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Prevalence of Psoriatic Arthritis in Primary Care Patients With Psoriasis

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Objective. **To estimate the prevalence of psoriatic arthritis (PsA) in primary care patients diagnosed as having psoriasis and to estimate the prevalence of musculoskeletal symptoms in psoriasis patients in primary care.**

Methods. **We conducted a cross-sectional study in adult primary care patients with psoriasis. Responding patients reporting pain in joints, entheses, or the lower back were interviewed by telephone to determine eligibility and, if eligible, were invited for clinical evaluation. During clinical evaluation, skin, nails, joints, and entheses were assessed. Additionally, ultrasound of the enthesis was performed by an independent trained examiner if a patient had at least 1 tender enthesis (determined by the Leeds Enthesitis Index and the Maastricht Ankylosing Spondylitis Enthesitis Score). Patients who fulfilled the Classification of Psoriatic Arthritis (CASPAR) Study Group criteria were classified as having PsA.**

Results. **We invited 2,564 psoriasis patients from databases of 97 participating general practitioners. Of 1,673 responders (65.2%), 841 (50.3%) were willing to participate. A total of 823 patients (32.1%) reported having musculoskeletal symptoms; 659 of these patients were determined to be eligible, 524 of whom were clinically evaluated. We identified 64 cases of established PsA and another 17 cases of newly diagnosed PsA, leading to a prevalence of 3.2% (95% confidence interval [95% CI] 2.5–3.9) among psoriasis patients in primary care. This prevalence would increase to 4.6% (95% CI 3.8–5.4) if PsA cases based on enthesitis were also taken into account.**

Conclusion. **Among psoriasis patients in primary care, the prevalence of PsA is conservatively estimated to be 3.2%, increasing to 4.6% if enthesitis is taken into account. The prevalence of musculoskeletal symptoms among psoriasis patients is comparable with the prevalence of musculoskeletal symptoms in the general population.**

Psoriatic arthritis (PsA) is the second most frequent inflammatory arthritis for which a rheumatologist is consulted (1). PsA is well treatable, and an increasing number of studies show that early diagnosis improves the outcome substantially (2–6). In most cases PsA is preceded by psoriasis, which affects 2–3% of the Western population (7–9). Estimates of the prevalence of PsA among psoriasis patients are numerous and range widely (6–42%) (10,11), and most data stem from secondary dermatologic care. However, most psoriasis patients at risk of PsA will visit their general practitioner first if having musculoskeletal symptoms, which enables early referral if PsA is recognized in a timely manner. Therefore, prevalence data from primary care are important. To our knowledge, only 2 studies have reported the prevalence of PsA in primary care. Both studies were performed in the UK and showed prevalences of 9.0% and 13.8% (12,13).

The primary objective of this study was to give an estimate of the prevalence of PsA, including enthesitis, in psoriasis patients in primary care. The second objective was to estimate the prevalence of musculoskeletal symptoms in psoriasis patients.

PATIENTS AND METHODS

Patients. Between June 2013 and March 2014, 270 general practitioners from the Greater Rotterdam area in The

