

CONCISE REPORT

Secukinumab efficacy in anti-TNF-naïve and anti-TNF-experienced subjects with active ankylosing spondylitis: results from the MEASURE 2 Study

Joachim Sieper,¹ Atul Deodhar,² Helena Marzo-Ortega,³ Jacob A Aelion,⁴ Ricardo Blanco,⁵ Tseng Jui-Cheng,⁶ Mats Andersson,⁷ Brian Porter,⁸ Hanno B Richards,⁷ on behalf of the MEASURE 2 Study Group

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For numbered affiliations see end of article.

Correspondence to Professor Joachim Sieper, Medical Department I, Rheumatology, Campus Benjamin Franklin, Charité Universitätsmedizin Berlin, Hindenburgdamm 30, Berlin 12203, Germany; joachim.sieper@charite.de

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ABSTRACT

Background There is significant unmet need in patients with ankylosing spondylitis (AS) who have inadequate response or intolerance to anti-tumour necrosis factor (TNF) treatment. Secukinumab, an anti-interleukin-17A monoclonal antibody, significantly improved signs and symptoms of AS in the MEASURE 2 study (NCT01649375).

Methods Subjects with active AS (N=219) received secukinumab (150 or 75 mg) or placebo at baseline, weeks 1, 2, 3 and 4, and every 4 weeks thereafter. Randomisation was stratified by prior anti-TNF use: anti-TNF-naïve or inadequate response/intolerance to one anti-TNF (anti-TNF-IR). The primary endpoint was Assessment of SpondyloArthritis International Society criteria (ASAS) 20 at week 16.

Results At week 16, 68.2% of anti-TNF-naïve subjects treated with secukinumab 150 mg achieved ASAS20 compared with 31.1% treated with placebo ($p<0.001$). In the anti-TNF-IR group, 50.0% of subjects treated with secukinumab 150 mg achieved an ASAS20 response compared with 24.1% treated with placebo ($p<0.05$). Numerically greater improvements were observed with secukinumab than with placebo for most secondary endpoints. Clinical responses were sustained through week 52.

Conclusions Secukinumab 150 mg provided sustained improvements in signs and symptoms of AS in anti-TNF-naïve and anti-TNF-IR subjects through 52 weeks of therapy.

Trial registration number NCT01649375.

intolerant to these agents or fail to achieve adequate disease control.^{5 6}

Treatment with secukinumab (human anti-interleukin (IL)-17A IgG1k monoclonal antibody) significantly improved the signs and symptoms of AS when compared with placebo treatment in two phase 3 trials (MEASURE 1 (intravenous followed by subcutaneous (s.c.) administration; NCT01358175) and MEASURE 2 (s.c. administration; NCT01649375)).⁷ In MEASURE 2, 61% and 41% of subjects treated with secukinumab 150 mg and 75 mg, respectively, achieved an Assessment of SpondyloArthritis International Society 20 (ASAS20) response at week 16, compared with 28% given placebo.⁷ All pre-defined secondary endpoints except ASAS partial remission were met with secukinumab 150 mg s.c. The clinical responses observed at week 16 were sustained through 52 weeks of therapy.⁷ Responses with secukinumab 75 mg were not significantly different from placebo for the primary endpoint or for secondary endpoints based on hierarchical testing.⁷ The safety profile was consistent with other studies of secukinumab in AS, psoriatic arthritis and moderate-to-severe plaque psoriasis.⁷⁻¹¹

Here, we present the results of a pre-specified subgroup analysis of MEASURE 2 to investigate the efficacy of secukinumab in subjects who were naïve to anti-TNF therapy (anti-TNF-naïve) and in those with a history of inadequate response or reported intolerance to anti-TNF therapy (anti-TNF-IR).

