RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Early clinical response associates with long-term outcomes with ixekizumab in radiographic axial spondyloarthritis

Sofia Ramiro ,[1,2] Cédric Lukas,[3] Louis Bessette,[4] Pendleton Wickersham,[5] Tommaso Panni,[6] Rebecca Bolce,[6] Soyi Liu-Leage,[6] Boris Janos,[6] Michael J Nissen ,[7] James Cheng-Chung Wei [8,9]

To cite: Ramiro S, Lukas C, Bessette L, *et al*. Early clinical response associates with long-term outcomes with ixekizumab in radiographic axial spondyloarthritis. *RMD Open* 2024;**10**:e004429. doi:10.1136/rmdopen-2024-004429

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/rmdopen-2024-004429).

Part of this data has been accepted and published as an abstract by the American College of Rheumatology, and it has been presented at the ACR Convergence on 12 November 2023. Reference: Ramiro S, Lukas C, Bessette L, et al. 0520 How Do Early Disease Activity and Early Clinical Response Associate with Long-Term Outcomes with Ixekizumab in Radiographic Axial Spondyloarthritis? Arthritis Rheumatol. 2023; 75(9). Available at:https://acrabstracts.org/abstract/how-do-early-disease-activity-and-early-clinical-response-associate-with-long-term-outcomes-with-ixekizumab-in-radiographic-axial-spondyloarthritis/.

Received 15 April 2024
Accepted 3 July 2024

For numbered affiliations see end of article.

Correspondence to
Dr Sofia Ramiro;
sofiaramiro@gmail.com

ABSTRACT

Background The Assessment of SpondyloArthritis international Society-European Alliance of Associations for Rheumatology recommendations for axial spondyloarthritis (axSpA) management include patient assessment for biological disease-modifying antirheumatic drug (bDMARD) treatment response after at least 12 weeks of treatment. The current treat-to-target strategy for axSpA is to achieve inactive disease (ID; Axial Spondyloarthritis Disease Activity Score (ASDAS) <1.3) or at least low disease activity (LDA; 1.3≤ASDAS<2.1).

To investigate the association between treatment response at week 12 and/or week 24 and attainment of the ASDAS<2.1 treat-to-target recommendation at week 52 in bDMARD-naïve patients with radiographic (r-)axSpA treated with ixekizumab (IXE).

Methods This post hoc analysis included patients randomly assigned to IXE 80 mg every 4 weeks from COAST-V (NCT02696785), a phase 3 trial in bDMARD-naïve patients with r-axSpA. The proportion of patients who achieved ASDAS<2.1 at week 52 was measured among those who attained or not clinically important improvement (CII, ΔASDAS≥1.1) response, and among those with ID, LDA and high or very high disease activity at week 12 and/or week 24. Non-response was assumed for missing data.

Results Amongst 81 patients, 47 (58.0%) achieved ASDAS CII at week 12, with 70.2% (n=33) achieving ASDAS<2.1 at week 52. At week 24, 52 (64.2%) patients achieved ASDAS CII, with 71.2% (n=37) achieving ASDAS<2.1 at week 52. Of the 24 patients who did not achieve ASDAS CII at either week 12 or week 24, 5 (20.8%) achieved ASDAS<2.1 at week 52.

Conclusion This analysis reinforces the current recommendation that continuing treatment in those achieving ASDAS CII at week 12 and/or week 24 increases the likelihood of obtaining ID/LDA at week 52.

Trial registration number NCT02696785.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The association of treatment response at week 12 and achievement of long-term response in patients with axial spondyloarthritis (axSpA) has been investigated for tumour necrosis factor inhibitors in two studies, but it has not been confirmed in other studies, neither has it been evaluated for other drug classes, such as interleukin-17A inhibitors.

WHAT THIS STUDY ADDS

⇒ Over 70% of patients who achieved Axial Spondyloarthritis Disease Activity Score (ASDAS) clinically important improvement (CII) at week 12 and/or week 24 subsequently achieved ASDAS<2.1 at week 52, while 20.8% of the patients who did not achieve ASDAS CII at either week 12 or week 24 then achieved ASDAS<2.1 at week 52.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This analysis informs clinicians on the relevance of continuing treatment in biological disease-modifying antirheumatic drug-naïve patients with radiographic axSpA that achieve ASDAS CII at week 12 and/or week 24, thus increasing the likelihood of attaining inactive disease or low disease activity at week 52.

⇒ At the same time, identifying patients unlikely to achieve the treatment target may help clinicians avoid unnecessary exposure of patients to treatment and consequently potentially lead to increased cost-effectiveness.

INTRODUCTION

Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic and musculoskeletal disease predominately affecting the axial skeleton (sacroiliac joints (SIJ) and spine).[1] AxSpA is also characterised by variable manifestations including peripheral arthritis, enthesitis, dactylitis and extramusculoskeletal manifestations including anterior uveitis, psoriasis and inflammatory bowel disease.[1] Disease progression can lead to new bone formation in the form of syndesmophytes and joint ankylosis, primarily in the axial skeleton.[1] The disease is known to affect up to 0.1%–1.4% of the adult population worldwide, with some heterogeneity across prevalence studies.[2 3] Patients are classified into

two subsets according to the presence of radiographical structural damage of the SIJ (radiographic (r)-axSpA, also known as ankylosing spondylitis) or its absence (non-radiographic (nr)-axSpA).[4–6] Nonetheless, these subsets have a similar clinical presentation and burden of illness, thus reinforcing that they are part of the same disease.[4–6]