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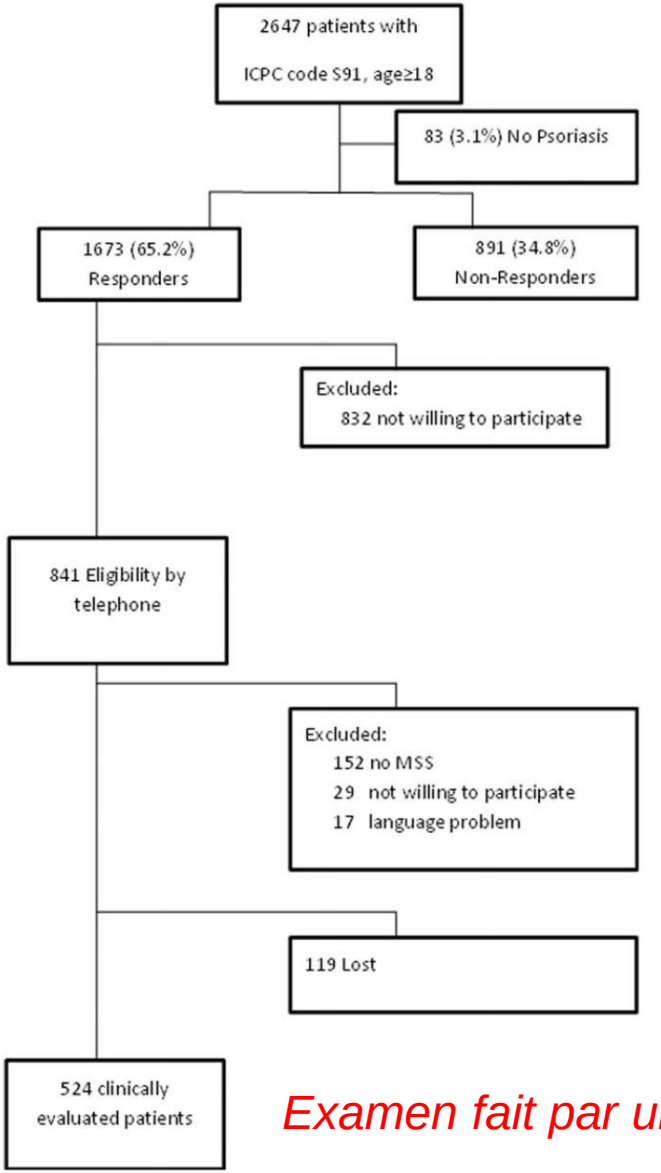
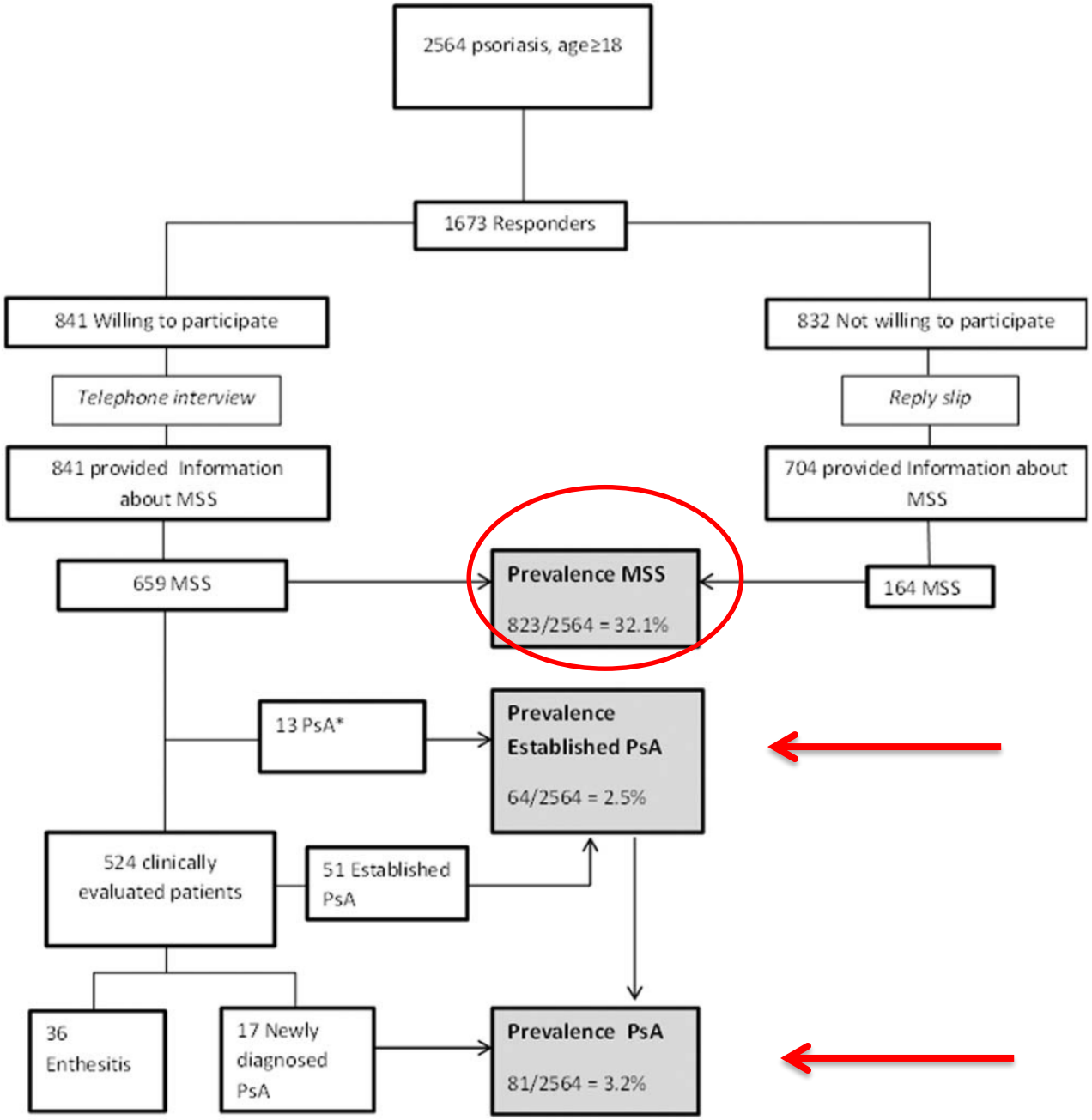
Base de donnée patients Pso:
97 MG

Douleurs articulaires,
tendineuses ou rachidienne ?



Examen fait par un rhumatologue

Figure 1. Recruitment of the psoriasis patients in primary care. ICPC = International Classification of Primary Care; MSS = musculoskeletal symptoms.


2564 psoriasis, age≥18
1673 Responders
841 Willing to participate
832 Not willing to participate
Telephone interview
Reply slip
841 provided Information about MSS
704 provided Information about MSS
659 MSS
Prevalence MSS
823/2564 = 32.1%
164 MSS
13 PsA*
Prevalence Established PsA
64/2564 = 2.5%
524 clinically evaluated patients
51 Established PsA
36 Enthesitis
17 Newly diagnosed PsA
Prevalence PsA
81/2564 = 3.2%

EXTENDED REPORT

Analysis of periarticular bone changes in patients with cutaneous psoriasis without associated psoriatic arthritis

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Handling editor Tore K Kvien

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ABSTRACT

Objectives To search for structural bone changes in the joints of psoriasis patients without psoriatic arthritis (PsA).

Methods 55 psoriasis patients without any current or past symptoms of arthritis or enthesitis and 47 healthy controls were examined by high-resolution peripheral quantitative CT scans of the metacarpophalangeal joints. Number, size and exact localisation of erosions and enthesiophytes were recorded by analysing axial scans of the metacarpal heads and phalangeal bases and were confirmed in additional coronal and/or sagittal sections. In addition, we collected demographic and clinical data including subtype, duration and severity of psoriasis.

Results Psoriasis patients showed a larger and significantly increased number of enthesiophytes (total number 306; mean±SD/patient 5.62±3.30) compared with healthy controls (total number 138; mean±SD/patient 3.04±1.81, p<0.001). Enthesiophytes were typically found at the dorsal and palmar sides of the metacarpal heads where functional entheses related to extensor and flexor tendons are localised. Bone erosions were rare and not significantly different between psoriasis patients and healthy controls. If present, erosions were almost exclusively found at the radial side of the second metacarpal head in both psoriasis patients and healthy controls.

Conclusions Psoriasis patients without PsA show substantial signs of enthesiophyte formation compared with healthy controls. These changes represent new bone formation at mechanically exposed sites of the joint and substantiate the concept of the existence of a 'Deep Koebner Phenomenon' at enthesial sites in psoriasis patients.