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory disease which primarily affects the axial skeleton.¹ It is characterised by the erosion and fusion of the spinal vertebrae and sacroiliac joints,² which often results in progressive, irreversible structural damage, deterioration of function, disability and reduced quality of life (QoL).^{3 4}

Current therapeutic options are limited for patients with AS. Non-steroidal anti-inflammatory drugs are often insufficient to control disease symptoms and, although anti-tumour necrosis factor (TNF) therapy is recommended for patients with persistent disease activity despite conventional treatment, up to 40% of patients with AS become

PATIENTS AND METHODS

MEASURE 2 is an ongoing randomised, double-blind, placebo-controlled, 5-year, phase 3 trial. A complete description of enrolment criteria, study procedures and study design has been reported previously.⁷

Eligible subjects were aged ≥ 18 years with AS fulfilling the modified New York criteria, a score of ≥ 4 (0–10) on the Bath AS Disease Activity Index (BASDAI), and a spinal pain score of ≥ 40 mm on a 100 mm visual analogue scale, despite treatment with their maximum tolerated dose of non-steroidal anti-inflammatory drugs (NSAIDs). Written informed consent was obtained from all subjects.

Subjects previously treated with only one anti-TNF agent were eligible to participate in the study if they had had an inadequate response after



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receiving the approved dose for ≥ 3 months or were unable to tolerate at least one dose (anti-TNF-IR). The online Supplementary Methods file provides further information regarding allowed medication and exclusion criteria.

Subjects with active AS were randomised 1:1:1 to secukinumab 150 mg, secukinumab 75 mg or placebo, administered at baseline, weeks 1, 2, 3 and 4, and every 4 weeks thereafter. Randomisation was stratified by anti-TNF history: anti-TNF-naïve, or inadequate response or intolerance to one previous anti-TNF agent (anti-TNF-IR).

The primary efficacy endpoint was the proportion of subjects achieving an ASAS20 response (improvement of $\geq 20\%$ and ≥ 1 unit on a 10-unit scale in at least three of the four core ASAS domains, with no worsening of $\geq 20\%$ and ≥ 1 unit in the fourth) at week 16. Secondary endpoints at week 16 are described in the online Supplementary Methods file. Exploratory endpoints included efficacy assessments through week 52.

Primary and secondary efficacy endpoint analyses included all subjects according to treatment assigned at randomisation. Efficacy analyses in anti-TNF-naïve and anti-TNF-IR subgroups were pre-specified.

Logistic regression with treatment regimen and anti-TNF status as factors, and weight as a covariate, was used to evaluate the effect of secukinumab versus placebo for binary variables.

Missing response values, including those due to discontinuation, were imputed as non-response (non-responder imputation (NRI)). A mixed-effects model (MMRM) was used to analyse continuous variables. Data are presented by NRI/MMRM and observed analyses at week 52. Further information is provided in the online Supplementary Methods file.

RESULTS

Subjects (N=219) were randomly assigned to treatment with s.c. secukinumab 150 mg (n=72), secukinumab 75 mg (n=73) or placebo (n=74) from 28 October 2012 through 29 July 2013. Of 219 randomised subjects, 61.2% were anti-TNF-naïve and 38.8% were anti-TNF-IR. Demographic and baseline characteristics were similar across the subgroups (table 1) with fewer female patients in the anti-TNF-naïve placebo group than in the respective secukinumab groups. Characteristics were comparable to the overall study population.⁷ At week 16, 200 (91.3%) subjects remained in the study and 181 (82.6%) subjects completed 52 weeks of treatment.

At week 16, a higher proportion of subjects treated with secukinumab 150 mg achieved ASAS20 responses in both anti-TNF-naïve and anti-TNF-IR subgroups than in the placebo group (table 2 and figure 1). In the anti-TNF-naïve group, 68.2% of subjects treated with secukinumab 150 mg achieved ASAS20