As per the 2022 Assessment of SpondyloArthritis international Society (ASAS)-European Alliance of Associations for Rheumatology (EULAR) recommendations, treatment of axSpA should be tailored to the patient's disease presentation and should include physical exercise, smoking cessation and physiotherapy. For symptomatic patients, non-steroidal anti-inflammatory drugs (NSAIDs) represent first-line pharmacology treatment and, for patients with persistently high disease activity (HDA), a tumour necrosis factor inhibitor (TNFi), an interleukin (IL)-17A inhibitor (IL-17i) or a Janus kinase inhibitor should be considered while TNFi and IL-17i are currently considered as first-line options.[7]

Furthermore, the ASAS-EULAR recommendations include assessing a patient's response to biological disease-modifying antirheumatic drug (bDMARD) and targeted synthetic disease-modifying antirheumatic drugs after at least 12 weeks of treatment. If a clinically important improvement (CII) in Axial Spondyloarthritis Disease Activity Score (ASDAS),[6] that is, improvement ≥1.1, is achieved, the treatment should be continued.[7] ASDAS, preferably calculated using C reactive protein (CRP), is a well-balanced index, containing patient-reported outcomes as well as an objective sign of inflammation, namely CRP, and it is used for monitoring axSpA activity in clinical practice, with existing validated cut-offs that define improvement and worsening stages.[7] While the efficacy of a treat-to-target strategy for axSpA has not been proven to be superior to usual care,[8] it has been shown to lead to better disease activity outcomes and has been recommended by an international taskforce.[9 10] In addition, the international recommendations encourage rheumatologists and patients to agree on a treatment strategy towards a predefined target, unless there are concomitant factors to impede this approach.[7] Considering the evidence of ASDAS being an appropriate target for axSpA treatment,[7] a reasonable strategy could be to achieve sustained inactive disease (ID) or at least low disease activity (LDA).[9 10]

While the association of treatment response at week 12 and achievement of long-term response in patients with axSpA has been investigated for TNFi in two studies,[11 12] it has been neither confirmed in other studies nor evaluated for other drug classes, such as IL-17i. Ixekizumab (IXE) is a monoclonal antibody that selectively targets IL-17A, which has been demonstrated to be efficacious in the treatment of axSpA (both nr-axSpA and r-axSpA) in either bDMARD-naïve or TNFi-experienced patients.[13–15]

The investigation of the association between early treatment response to IXE and long-term response may help rheumatologists to optimise patient treatment. Similarly, by identifying patients who are unlikely to achieve the treatment target, this may help avoid unnecessary exposure to treatment and consequently potentially lead to increased cost-effectiveness. The identification of patients unlikely to achieve the desirable long-term targets is very informative for clinicians in daily clinical practice.

Therefore, this post hoc analysis aimed to fill this knowledge gap by investigating the association between treatment response to IXE at week 12 and/or week 24 and long-term response, namely, achievement of ASDAS<2.1 at week 52, in bDMARD-naïve patients with r-axSpA.

METHODS

Study design and patient population

COAST-V (NCT02696785) was a 52-week, phase 3, multicentre, randomised, double-blind, active-controlled and placebo-controlled trial investigating the efficacy of IXE in bDMARD-naïve patients with r-axSpA. The COAST-V trial design has been published previously.[13]

Eligible patients were aged 18 years or over with an established diagnosis of r-axSpA fulfilling ASAS criteria (sacroiliitis on a pelvis radiograph defined by modified New York criteria and at least one spondyloarthritis feature according to ASAS axSpA classification criteria) who had active disease defined as a score of at least 4 on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and a score of at least 4 in the total back pain numeric rating scale at screening and baseline. Patients were bDMARD-naïve with an inadequate response to at least 2 NSAIDs or a history of intolerance to NSAIDs.

Eligible patients were randomised 1:1:1:1 to receive 80 mg IXE every 2 weeks, 80 mg IXE every 4 weeks (IXE Q4W), 40 mg adalimumab every 2 weeks (active reference group) or placebo. At week 16, patients entered an extended treatment period (weeks 16–52) and, during this period, IXE treatment groups remained on their assigned treatment, and patients originally randomised to placebo or adalimumab were re-randomised 1:1 to IXE every 2 weeks or IXE Q4W. This post hoc analysis includes only those patients randomised to the currently approved treatment IXE dose, IXE Q4W (N=81).

Time points

The results at week 16 of COAST-V have been published previously,[13] including the patient population of this post hoc analysis. Time points at 12, 24 and 52 weeks were chosen to highlight the time points indicated by the ASAS-EULAR recommendations (week 12) for treatment review, and a further 12 weeks of treatment, thus leading to week 24, which also reflects the common practice of assessing patients approximately every 3 months, especially after a period of HDA and therapeutic changes (as it was the trial baseline). Finally, outcomes at week 52 were also assessed, representing the conclusion of the clinical trial and reflecting longer-term treatment outcome.

Disease activity and clinical response

The proportion of patients achieving an ASDAS<2.1 (target) or <1.3 (ideal and most conservative target) at