INTRODUCTION

The spectrum of psoriatic disease comprises three major entities, skin disease, psoriatic arthritis (PsA) and psoriatic nail disease.[1] Skin disease is substantially more common (2%–3%) than PsA, whose prevalence is considered ranging from 0.3% to 1.0%.[2] Some 39% of patients with psoriasis have PsA in hospital settings and some 11% in the community.[3 4] In the majority of cases (up to 60%),[5] skin disease is reported to predate arthritis while in the remaining cases it can precede or concomitantly start with skin disease. Diagnosis of PsA requires the presence of clinical signs of musculoskeletal disease, such as arthritis, enthesitis or inflammatory back pain. Also, Classification Criteria for Psoriatic Arthritis (CASPAR) criteria for the classification of PsA[6] explicitly mention that for classification of PsA, clinical signs of inflammation have to be present. Whereas the term PsA is reserved for clinical manifestations of psoriatic disease affecting the musculoskeletal system, discrete subclinical changes in the joints and the entheses may occur before the onset of PsA and/or may affect a larger proportion of patients with psoriatic skin disease. This concept would also suggest an even tighter link between the skin and the joints in psoriatic disease, representing two organ manifestations of the same underlying disease process. Support for this notion comes from imaging studies providing evidence for the existence of subclinical inflammatory changes in patients with psoriatic skin disease using MRI or high-resolution ultrasound scans.[7–9] It has to be defined, however, if such changes really impact on joint architecture in psoriasis patients. Furthermore, in contrast to rheumatoid arthritis (RA), inflammation may not be the only responsible factor for articular changes in psoriatic disease but biomechanical factors related to entheseal stress may substantially contribute to the disease as well.

That PsA is accompanied by changes of the joint structure is well described.[10–13] However, whether such changes are found even in patients with psoriatic skin disease without PsA is currently partially explored.[14] One key aspect of structural changes in PsA is new bone formation, which strikingly differs from what is observed in RA and particularly affects the entheseal regions of the joints (enthesiophytes).[13] Recent work has identified entheseal pathology as a specific part of the PsA disease process. Entheses may represent the primary site of musculoskeletal changes in psoriasis patients developing PsA. In particular, the understanding of entheseal structures as an organ with a high degree of structural and functional organisation and the coining of the term 'synovio-entheseal complex' have extended our view on PsA.[15–17] These concepts are of potential importance in searching for the discrete changes of the joints in patients with psoriatic skin disease.

The aim of this work was to investigate the skeletal micro-architecture of the joints in psoriasis patients with skin disease but no evidence for PsA

To cite: Simon D, Faustini F, Kleyer A, *et al*. *Ann Rheum Dis* 2016;**75**:660–666.

Base de P1
Tête MCP

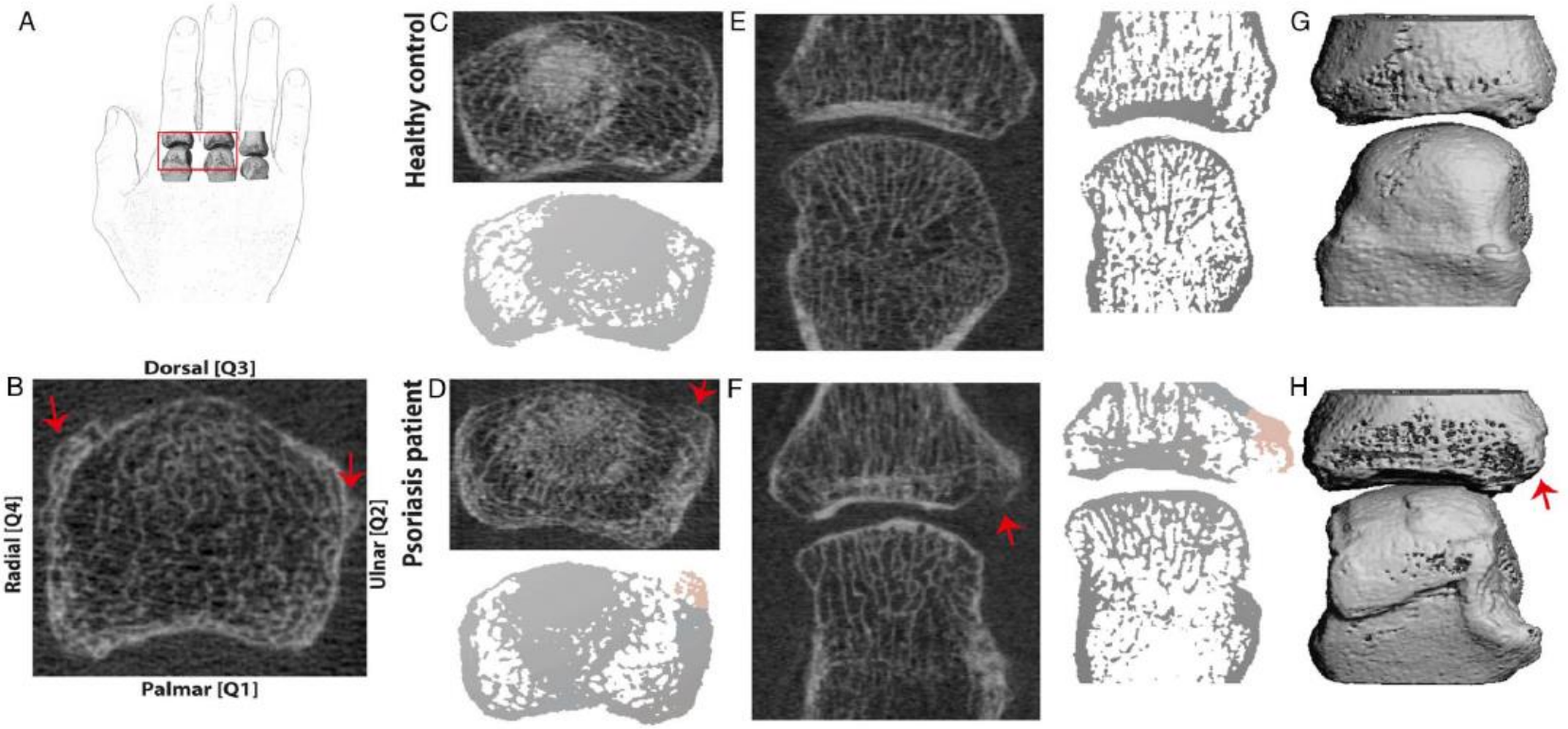
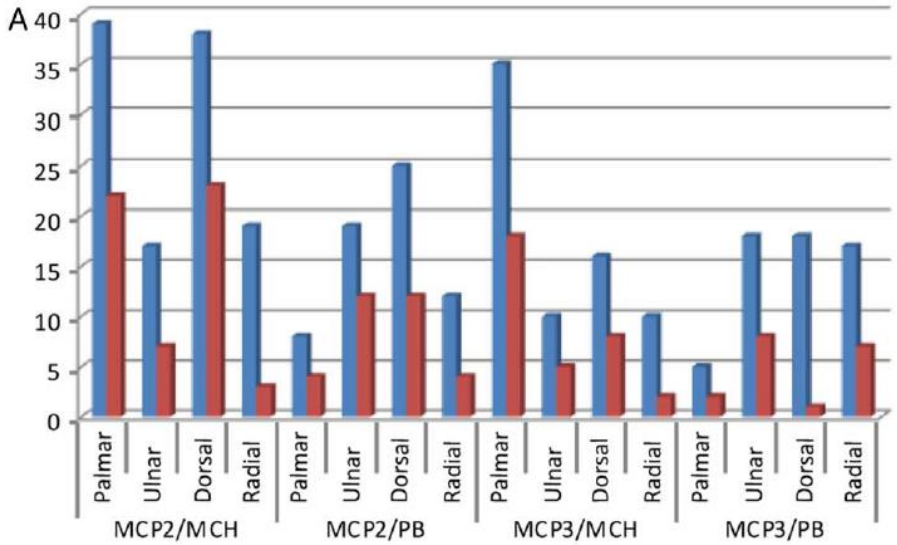