Table 1 Demographic and baseline characteristics

	Anti-TNF-naïve			Anti-TNF-IR		
	Secukinumab s.c.			Secukinumab s.c.		
	150 mg (N=44)	75 mg (N=45)	Placebo (N=45)	150 mg (N=28)	75 mg (N=28)	Placebo (N=29)
Age (years), mean (SD)	43.7 (12.9)	43.9 (14.1)	43.5 (13.3)	39.3 (11.6)	45.2 (11.3)	43.8 (13.2)
Female, n (%)	18 (40.9)	14 (31.1)	10 (22.2)	8 (28.6)	8 (28.6)	8 (27.6)
Race, n (%)						
White	44 (100)	42 (93.3)	41 (91.1)	25 (89.3)	28 (100)	29 (100)
Asian	0	3 (6.7)	4 (8.9)	2 (7.1)	0	0
American Indian or Alaskan Native	0	0	0	1 (3.6)	0	0
Ethnicity, n (%)						
Hispanic/Latino	0	3 (6.7)	3 (6.7)	5 (17.9)	3 (10.7)	5 (17.2)
Not Hispanic/Latino	40 (90.9)	38 (84.4)	36 (80.0)	19 (67.9)	21 (75.0)	21 (72.4)
Unknown or not reported	4 (9.1)	4 (8.9)	6 (13.3)	4 (14.3)	4 (14.3)	3 (10.3)
Weight (kg), mean (SD)	80.4 (16.8)	80.0 (18.3)	81.8 (14.1)	85.4 (19.6)	83.8 (15.9)	77.9 (16.7)
BMI (kg/m ²), mean (SD)	27.0 (6.0)	27.7 (6.2)	27.4 (6.2)	28.1 (5.5)	28.6 (5.4)	26.5 (4.9)
Time since AS diagnosis (years), mean (SD)	6.1 (8.6)	3.7 (5.7)	3.9 (6.2)	8.5 (7.6)	7.7 (9.0)	10.2 (11.0)
Disease activity						
BASDAI, mean total score (SD)	6.7 (1.4)	6.4 (1.3)	6.8 (1.3)	6.5 (1.7)	6.8 (1.2)	6.7 (1.3)
Total back pain (0–100 mm scale), mean score (SD)	66.9 (15.4)	63.2 (17.7)	67.7 (17.7)	65.2 (18.7)	68.0 (17.5)	71.6 (20.5)
Patient's global assessment of disease activity (0–100 mm scale), mean (SD)	66.7 (15.9)	60.1 (17.5)	68.6 (15.8)	68.6 (18.4)	71.9 (16.3)	73.5 (15.5)
hsCRP (mg/L), mean (SD)	23.8 (47.0)	15.7 (20.1)	16.6 (19.7)	29.0 (55.3)	14.7 (19.7)	14.3 (16.6)
ESR (mm/h), mean (SD)	34.3 (24.1)	28.2 (19.2)	33.0 (15.5)	33.3 (26.2)	29.2 (23.1)	24.2 (20.0)
HLA-B27						
Negative	8 (18.2)	9 (20.0)	8 (18.2)	4 (14.3)	6 (21.4)	4 (14.3)
Positive	33 (75.0)	32 (71.1)	33 (75.0)	24 (85.7)	21 (75.0)	24 (85.7)
Missing	3 (6.8)	4 (8.9)	3 (6.8)	0 (0.0)	1 (3.6)	0 (0.0)
Previous treatment						
MTX use at randomisation	6 (13.6)	5 (11.1)	4 (8.9)	2 (7.1)	4 (14.3)	5 (17.2)
Sulfasalazine use at randomisation	4 (9.1)	8 (17.8)	9 (20.0)	0 (0.0)	6 (21.4)	10 (11.8)

AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; ESR, erythrocyte sedimentation rate; HLA, human leukocyte antigen; hsCRP, high-sensitivity C-reactive protein; MTX, methotrexate; s.c., subcutaneously; TNF, tumour necrosis factor.

Table 2 Measures of disease activity and health-related quality of life (secondary endpoints) at week 16 (NRI and MMRM analysis)