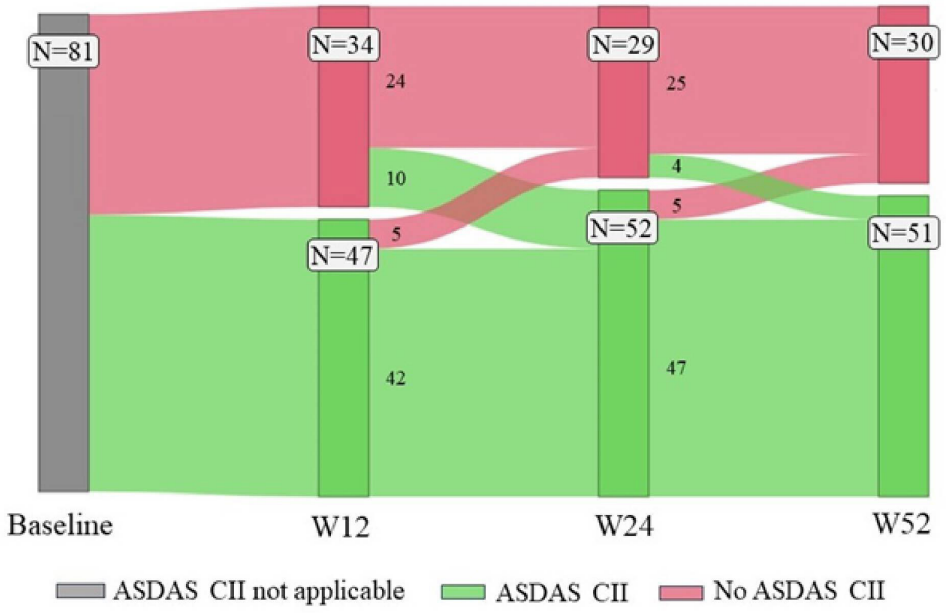

Figure 1 Trajectory of response from baseline to week 52—ASDAS CII. ASDAS, Axial Spondyloarthritis Disease Activity Score; CII, clinical important improvement; N, number of patients; W, week.

week 52 was measured among those attaining a meaningful clinical response at week 12 and/or week 24 and those who did not. Response at week 12 and/or 24 was measured by achievement or not (non-responders) of ASDAS CII; ASDAS major improvement (MI), defined as a change of ≥2.0 units; BASDAI50, representing an improvement of ≥50% of the BASDAI from baseline; and BASDAI<4, which is considered as not active disease.

Furthermore, the proportion of patients who achieved an ASDAS<2.1 or <1.3 at week 52 was evaluated among those with ID (ASDAS<1.3), LDA (1.3≤ASDAS<2.1), HDA (2.1≤ASDAS<3.5) or very HDA (VHDA; ASDAS≥3.5) at week 12 and/or week 24.

Statistical analyses

Sankey diagrams were used to illustrate the response trajectory of the 81 patients in achieving ASDAS CII and ASDAS<2.1 from baseline to week 52.

The proportion of patients achieving an ASDAS<2.1 (or <1.3) at week 52 was measured according to the disease activity or clinical response at weeks 12 and/or 24 as previously described. In order to gain further insight

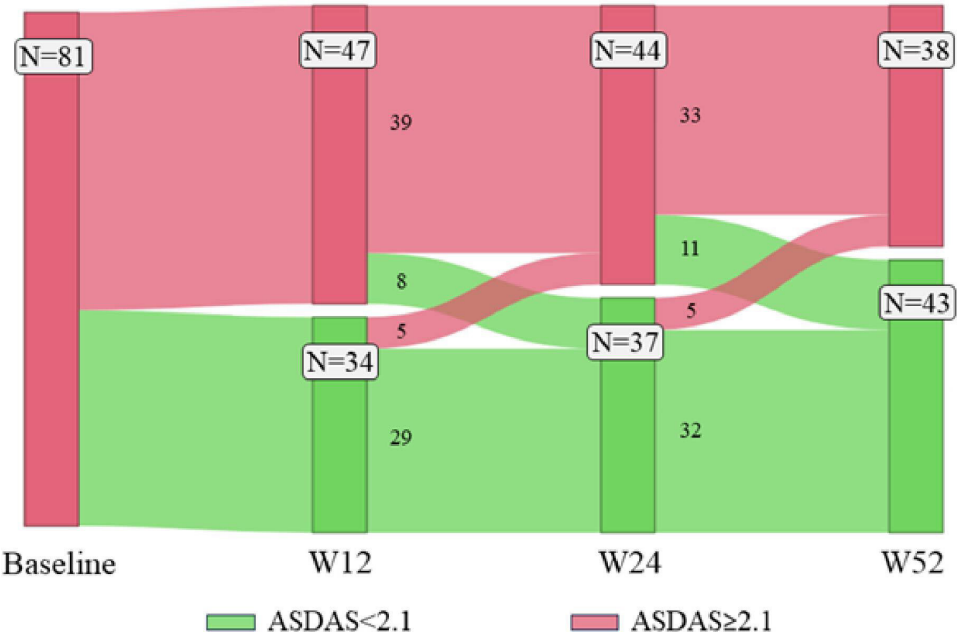

Figure 2 Trajectory of ASDAS<2.1 from baseline to week 52. ASDAS, Axial Spondyloarthritis Disease Activity Score; N, number of patients; W, week.

into the likelihood of achieving a long-term target among those not achieving an early response, the probability of ASDAS<2.1 (or <1.3) at week 52 was also calculated in those not achieving ASDAS CII or the other response measures at week 12, at week 24 and at none of the time points.

Additionally, baseline demographic and disease characteristics were analysed by ASDAS CII achievement status at weeks 12 and 24, which allowed categorisation of response in four groups (response at week 12 and week 24, at none of the time points,and at each of the time points only).

Missing data at the predefined time points (week 12, week 24 and week 52) were computed using non-responder imputation, assuming non-response for all missing data.

RESULTS

The 81 patients treated with IXE Q4W that were included in this post hoc analysis had a mean (SD) age of 41.0 (12.1) years, with 84% being males, 93% being positive for human leucocyte antigen-B27 and a mean ASDAS of 3.7 (0.7) (online supplemental table S1).

