evaluate the effect of starting dose on the ASAS40 results at weeks 16 and 52. 2. At week 0, patients were randomly assigned to receive placebo (placebo group), 80

	mg subcutaneous ixekizumab every 4 weeks (Q4W; ixekizumab Q4W group) or ixekizumab every 2 weeks (Q2W; ixekizumab Q2W group; appendix p 32). 3. Added value of this study The COAST-X study met the primary endpoints, showing superiority of ixekizumab over placebo for achievement of Assessment of SpondyloArthritis international Society-40 response at weeks 16 and 52 in patients with non-radiographic axial spondyloarthritis and objective signs of inflammation.
Outcomes	1. An ASAS40 response is defined as an improvement of 40% or more and an absolute improvement from baseline of 2 or more units (range 0-10) in at least three of the fol lowing four domains: patient global score (patient global assessment of disease activity), spinal pain score (spinal pain numerical rating score), function score (Bath Ankylosing Spondylitis Functional Index [BASFI]), 25 and inflam mation score (mean of BASDAI question 5 [intensity of morning stiffness] and question 6 [duration of morning stiffness]), without any worsening in the one remaining domain. 2. Added value of this study The COAST-X study met the primary endpoints, showing superiority of ixekizumab over placebo for achievement of Assessment of SpondyloArthritis international Society-40 response at weeks 16 and 52 in patients with non-radiographic axial spondyloarthritis and objective signs of inflammation. 3. 24 Other key inclusion criteria were active disease at screening and baseline (defined as a Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] 25 score of ,â•4 and total back pain score of ,â•4 on a 0-10 scale) and either an inadequate response to two or more NSAIDs or a history of intolerance of NSAIDs.

Bias	Judgement	Support for judgement
Random sequence generation	low	1. Randomisation and masking Patients were allocated to treatment by a computer generated random sequence, with stratification by country and MRI and CRP status at screening (MRI-positive and CRP-positive, MRI-positive and CRP-negative, or MRI- negative and CRP-positive). 2. At week 0, patients were randomly assigned to receive placebo (placebo group), 80 mg subcutaneous ixekizumab every 4 weeks (Q4W; ixekizumab Q4W group) or ixekizumab every 2 weeks (Q2W; ixekizumab Q2W group; appendix p 32). 3. Patients were randomly assigned (1:1:1) to receive sub cutaneous injections of 80 mg ixekizumab Q2W, 80 mg ixekizumab Q4W, or matching placebo Q2W. Patients assigned to ixekizumab treatment regimens were randomly assigned (1:1) to receive a starting dose of either 80 mg ixekizumab or 160 mg ixekizumab (two 80 mg injections) at week 0 to evaluate the effect of starting dose on the ASAS40 results at weeks 16 and 52.
Allocation concealment	low	1. Patients, investigators, and all other personnel involved in the conduct of the study were unaware of individual treatment assignments during the 52-week blinded period. 2. For patients who switched to open-label treatment with ixekizumab Q2W, the study site personnel, patients, and study team remained masked to the initial ran- domisation. 3. Randomisation and masking Patients were allocated to treatment by a computer generated random sequence, with stratification by country and MRI and CRP status at screening (MRI-positive and CRP-positive, MRI-positive and CRP-negative, or MRI- negative and CRP-positive).
Blinding of participants and personnel	low	1. Patients, investigators, and all other personnel involved in the conduct of the study were unaware of individual treatment assignments during the 52-week blinded period. 2. To maintain masking, all patients received two injections at week 0

		and one injection every 2 weeks during the remainder of the masked treatment dosing period. 3. For patients who switched to open-label treatment with ixekizumab Q2W, the study site personnel, patients, and study team remained masked to the initial ran- domisation.
Blinding of outcome assessment	low	1. Patients, investigators, and all other personnel involved in the conduct of the study were unaware of individual treatment assignments during the 52-week blinded period. 2. To maintain masking, all patients received two injections at week 0 and one injection every 2 weeks during the remainder of the masked treatment dosing period. 3. For patients who switched to open-label treatment with ixekizumab Q2W, the study site personnel, patients, and study team remained masked to the initial ran- domisation.

References

1. Deodhar A et al. Ixekizumab for patients with non-radiographic axial spondyloarthritis (COAST-X): a randomised, placebo-controlled trial Ann. Rheum. Dis. 2019. 10217(6); 53-64 PMID: 22772328