	Anti-TNF-naive			Anti-TNF-IR		
	Secukinumab s.c.			Secukinumab s.c.		
	150 mg (N=44)	75 mg (N=45)	Placebo (N=45)	150 mg (N=28)	75 mg (N=28)	Placebo (N=29)
ASAS20, n (%) responders¶	30 (68.2)†	23 (51.1)	14 (31.1)	14 (50.0)‡	7 (25.0)	7 (24.1)
ASAS40, n (%) responders**	19 (43.2)‡	14 (31.1)	8 (17.8)	7 (25.0)§	5 (17.9)‡	0 (0.0)
ASAS 5/6, n (%) responders††	22 (50.0)†	18 (40.0)§	6 (13.3)	9 (32.1)§	7 (25.0)§	0 (0.0)
ASAS partial remission, n (%) responders‡‡	8 (18.2)	9 (20.0)	3 (6.7)	2 (7.1)	2 (7.1)	0 (0.0)
BASDAI,§§ LS mean change from baseline (SE)¶¶	2.6§ (0.3) n=43	2.3‡ (0.3) n=45	1.2 (0.3) n=42	1.6 (0.4) n=24	1.4 (0.4) n=22	0.6 (0.4) n=22
hsCRP, geometric mean post-baseline/baseline ratio*** (SE)¶¶	0.46* (1.1) n=43	0.49* (1.1) n=45	1.00 (1.1) n=42	0.69‡ (1.2) n=25	0.84 (1.2) n=24	1.27 (1.2) n=24
SF-36 PCS,††† LS mean change from baseline (SE)¶¶	7.5§ (1.0) n=43	6.0‡ (1.0) n=45	3.0 (1.0) n=43	4.5‡ (1.2) n=24	3.6 (1.3) n=21	0.3 (1.2) n=23
ASQoL,‡‡‡ LS mean change from baseline (SE)¶¶	5.0§ (0.7) n=43	4.0‡ (0.7) n=44	1.9 (0.7) n=43	2.4 (0.8) n=23	2.5 (0.9) n=22	0.5 (0.8) n=23

*p<0.0001; †p<0.001; ‡p<0.01; §p<0.05 vs placebo.

At week 16 missing response values were imputed as non-response (non-responder imputation). Continuous results are from MMRM.

¶≥20% improvement in three of four core ASAS response criteria, with no worsening of ≥20% in the fourth.

**≥40% improvement in three of four core ASAS response criteria, with no worsening in the fourth.

††≥20% improvement in five of the six ASAS response criteria.

‡‡A score of ≤2 units (from 0 to 10) in each of the four core ASAS domains.

§§Scores range from 0 to 10, with 0 representing no problem and 10 the worst problem.

¶¶n=number of subjects with measurements at both baseline and the post-baseline visit.

***Exponentially transformed least square mean (LSM), the geometric mean ratio of post-baseline/baseline. A value <1 indicates a reduced CRP.

†††SF-36 PCS v2; scores range from 0 to 100 for individual domains (0 representing maximum disability and 100 no disability), with a normative score of 50 for the composite PCS.

‡‡‡Scores range from 0 to 18, with 0 representing lowest severity and 18 highest severity.

ASAS, Assessment of SpondyloArthritis International Society criteria; ASQoL, Ankylosing Spondylitis Quality of Life questionnaire; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; hsCRP, high-sensitivity C-reactive protein; LS, least squares; MMRM, mixed-effect model repeated-measures; NRI, non-responder imputation; SF-36 PCS, Short Form-36 Physical Component Summary; TNF, tumour necrosis factor.

responses ($p<0.001$ vs placebo), compared with 51.1% of subjects treated with secukinumab 75 mg ($p>0.05$ vs placebo) and 31.1% of subjects treated with placebo. In the anti-TNF-IR group, 50.0% of subjects treated with secukinumab 150 mg achieved ASAS20 responses ($p<0.05$ vs placebo), compared with 25.0% of subjects treated with secukinumab 75 mg ($p>0.05$ vs placebo), and 24.1% of subjects treated with placebo.

At week 16, secukinumab 150 mg also achieved greater improvements versus placebo for ASAS40, ASAS 5/6, high-sensitivity C-reactive protein and the Short Form-36 Physical Component Summary (SF-36 PCS) in both anti-TNF-naive and anti-TNF-IR subjects and for the Ankylosing Spondylitis Quality of Life questionnaire (ASQoL) and BASDAI for anti-TNF-naive subjects ($p<0.05$ for all comparisons vs placebo) (table 2 and figure 1). There were also numerical improvements in ASAS partial remission with secukinumab 150 mg, which did not reach statistical significance versus placebo. Responses were generally greater in anti-TNF-naive than in anti-TNF-IR subjects.