Figure 1 Region of interest (ROI) and examples of periarticular bone changes in psoriasis patients and healthy controls. (A) 3D view of the ROI. (B) Distribution of the axial quadrants and examples of enthesiophytes (red arrows). (C and D) Axial, (E and F) sagittal and (G and H) 3D reconstruction (dorsal view) of a metacarpophalangeal joint in a healthy control (upper row, C, E and G) and a psoriasis patient (lower row, D, F and H) showing an enthesiophyte (red arrows) at the insertion of the collateral ligament at the phalangeal base.

Table 1 Demographic and disease specific characteristics

	Psoriasis patients	Healthy controls
Demographic characteristics		
N of subjects	55	47
Sex (male/female)	35/20	24/23
Age (years)	49.0±11.4	45.7±12.9
Height (cm)	174.2±9.3	174.0±10.4
Weight (kg)	84.9±20.1	78.0±18.4
BMI	27.9±5.6	25.0±4.7
Smokers N (%)	16 (29.1)	11 (23.4)
Disease specific characteristics		
Duration of skin psoriasis (years)	15.2±15.4	–
PASI	6.2±8.0	–
DLQI	6.3±6.1	–
Phenotypic characteristics		
Psoriasis vulgaris N (%)	40 (72.7)	–
Other subtypes N (%)	15 (27.3)	–
Nail involvement N (%)	28 (50.9)	–
Scalp involvement N (%)	16 (29.1)	–
Other clinical characteristics		
ACPA positive N (%)	0	–
RF positive N (%)*	4 (7.3)	–
C reactive protein (mg/L)†	3.8±4.6	–
Treatment modalities		
No current treatment N (%)	15 (27.3)	–
Topical therapies N (%)	25 (45.5)	–
Fumaric acid N (%)	11 (20.0)	–
Systemic agents N (%)	9 (16.4)	–
TNF-i N (%)	3 (5.5)	–
Ustekinumab N (%)	1 (1.8)	–



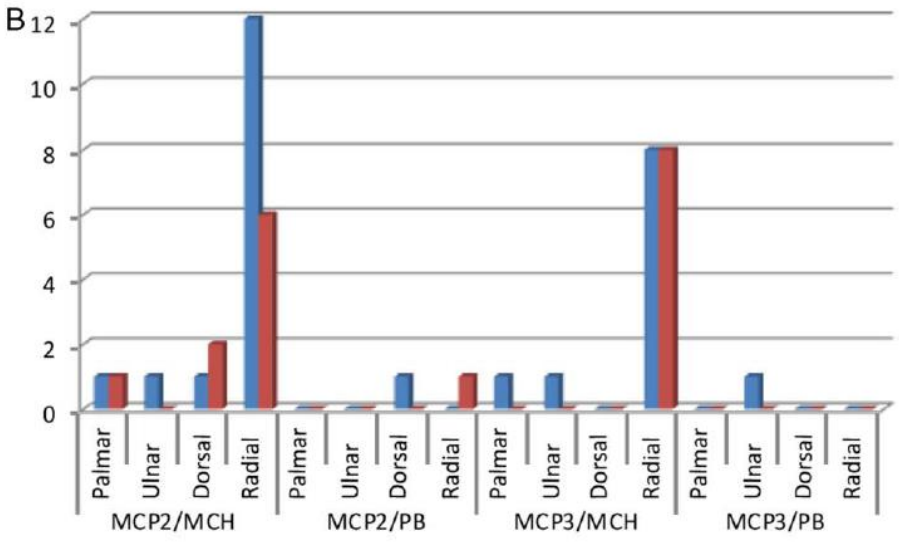


Table 2 Periarticular bone changes in the psoriasis patients and healthy controls