Response trajectory of patients achieving ASDAS CII at week 12, week 24 and week 52

Of the 81 patients, 47 (58.0%) and 52 (64.2%) patients achieved ASDAS CII at weeks 12 and 24 of the treatment,

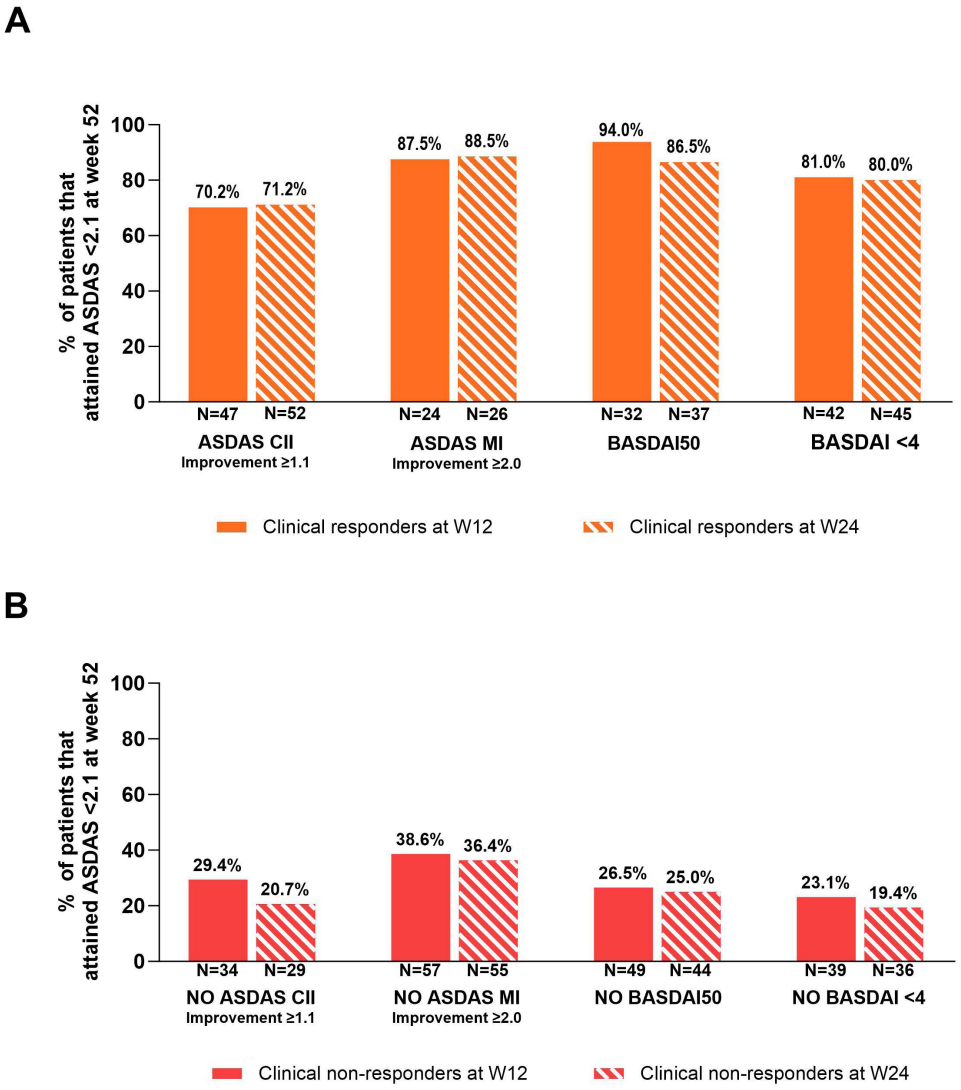

Figure 3 Association between clinical response at weeks 12 and 24 of ixekizumab treatment and attainment of ASDAS<2.1 at week 52. (A) Proportion of patients who attained ASDAS<2.1 at week 52 among clinical responders at week 12 and/or week 24. (B) Proportion of patients who attained ASDAS<2.1 at week 52 among clinical non-responders at week 12 and/or week 24. Clinical responders are defined as those that achieve ASDAS CII, ASDAS MI, BASDAI50, or BASDAI<4. ASDAS CII is defined as a change of ≥1.1 units, and ASDAS MI is defined as a change of ≥2.0 units. BASDAI50 represents an improvement of ≥50% of the BASDAI from baseline. A BASDAI of <4 is not considered active disease. ASDAS, Axial Spondyloarthritis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CII, clinically important improvement; MI, major improvement; N, number of patients; W, week.