Improvements in ASAS20 response rates observed at week 16 with secukinumab 150 mg were sustained or continued to improve through week 52 in both anti-TNF-naive and anti-TNF-IR subjects (see figure 1 and online supplementary table S1 (observed data at week 52)). Using a conservative estimate of efficacy at week 52, with missing values imputed as non-response (see online supplementary table S2), the proportions of subjects with an ASAS20 response at week 52 in the anti-TNF-naive group were 72.7% (150 mg) and 66.7% (75 mg). In the anti-TNF-IR group, ASAS20 response rates were 46.4% (150 mg) and 32.1% (75 mg).

Improvements in secondary endpoints observed at week 16 were sustained or continued to improve through week 52 in

anti-TNF-naive and anti-TNF-IR subjects (see online supplementary figure S1 and online supplementary tables S1 and S2).

DISCUSSION

Previous results from MEASURE 1 and MEASURE 2 have shown that secukinumab 150 mg provides clinically significant and sustained improvements in the signs and symptoms of AS.⁷ The data from this pre-specified subgroup analysis demonstrated that secukinumab 150 mg was effective for subjects who were naive to anti-TNF treatment as well as those who had failed to achieve adequate disease control with, or who were intolerant to, anti-TNF treatment. The improvements observed with secukinumab were generally higher in the anti-TNF-naive subjects compared with anti-TNF-IR subjects.

Secukinumab 150 mg was associated with a reduction in inflammation and improvements in physical function and health-related QoL in both anti-TNF-naive and anti-TNF-IR subjects. Improvements at week 16 were sustained or continued to improve through week 52 in both anti-TNF subgroups.

Responses with the secukinumab 75 mg dose were consistently lower than those with the 150 mg dose in both anti-TNF-naive and anti-TNF-IR subjects. These data provide confirmation that secukinumab 150 mg is an appropriate dose for subjects with active AS. Secukinumab 150 mg has recently been approved (US and EU) for the treatment of adults with active AS.

Reported ASAS20 response rates for anti-TNF agents in anti-TNF-naive subjects are 58–61%^{12–15} at weeks 12–24, which, by indirect comparison, is comparable to that observed with secukinumab 150 mg in anti-TNF-naive subjects in this study (68.2%).