	Psoriasis patients	Healthy controls	p Value*
Number of subjects	55	47	
Erosions total, N	27	18	
Erosions/patient, N	0.5	0.4	
Erosions, mean±SD	0.49±0.94	0.39±0.65	0.99
Metacarpal head 2 N (%)	15 (55)	9 (50)	
Phalangeal base 2 N (%)	1 (4)	1 (6)	
Metacarpal head 3 N (%)	10 (37)	8 (44)	
Phalangeal base 3 N (%)	1 (4)	0 (0)	
Enthesiophytes total, N	306	138	
Enthesiophytes/patient, N	6	3	
Enthesiophytes, mean±SD	5.62±3.30	3.04±1.81	<0.001
Metacarpal head 2, N (%)	113 (37)	55 (40)	
Phalangeal base 2, N (%)	64 (21)	32 (24)	
Metacarpal head 3, N (%)	71 (23)	33 (23)	
Phalangeal base 3, N (%)	58 (19)	18 (13)	

EXTENDED REPORT

European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update

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ABSTRACT

Background Since the publication of the European League Against Rheumatism recommendations for the pharmacological treatment of psoriatic arthritis (PsA) in 2012, new evidence and new therapeutic agents have emerged. The objective was to update these recommendations.

Methods A systematic literature review was performed regarding pharmacological treatment in PsA. Subsequently, recommendations were formulated based on the evidence and the expert opinion of the 34 Task Force members. Levels of evidence and strengths of recommendations were allocated.

Results The updated recommendations comprise 5 overarching principles and 10 recommendations, covering pharmacological therapies for PsA from non-steroidal anti-inflammatory drugs (NSAIDs), to conventional synthetic (csDMARD) and biological (bDMARD) disease-modifying antirheumatic drugs, whatever their mode of action, taking articular and extra-articular manifestations of PsA into account, but focusing on musculoskeletal involvement. The overarching principles address the need for shared decision-making and treatment objectives. The recommendations address csDMARDs as an initial therapy after failure of NSAIDs and local therapy for active disease, followed, if necessary, by a bDMARD or a targeted synthetic DMARD (tsDMARD). The first bDMARD would usually be a tumour necrosis factor (TNF) inhibitor. bDMARDs targeting interleukin (IL)12/23 (ustekinumab) or IL-17 pathways (secukinumab) may be used in patients for whom TNF inhibitors are inappropriate and a tsDMARD such as a phosphodiesterase 4-inhibitor (apremilast) if bDMARDs are inappropriate. If the first bDMARD strategy fails, any other bDMARD or tsDMARD may be used.

Conclusions These recommendations provide stakeholders with an updated consensus on the pharmacological treatment of PsA and strategies to reach optimal outcomes in PsA, based on a combination of evidence and expert opinion.

INTRODUCTION

The management of psoriatic arthritis (PsA) rests on non-pharmacological and pharmacological measures. The so-called disease-modifying antirheumatic drugs (DMARDs) are commonly characterised by their capacity to reduce or reverse signs and symptoms, disability, impairment of quality of life, inability to work and progression of joint damage and thus can interfere with the entire disease process.[1 2] There are three major classes of DMARDs, loosely grouped according to different mechanisms of action: conventional synthetic (cs) DMARDs such as methotrexate (MTX), sulfasalazine and leflunomide; biological agents (bDMARDs) and targeted synthetic (ts) DMARDs, such as phosphodiesterase (PDE) inhibitors or JAK-inhibitors such as tofacitinib.[3] Tumour necrosis factor inhibitors (TNFis) have been shown to be efficacious in PsA.[4] In contrast with rheumatoid arthritis (RA), until recently only TNFis were available as therapeutic agents in PsA, if csDMARDs failed to exhibit efficacy. Recently however, novel therapies with utility in PsA have emerged. PsA is heterogeneous by virtue of its broad phenotypes of musculoskeletal involvement (peripheral arthritis, dactylitis, enthesitis and axial disease), and its spectrum of extra-articular manifestations, especially skin and nails, and other organ involvement.[5–7] csDMARDs and bDMARDs have differential effects on the various disease manifestations.

With several therapeutic options available and insufficient information on differential efficacy and safety, treatment decisions in clinical practice remain challenging. Therefore, the European League Against Rheumatism (EULAR) developed recommendations for the management of PsA with these drugs in 2011.[8] These recommendations were based on two systematic literature reviews (SLRs)[4] and focused on indications for the use of and suggestions for differential and strategic employment of csDMARDs and bDMARDs based on treatment targets and disease risk assessment,

AMM

Rhumatisme psoriasique
STELARA, seul ou en association avec le méthotrexate (MTX), est indiqué dans le traitement du rhumatisme psoriasique actif chez l'adulte lorsque la réponse à un précédent traitement de fond antirhumatismal non-biologique (DMARD) a été inadéquate.

AMM
Otezla, seul ou en association avec un traitement de fond antirhumatismal (DMARD), est indiqué dans le traitement du rhumatisme psoriasique (RP) actif chez les patients adultes ayant présenté une réponse insuffisante ou une intolérance à un traitement de fond antérieur.

AMM
PsA :« Cosentyx, seul ou en association avec le méthotrexate (MTX), est indiqué dans le traitement du rhumatisme psoriasique actif chez l'adulte lorsque la réponse aux traitements de fond antirhumatismaux (DMARDs) antérieurs a été inadéquate (voir rubrique 5.1). »

ARD Online First, published on August 26, 2016 as 10.1136/annrheumdis-2016-209709

OPEN ACCESS

EXTENDED REPORT

Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1

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Handling editor Tore K Kvien

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2016-209709).

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ABSTRACT

Objective To assess the safety and efficacy of ixekizumab, a monoclonal antibody that inhibits interleukin-17A, in a double-blind phase III trial enrolling patients with active psoriatic arthritis (PsA).