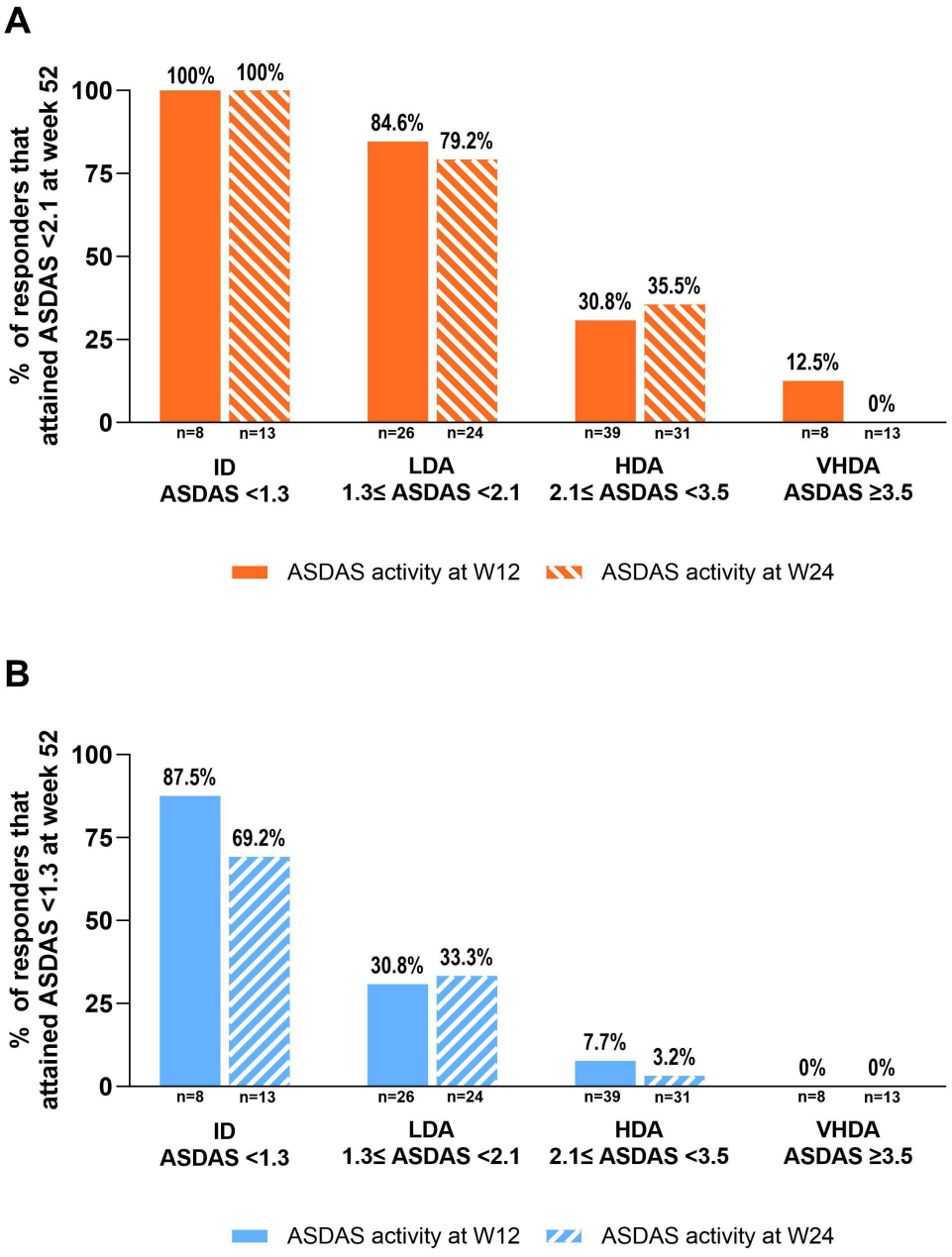

Figure 4 Association between disease activity at weeks 12 and 24 of ixekizumab treatment and attainment of ASDAS<2.1 or ASDAS<1.3 at week 52. ID is defined as ASDAS<1.3, LDA is defined as 1.3≤ASDAS<2.1, HDA is defined as 2.1≤ASDAS<3.5 and VHDA is defined as ASDAS≥3.5. ASDAS, Axial Spondyloarthritis Disease Activity Score; HDA, high disease activity; ID, inactive disease; LDA, low disease activity; n, number of patients; VHDA, very high disease activity; W, week.

respectively. Of the 34 (42.0%) patients who did not achieve ASDAS CII at week 12, 10 (29.4%) then reached it at week 24, and an additional 4 (13.8%) patients achieved ASDAS CII at week 52 (figure 1). However, after week 12, five (10.6%) patients lost their ASDAS CII response, and after week 24, an additional five (9.6%) patients lost response.

Achievement of ASDAS<2.1 at week 12, week 24 and week 52

At baseline, all 81 patients had ASDAS≥2.1, and at week 12, 34 (42.0%) achieved ASDAS<2.1, with 29 (85.3%) maintaining the response at week 24. Of the 47 (58.0%) patients with ASDAS≥2.1 at week 12, 8 (29.4%) reported an ASDAS<2.1 at week 24. Notably, 11 (25.0%) patients who had ASDAS≥2.1 at week 24 ended up having an ASDAS<2.1 at week 52. However, five (14.7%) patients after week 12 and an additional five (13.5%) patients after week 24 did not maintain their ASDAS<2.1 at the following time point (figure 2).

Association of clinical response measures at week 12 and week 24 with the achievement of ASDAS<2.1 or ASDAS<1.3 at week 52

At week 52, 43 (53.1%) patients achieved ASDAS<2.1. Among the patients who met ASDAS CII, ASDAS MI, BASDAI50 and BASDAI<4 response at week 12,

Table 1 Baseline demographics and disease characteristics of patients who achieved or did not achieve ASDAS CII at week 12 and/or week 24

	Week 12 Achieved ASDAS CII (N=47)		Week 12 Did not achieve ASDAS CII (N=34)	
	Week 24 Achieved ASDAS CII (n=42)	Week 24 Did not achieve ASDAS CII (n=5)	Week 24 Achieved ASDAS CII (n=10)	Week 24 Did not achieve ASDAS CII (n=24)
Age, years	39.4 (12.6)	40.0 (9.3)	40.3 (7.9)	44.1 (13.2)
Male, n (%)	35 (83.3)	4 (80.0)	8 (80.0)	21 (87.5)
HLA-B27 positive, n (%)	41 (97.6)	5 (100.0)	9 (90.0)	20 (83.3)
Symptom duration, years	14.2 (10.8)	13.0 (11.8)	15.8 (11.4)	19.2 (11.5)
MRI-SIJ Spondylarthritis Research Consortium of Canada score≥2, n (%)	17 (40.5)	3 (60.0)	2 (20.0)	5 (20.8)
CRP>5 mg/L, n (%)	34 (81.0)	3 (60.0)	8 (80.0)	7 (29.2)
ASDAS score at baseline	4.0 (0.7)	3.8 (1.0)	3.6 (0.6)	3.2 (0.6)
ASDAS score at week 12	1.9 (0.7)	2.1 (0.4)	2.8 (0.6)	2.8 (0.6)
ASDAS score at week 24	1.8 (0.7)	2.6 (0.8)	2.2 (0.8)	3.0 (0.8)

Data are mean (SD) unless stated otherwise.
ASDAS, Axial Spondyloarthritis Disease Activity Score; CII, clinically important improvement; CRP, C reactive protein; HLA-B27, human leucocyte antigen B27; MRI-SIJ, magnetic resonance imaging of the sacroiliac joints; N/n, number of patients.