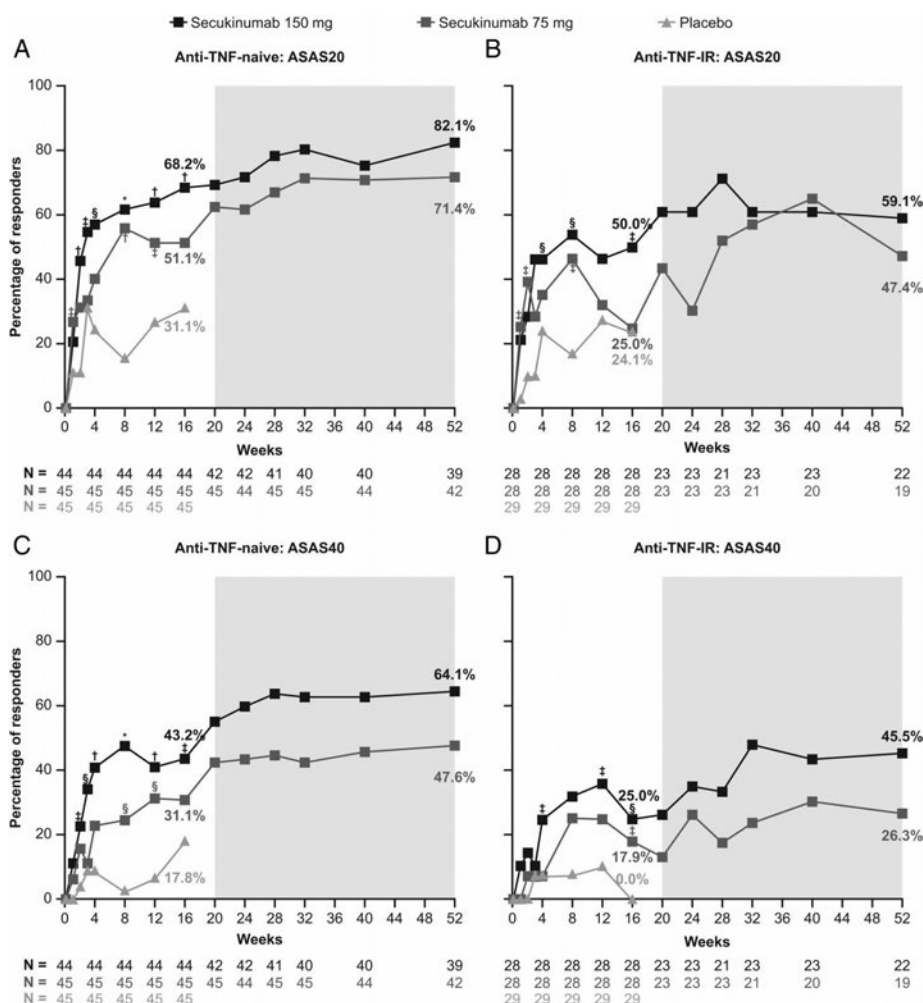


Figure 1 Assessment of SpondyloArthritis International Society 20 (ASAS20) and ASAS40 response in anti-TNF-naïve and anti-TNF-IR subjects (non-responder imputation (NRI) data to week 16; observed data from weeks 20–52). Shown are the proportions of subjects with ASAS20 responses (improvement of $\geq 20\%$ and absolute improvement of ≥ 1 unit (on a 10-unit scale) in at least three of the four main Assessment of SpondyloArthritis International Society criteria (ASAS) domains, with no worsening of $\geq 20\%$ in the remaining domain) and the proportion with ASAS40 responses (improvement of $\geq 40\%$ and absolute improvement of ≥ 2 units (on a 10-unit scale) in at least three of the four main ASAS domains, with no worsening in the remaining domain) in MEASURE 2. Randomisation was stratified by prior anti-TNF use: anti-TNF-naïve (left panels) or inadequate response/intolerance to one anti-TNF (anti-TNF-IR; right panels). Missing data were imputed as non-response (NRI) up to week 16. Observed data are presented from week 20 to week 52 (indicated by the grey box in each panel). * $p < 0.0001$; † $p < 0.001$; § $p < 0.01$; ‡ $p < 0.05$ vs placebo. TNF, tumour necrosis factor.

There are several anti-TNF therapies available for the treatment of AS; however, up to 40% of patients are unresponsive (primary or secondary treatment failure) or intolerant to these agents.^{5,6} According to recent results from the Danish DANBIO registry, ASAS20 response rates for anti-TNF-IR patients are typically lower than those for anti-TNF-naïve patients^{16–19} as observed in this study. The data from MEASURE 2 suggest that IL-17A inhibition may also be an effective therapeutic strategy for patients with an inadequate response/intolerance to TNF antagonists.

A limitation of this study is that it was not designed to show statistical superiority versus placebo by anti-TNF status. It also did not investigate the efficacy of secukinumab in subjects who were unresponsive or intolerant to multiple anti-TNF agents. In addition, the anti-TNF-IR group was not large enough to allow conclusions to be drawn regarding comparative efficacy when further subdivided into primary versus secondary treatment failure or intolerance categories.

In conclusion, secukinumab 150 mg s.c. provided clinically significant and sustained improvements in the signs and symptoms of AS in both anti-TNF-naïve and anti-TNF-IR subjects through 52 weeks of therapy.