Methods Patients naive to biologic therapy with active PsA were randomised to subcutaneous injections of placebo (N=106), adalimumab 40 mg once every 2 weeks (active reference; N=101), ixekizumab 80 mg once every 2 weeks (IXEQ2W) (N=103), or ixekizumab 80 mg once every 4 weeks (IXEQ4W) (N=107). Both ixekizumab regimens included a 160-mg starting dose. The primary objective was to assess the superiority of IXEQ2W or IXEQ4W versus placebo as measured by the proportion of patients achieving an American College of Rheumatology 20 (ACR20) response at week 24.

Results Significantly more patients treated with ixekizumab achieved an ACR20 response with IXEQ2W (62.1%) or IXEQ4W (57.9%) than placebo (30.2%) ($p \leq 0.001$; non-responder imputation method). Disease activity and functional disability were significantly improved with both ixekizumab doses versus placebo at weeks 12 and 24, and there was significantly less progression of structural damage at week 24 ($p \leq 0.01$). Clearance of plaque psoriasis was greater with ixekizumab than placebo ($p \leq 0.001$). Efficacy results with adalimumab, the active reference arm, showed significant improvements versus placebo. Treatment-emergent adverse events were more frequent with ixekizumab (65.7–66.4%) and adalimumab (64.4%) than placebo (47.2%) ($p<0.05$).

Conclusions In biologic-naive patients with active PsA, ixekizumab treatment resulted in improvements in disease activity and physical function, as well as in the inhibition of structural damage progression. Overall, adverse events were more frequent in all active groups compared with placebo.

Trial registration number NCT01695239; EudraCT2011-002326-49; Results.

INTRODUCTION

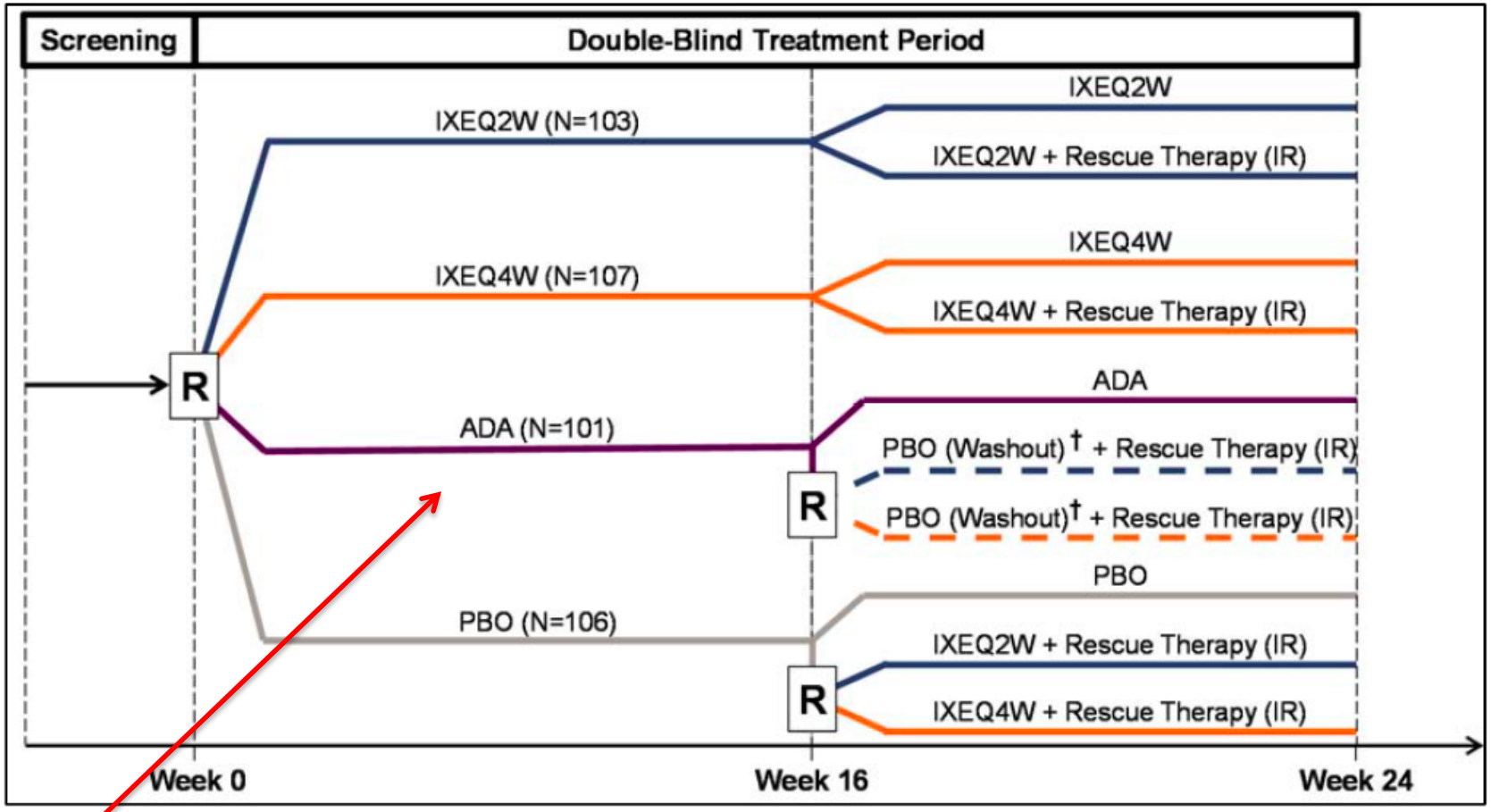
Psoriatic arthritis (PsA) is a chronic, systemic, immune-mediated, inflammatory arthritis commonly associated with plaque psoriasis, joint damage, dactylitis, enthesitis and axial involvement.[1 2] PsA can be progressive and destructive, resulting in physical deformities, impaired function, decreased quality of life and increased mortality.[3 4] The cytokine interleukin (IL)-17A promotes joint inflammation and damage by triggering the activation and trafficking of immune cells, inducing proinflammatory cytokines and chemokines, acting as a chemoattractant to neutrophils and monocytes, and stimulating release of matrix metalloproteases and receptor activator of nuclear factor kappa-B ligand, which contribute to cartilage and bone destruction, respectively.[5] Increased numbers of IL-17A-producing cells are present in the peripheral blood, synovial tissue and fluid, and skin plaques of patients with PsA;[6–11] the concentration of IL-17A-producing cells correlates with disease activity.[10] Based on these findings, specific inhibition of IL-17A represents an emerging targeted approach to PsA management.[12 13]