70.2%–93.8% of them subsequently achieved ASDAS<2.1 at week 52. Among those who met ASDAS CII, ASDAS MI, BASDAI50 and BASDAI<4 response at week 24, 71.2%–88.5% of them later achieved ASDAS<2.1 at week 52 (figure 3A).

As shown in figure 3B, 10 (29.4%) of the 34 patients who did not achieve ASDAS CII at week 12 and equally 6 (20.7%) of the 29 patients who did not achieve ASDAS CII at week 24 attained an ASDAS<2.1 at week 52.

Of the 24 patients who did not achieve ASDAS CII at either week 12 or week 24, 5 (20.8%) achieved ASDAS<2.1 at week 52.

At week 52, 18 (22.2%) of the patients achieved ASDAS<1.3. The proportion of patients who achieved an ASDAS<1.3 at week 52 among those who attained ASDAS CII, ASDAS MI, BASDAI 50 and BASDAI<4 at week 12 and week 24, ranged from 36.2% to 50.0% and from 34.6% to 50.0%, respectively (online supplemental figure S1A).

Finally, only one (2.9%) of the patients who did not achieve ASDAS CII at week 12 and none of the patients who did not achieve ASDAS CII at week 24 then achieved an ASDAS<1.3 at week 52 (online supplemental figure S1B).

Association between disease activity at weeks 12 and 24 of ixekizumab treatment and attainment of ASDAS<2.1 or ASDAS<1.3 at week 52

All eight (9.9%) patients who achieved ASDAS<1.3 (ID) at week 12 subsequently attained an ASDAS<2.1 at week 52, with 7 (87.5%) maintaining the ID status at week 52 (figure 4A,B). At week 52, 84.6% (n=22) of patients with LDA (1.3≤ASDAS<2.1) at week 12 achieved ASDAS<2.1 while 30.8% (n=8) of these patients achieved ID.

Among the 13 (16.0%) patients with ID at week 24, 9 (69.2%) patients maintained ID, and all (100%) had an ASDAS<2.1 at week 52. Nineteen (79.2%) of those who had achieved LDA at week 24 attained ASDAS<2.1 at week 52 while 33.3% (n=8) achieved ID.

At weeks 12 and 24, 48.1% (n=39) and 38.3% (n=31) of patients had HDA (2.1≤ASDAS<3.5), respectively, and of those, 12 (30.8%) and 11 (35.5%) patients achieved ASDAS<2.1, while 3 (7.7%) patients and 1 (3.2%) patient achieved ID at week 52, respectively (figure 4).

At week 12, eight (9.9%) patients had VHDA (ASDAS≥3.5), while at week 52, one patient in this group achieved ASDAS<2.1, and none in this group achieved ASDAS ID.

In total, 24 patients did not achieve ASDAS CII neither at week 12 nor at week 24 (70.6% of the 34 patients who did not achieve ASDAS CII at week 12). Compared with patients achieving ASDAS CII at both weeks 12 and 24 (n=42), patients who did not meet ASDAS CII at weeks 12 nor 24 (n=24) had higher mean age and symptom duration, lower level of inflammation on magnetic resonance imaging of the SIJ (MRI-SIJ) and the proportion of patients with elevated CRP was lower (table 1).

Of the 24 patients who did not reach ASDAS CII at either week 12 or 24, 3 (12.5%) patients subsequently achieved ASDAS CII at week 52, while 21 (87.5%) patients did not reach ASDAS CII at any visit (weeks 12, 24 and 52). Their baseline characteristics are summarised in online supplemental table S2.

DISCUSSION

The current ASAS-EULAR recommendations endorse that patients with r-axSpA receiving a bDMARD should

be assessed after at least 12 weeks of treatment, and if a substantial reduction in disease activity (≥1.1 improvement in ASDAS score (ASDAS CII)) is obtained, along with a positive opinion from the rheumatologist, the medication should be continued.[7]

In COAST-V, 47 (58.0%) of the bDMARD-naïve patients with r-axSpA treated with IXE achieved an ASDAS CII at week 12, and 70.2% of them then achieved ASDAS<2.1 at week 52, the current treat-to-target recommendation.[7] Similarly, 71.2% of the patients who achieved ASDAS CII at week 24 then attained an ASDAS<2.1 at week 52. Overall, the achievement of ASDAS CII at week 12 was maintained through week 52. However, a fluctuation of response was reported among the 81 patients for ASDAS CII from baseline to week 52, thus prompting further analyses on other factors that may be associated with maintaining long-term response.

In this analysis, patients achieving an ASDAS CII at weeks 12 and/or 24 were more likely to have a shorter symptom duration and higher inflammation on MRI-SIJ and CRP and to be younger. These results are aligned with a recent systematic review of the factors associated with sustained remission (defined as achieving and maintaining ASDAS ID) in axSpA, which highlighted that being younger, having shorter duration of disease, and male gender were common predictors of remission,[16] as well as other observational studies assessing predictors of response to TNFi,[17 18] and the 2022 ASAS-EULAR recommendations.[7]

If patients with r-axSpA in this cohort naïve to previous bDMARD therapy have not reached an ASDAS CII at weeks 12 or 24, it is unlikely that they will attain the treat-to-target goal of at least an ASDAS<2.1 at week 52. However, of the 24 patients who did not achieve ASDAS CII at either week 12 or week 24, only 5 (20.8%) later achieved ASDAS<2.1 at week 52.