Author affiliations

- ¹Charité University Medicine Berlin, Berlin, Germany
- ²Oregon Health & Science University, Portland, Oregon, USA
- ³NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust and Leeds Institute for Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK
- ⁴Arthritis Clinic, Jackson, Tennessee, USA
- ⁵Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain
- ⁶Kaohsiung Veterans General Hospital, Kaohsiung City, Taiwan
- ⁷Novartis Pharma AG, Basel, Switzerland
- ⁸Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, USA

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REFERENCES

- 1 Tam LS, Gu J, Yu D. Pathogenesis of ankylosing spondylitis. *Nat Rev Rheumatol* 2010;6:399–405.
- 2 Ghasemi Rad M, Attaya H, Lesha E, et al. Ankylosing spondylitis: a state of the art factual backbone. *World J Radiol* 2015;7:236–52.
- 3 Gao X, Wendling D, Botteman MF, et al. Clinical and economic burden of extra articular manifestations in ankylosing spondylitis patients treated with anti tumor necrosis factor agents. *J Med Econ* 2012;15:1054–63.
- 4 Giacomelli R, Gorla R, Trotta F, et al. Quality of life and unmet needs in patients with inflammatory arthropathies: results from the multicentre, observational RAPSODIA study. *Rheumatology* 2015;54:792–7.
- 5 Dougados M, Baeten D. Spondyloarthritis. *Lancet* 2011;377:2127–37.
- 6 Braun J, van den Berg R, Baraliakos X, et al. 2010 Update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;70:896–904.
- 7 Baeten D, Sieper J, Braun J, et al. Secukinumab, an interleukin 17A inhibitor, in ankylosing spondylitis. *N Engl J Med* 2015;373:2534–48.
- 8 Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis: results of two phase 3 trials. *N Engl J Med* 2014;371:326–8.
- 9 Baeten D, Baraliakos X, Braun J, et al. Anti interleukin 17A monoclonal antibody secukinumab in treatment of ankylosing spondylitis: a randomised, double blind, placebo controlled trial. *Lancet* 2013;382:1705–13.
- 10 Mease PJ, McInnes IB, Kirkham B, et al. Secukinumab inhibition of interleukin 17A in patients with psoriatic arthritis. *N Engl J Med* 2015;373:1329–39.
- 11 McInnes IB, Mease PJ, Kirkham B, et al. Secukinumab, a human anti interleukin 17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double blind, placebo controlled, phase 3 trial. *Lancet* 2015;386:1137–46.
- 12 van der Heijde D, Kivitz A, Schiff MH, et al. Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double blind, placebo controlled trial. *Arthritis Rheum* 2006;54:2136–46.
- 13 Davis JC Jr, Van Der Heijde D, Braun J, et al. Recombinant human tumor necrosis factor receptor (etanercept) for treating ankylosing spondylitis: a randomized, controlled trial. *Arthritis Rheum* 2003;48:3230–6.
- 14 Inman RD, Davis JC Jr, Heijde Dv, et al. Efficacy and safety of golimumab in patients with ankylosing spondylitis: results of a randomized, double blind, placebo controlled, phase III trial. *Arthritis Rheum* 2008;58:3402–12.
- 15 van der Heijde D, Dijkmans B, Geusens P, et al. Efficacy and safety of infliximab in patients with ankylosing spondylitis: results of a randomized, placebo controlled trial (ASSERT). *Arthritis Rheum* 2005;52:582–91.
- 16 Glinborg B, Østergaard M, Krogh NS, et al. Clinical response, drug survival and predictors thereof in 432 ankylosing spondylitis patients after switching tumour necrosis factor α inhibitor therapy: results from the Danish nationwide DANBIO registry. *Ann Rheum Dis* 2013;72:1149–55.
- 17 Lie E, van der Heijde D, Uhlig T, et al. Effectiveness of switching between TNF inhibitors in ankylosing spondylitis: data from the NOR DMARD register. *Ann Rheum Dis* 2011;70:157–63.
- 18 Rudwaleit M, Van den Bosch F, Kron M, et al. Effectiveness and safety of adalimumab in patients with ankylosing spondylitis or psoriatic arthritis and history of anti tumor necrosis factor therapy. *Arthritis Res Ther* 2010;12:R117.
- 19 Song IH, Heldmann F, Rudwaleit M, et al. Different response to rituximab in tumor necrosis factor blocker naive patients with active ankylosing spondylitis and in patients in whom tumor necrosis factor blockers have failed: a twenty four week clinical trial. *Arthritis Rheum* 2010;62:1290–7.