Ixekizumab, a recombinant, high-affinity, humanised, immunoglobulin G4κ monoclonal antibody selectively binds and neutralises IL-17A. The safety and efficacy of ixekizumab in patients with active PsA not previously treated with biologic agents are under investigation in a phase III study (SPIRIT-P1). Here we report the results from the 24-week, placebo-controlled and active-controlled, double-blind period of this study.

METHODS

Study design and patient population

The SPIRIT-P1 study (NCT01695239, EudraCT 2011-002326-49) is a 3-year, phase III, randomised, double-blind, placebo-controlled and active-controlled clinical trial comparing two regimens of ixekizumab and an active reference arm adalimumab (Humira; AbbVie) at the approved dose and regimen to treatment with placebo in patients not previously treated with biologic agents for plaque psoriasis or PsA. The double blind period of the study occurred in the first 24 weeks. Enrolled



Abbreviations: ADA=40 mg adalimumab every 2 weeks (active reference arm); IR=Inadequate Responder; IXEQ2W=80 mg ixekizumab every 2 weeks; IXEQ4W=80 mg ixekizumab every 4 weeks; PBO=placebo every 2 weeks; R=randomization.

The primary efficacy end point was the proportion of patients achieving an American College of Rheumatology (ACR) 20 response at week 24 versus placebo.

Table 1 Baseline characteristics of the patients according to treatment group

	Placebo N=106	IXEQ4W N=107	IXEQ2W N=103	Adalimumab 40 mg Q2W* N=101	Total N=417
Age (years), mean (SD)	50.6 (12.3)	49.1 (10.1)	49.8 (12.6)	48.6 (12.4)	49.5 (11.9)
Male, n (%)	48 (45.3)	45 (42.1)	48 (46.6)	51 (50.5)	192 (46.0)
Weight (kg), mean (SD)	83.8 (19.6)	85.5 (23.0)	81.6 (17.5)	91.6 (21.9)†	85.6 (20.9)
BMI (kg/m^2), mean (SD)	29.2 (6.3)	30.2 (8.4)	28.6 (6.6)	32.1 (11.4)‡	30 (8.5)
Race, n (%)					
White	99 (93.4)	102 (95.3)	96 (93.2)	95 (94.1)	392 (94.0)
Asian	5 (4.7)	2 (1.9)	5 (4.9)	3 (3.0)	15 (3.6)
American Indian or Alaska native	2 (1.9)	2 (1.9)	2 (1.9)	3 (3.0)	9 (2.2)
Other	0	1 (0.9)	0	0	1 (0.2)
Time since psoriatic arthritis diagnosis (years), mean (SD)	6.3 (6.9)	6.2 (6.4)	7.2 (8.0)	6.9 (7.5)	6.7 (7.2)
Time since psoriasis diagnosis (years), mean (SD)	16.0 (13.8)	16.5 (13.8)	17.0 (14.0)	15.7 (12.7)	16.3 (13.5)

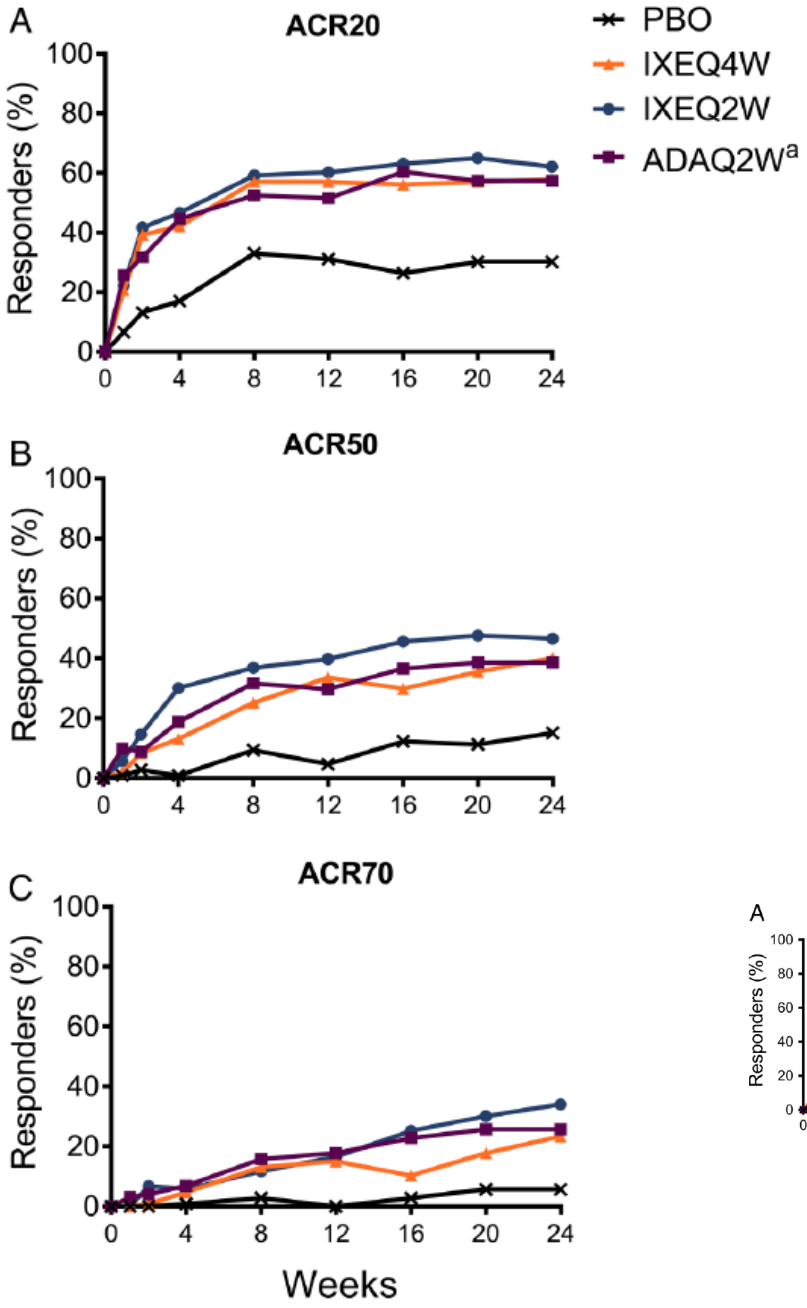
- âge moyen était de 49,5 ans,
- 46,0% étaient des hommes
- 94% caucasien
- IMC statistiquement supérieur dans le groupe adalimumab
- en moyenne 6 ans que le rhumatisme articulaire était connu et 16ans pour le diagnostic que psoriasis