Furthermore, of the eight patients with VHDA at week 12, only one patient achieved ASDAS<2.1 at week 52, and none attained an ASDAS<1.3, thus suggesting that for patients who remain in VHDA after 12 weeks of treatment, the likelihood of the desired long-term outcome is low and treatment cessation should be considered. Moreover, this analysis demonstrates that the response at weeks 12 and 24 also increases the chance of obtaining the state of ID.

This post hoc analysis is not exempted from limitations. First, the objective and the methods of this post hoc analysis were not included in the original trial. Second, the small sample size and strict selection criteria in a randomised clinical trial may not result in a population representative of the general population with the disease, especially considering that the patient population was predominantly male (84%) and white (64%). However, treatment dosage and clinical response measures were used as standard in clinical practice, providing information on patterns and expected outcomes in the real world, and these results are similar to those observed in patients with TNFi,[11 12] and therefore, this adds to the generalisability of the current data. Finally, the sample size was small, and an analysis of predictors was not conducted because it was outside the scope of this post hoc analysis; therefore, the results on the factors identified as different between groups are descriptive only and should be interpreted with caution. However, these factors have been previously identified as predictors of response in other papers.[7 16 17]

This post hoc analysis suggests that in patients with r-axSpA who are naïve to previous bDMARD therapy and treated with IXE Q4W, and who have not reached an ASDAS CII at weeks 12 or 24, it is unlikely that they will attain the treat-to-target goal of at least an ASDAS<2.1 at week 52.

These results reinforce the ASAS-EULAR recommendation to continue treatment if ASDAS CII is reached at the assessment of response, occurring from week 12, which is associated with a higher likelihood of reaching ASDAS<2.1 at week 52.

These results can assist rheumatologists in their treatment decisions in daily clinical practice.

Author affiliations
[1]Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands
[2]Department of Rheumatology, Zuyderland Medical Centre, Heerlen, The Netherlands
[3]University Hospital Centre of Montpellier, Montpellier, France
[4]Department of Medicine, Laval University, Quebec, Quebec, Canada
[5]Arthritis Associates, San Antonio, Texas, USA
[6]Eli Lilly and Company, Indianapolis, Indiana, USA
[7]Department of Rheumatology, Geneva University Hospitals, Geneve, Switzerland
[8]Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan
[9]Department of Nursing, Chung Shan Medical University, Taichung, Taiwan

X Michael J Nissen @#michaelnissen

Contributors SR contributed to the conception and design of the work, analysis and interpretation of data for the work and reviewed the work critically for important intellectual content. CL contributed to the acquisition, analysis and interpretation of data for the work and reviewed the work critically for important intellectual content. LB contributed to the interpretation of data for the work and reviewed the work critically for important intellectual content. PW contributed to the design of the work, interpretation of data for the work and reviewed the work critically for important intellectual content. TP contributed to the design of the work, acquisition, analysis and interpretation of data for the work, and reviewed the work critically for important intellectual content. RB contributed to the design of the work, analysis and interpretation of data for the work and reviewed the work critically for important intellectual content. She is the guarantor of the authors' contributorship. SL-L contributed to the conception and design of the work, analysis and interpretation of data for the work, she also reviewed the work critically for important intellectual content. BJ contributed to the interpretation of data for the work and reviewed it critically for important intellectual content. MJN contributed to the interpretation of the data for the work and reviewed the work critically for important intellectual content. JC-CW has contributed to the acquisition of data for the work and reviewed the work critically for important intellectual content.

Funding This study is sponsored by Eli Lilly and Company, Indianapolis, Indiana, USA. Medical writing assistance in the preparation of this article was provided by Valeria Maria Cortesi, MD, of Eli Lilly and Company. Support for this assistance was funded by Eli Lilly and Company.

Competing interests SR has received speaker and/or consultation fees and/or research support/grants from AbbVie, Eli Lilly and Company, Galapagos NV, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Sanofi and UCB Pharma. CL has received speaker and/or consultation fees and/or research support/grants from AbbVie, Amgen, Bristol Myers Squibb, Chugai Pharmaceutical, Eli Lilly and Company, Galapagos NV, Merck Sharp & Dohme, Novartis, Pfizer and Roche. LB has received speaker and/or consultation fees and/or research support/grants

from Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Sanofi, Eli Lilly and Company, Gilead, JAMP Pharma, Fresenius Kabi, Teva, Organon and Sandoz. PW has received consulting payments, research funding, and/or honoraria from Abbvie, Amgen, Novartis, Eli Lilly and Company, Sanofi-Genzyme, SetPoint, Sun Pharma, Viela Bio, RegenLab, Paradigm, AstraZeneca, Janssen, Horizon and LG Chem. TP is an employee and shareholder of Eli Lilly and Company. RB is an employee and shareholder of Eli Lilly and Company. SL-L is a former employee of Eli Lilly and Company. BJ is an employee and shareholder of Eli Lilly and Company. MJN has received speaker and/or consultation fees and/or research support/grants from AbbVie, Amgen, Celgene, Eli Lilly and Company, Janssen, Novartis and Pfizer and has received grant and/or research support from Novartis. JC-CW has received speaker and/or consultation fees and/or research support/grants from AbbVie, Bristol Myers Squibb, Celgene, Chugai Pharmaceutical, Eisai, Eli Lilly and Company, Janssen, Novartis, Pfizer, Sanofi-Aventis, TSH Biopharm and UCB Pharma.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and the COAST-V trial was conducted in accordance with the standards of the Declaration of Helsinki. All patients provided written informed consent before undergoing study-related procedures. The study protocols and consent forms were approved by each site's institutional review board (IRB) or ethics committee. The main ethics committee was Schulman Associates IRB, Cincinnati, Ohio, USA (number 201506061).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Lilly provides access to all individual participant data collected during the trial, after anonymisation, with the exception of pharmacokinetic or genetic data. Data are available to request 6 months after the indication studied has been approved in the USA and EU and after primary publication acceptance, whichever is later. No expiration date of data requests is currently set once data are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, blank or annotated case report forms, will be provided in a secure data sharing environment. For details on submitting a request, see the instructions provided at www.vivli.org.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

ORCID iDs
Sofia Ramiro http://orcid.org/0000-0002-8899-9087
Michael J Nissen http://orcid.org/0000-0002-6326-1764
James Cheng-Chung Wei http://orcid.org/0000-0002-8285-1700

REFERENCES

1 Navarro-Compán V, Sepriano A, El-Zorkany B, *et al*. Axial Spondyloarthritis. *Ann Rheum Dis* 2021;80:1511–21.
2 Reveille JD, Witter JP, Weisman MH. Prevalence of axial Spondylarthritis in the United States: estimates from a cross-sectional survey. *Arthritis Care Res (Hoboken)* 2012;64:905–10.
3 Strand V, Rao SA, Shillington AC, *et al*. Prevalence of axial Spondyloarthritis in United States rheumatology practices: assessment of Spondyloarthritis International society criteria versus rheumatology expert clinical diagnosis. *Arthritis Care Res (Hoboken)* 2013;65:1299–306.
4 López-Medina C, Ramiro S, van der Heijde D, *et al*. Characteristics and burden of disease in patients with radiographic and non-radiographic axial Spondyloarthritis: a comparison by systematic literature review and meta-analysis. *RMD Open* 2019;5:e001108.
5 Boel A, Molto A, van der Heijde D, *et al*. Do patients with axial Spondyloarthritis with radiographic Sacroiliitis fulfil both the modified New York criteria and the ASAS axial Spondyloarthritis criteria? Results from eight cohorts. *Ann Rheum Dis* 2019;78:1545–9.
6 van der Heijde D, Molto A, Ramiro S, *et al*. Goodbye to the term 'Ankylosing Spondylitis', hello 'axial Spondyloarthritis': time to embrace the ASAS-defined nomenclature. *Ann Rheum Dis* 2024;83:547–9.
7 Ramiro S, Nikiphorou E, Sepriano A, *et al*. ASAS-EULAR recommendations for the management of axial Spondyloarthritis: 2022 update. *Ann Rheum Dis* 2023;82:19–34.
8 Molto A, López-Medina C, Van den Bosch FE, *et al*. Efficacy of a tight-control and treat-to-target strategy in axial Spondyloarthritis: results of the open-label, pragmatic, cluster-randomised TICOSPA trial. *Ann Rheum Dis* 2021;80:1436–44.
9 Smolen JS, Schöls M, Braun J, *et al*. Treating axial Spondyloarthritis and peripheral Spondyloarthritis, especially Psoriatic arthritis, to target: 2017 update of recommendations by an international task force. *Ann Rheum Dis* 2018;77:3–17.
10 Machado PM, Landewé R, van der Heijde D. Ankylosing Spondylitis disease activity score (ASDAS): 2018 update of the nomenclature for disease activity states. *Ann Rheum Dis* 2018;77:1539–40.
11 van der Heijde D, Deodhar A, Fleischmann R, *et al*. Early disease activity or clinical response as predictors of long-term outcomes with Certolizumab Pegol in axial Spondyloarthritis or Psoriatic arthritis. *Arthritis Care Res (Hoboken)* 2017;69:1030–9.
12 Maksymowych WP, Kumke T, Auteri SE, *et al*. Predictors of long-term clinical response in patients with non-radiographic axial Spondyloarthritis receiving Certolizumab Pegol. *Arthritis Res Ther* 2021;23:274.
13 van der Heijde D, Cheng-Chung Wei J, Dougados M, *et al*. Ixekizumab, an Interleukin-17A antagonist in the treatment of Ankylosing Spondylitis or radiographic axial Spondyloarthritis in patients previously untreated with biological disease-modifying anti-rheumatic drugs (COAST-V): 16 week results of a phase 3 randomised, double-blind, active-controlled and placebo-controlled trial. *Lancet* 2018;392:2441–51.
14 Dougados M, Wei JC-C, Landewé R, *et al*. Efficacy and safety of Ixekizumab through 52 weeks in two phase 3, randomised, controlled clinical trials in patients with active radiographic axial Spondyloarthritis (COAST-V and COAST-W). *Ann Rheum Dis* 2020;79:176–85.
15 Deodhar A, Poddubnyy D, Rahman P, *et al*. Long-term safety and efficacy of Ixekizumab in patients with axial Spondyloarthritis: 3-year data from the COAST program. *J Rheumatol* 2023;50:1020–8.
16 Pinto AS, Farisogullari B, Machado PM. Predictors of remission in people with axial Spondyloarthritis: a systematic literature review. *Semin Arthritis Rheum* 2022;56:152078.
17 Arends S, Brouwer E, van der Veer E, *et al*. Baseline predictors of response and discontinuation of tumor necrosis factor-alpha blocking therapy in Ankylosing Spondylitis: a prospective longitudinal observational cohort study. *Arthritis Res Ther* 2011;13:R94.
18 Arends S, van der Veer E, Kallenberg CGM, *et al*. Baseline predictors of response to TNF-alpha blocking therapy in Ankylosing Spondylitis. *Curr Opin Rheumatol* 2012;24:290–8.