Mease PJ, *et al*. *Ann Rheum Dis* 2016;**0**:1–9. doi:10.1136/annrheumdis-2016-209709

Table 2 Comparison of efficacy during the 24 weeks of placebo-controlled therapy

	Placebo		IXEQ4W		IXEQ2W		Adalimumab 40 mg Q2W*	
	12 weeks	24 weeks	12 weeks	24 weeks	12 weeks	24 weeks	12 weeks	24 weeks
Responder rate:								
	N=106	p<0,001	N=107		N=103		N=101	
ACR20, %	31.1	30.2	57.0†	57.9†	60.2†	62.1†	51.5‡	57.4†
ACR50, %	4.7	15.1	33.6†	40.2†	39.8†	46.6†	29.7†	38.6†
ACR70, %	0	5.7	15.0	23.4†	16.5	34.0†	17.8	25.7†
	N=92		N=100		N=90		N=89	
HAQ-DI MCID, %§	29.3	26.1	49.0‡	49.0†	64.4†	57.8†	49.4‡	49.4†
	N=28		N=39		N=26		N=18	
LDI-B (0), %¶,**	53.6	25.0	74.4	79.5†	69.2	76.9†	61.1	77.8†
	N=57		N=68		N=57		N=54	
LEI (0), %¶,††	28.1	19.3	27.9	42.6‡	47.4‡‡	38.6§§	35.2	33.3
	N=67		N=73		N=59		N=68	
PASI 75, %¶¶	7.5	10.4	75.3†	71.2†	69.5†	79.7†	33.8†	54.4†
PASI 90, %¶¶	1.5	6.0	52.1†	56.2†	57.6†	67.8†	22.1‡	36.8†
PASI 100, %¶¶	1.5	3.0	31.5†	42.5†	40.7†	52.5†	14.7§§	23.5‡
	N=41		N=52		N=41		N=37	
sPGA (0, 1), %***	7.3	17.1	75.0†	65.4†	80.5†	73.2†	45.9†	62.2†
sPGA (0), %***	2.4	2.4	30.8‡	38.5‡	36.6‡	39.0‡	10.8	18.9‡‡
	N=74		N=70		N=74		N=71	
NAPSI (0), %†††	8.1	18.9	20.0‡‡	25.7	27.0‡	36.5§§	19.7‡‡	39.4‡

Mease PJ, *et al*. *Ann Rheum Dis* 2016;**0**:1–9. doi:10.1136/annrheumdis-2016-209709


A
ACR20
Responders (%)
100
80
60
40
20
0
0
4
8
12
16
20
24
PBO
IXEQ4W
IXEQ2W
ADAQ2W[a]
B
ACR50
Responders (%)
C
ACR70
Responders (%)
Weeks

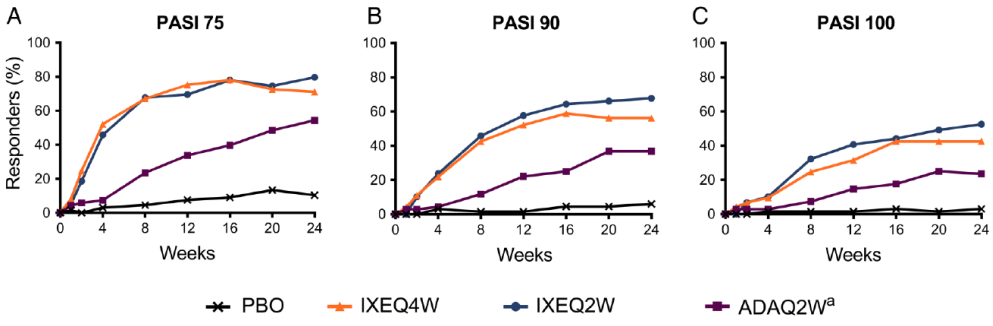

A
PASI 75
B
PASI 90
C
PASI 100
Responders (%)
Weeks
PBO
IXEQ4W
IXEQ2W
ADAQ2W[a]

Table 3 Effect on structural disease progression

		Placebo N=106	IXEQ4W N=107	IXEQ2W N=103	Adalimumab 40 mg Q2W* N=101
LS mean change from baseline mTSS (SE)†	Week 16	0.36 (0.07)	0.13 (0.07)‡	0.06 (0.07)§	0.12 (0.08)‡
	Week 24	0.49 (0.09)	0.17 (0.08)§	0.08 (0.08)¶	0.10 (0.09)¶
Percentage of patients with change in mTSS at week 24	≤0	72.0	83.0	83.5	91.6¶
	≤0.5	77.4	89.0**	94.8¶	95.8¶
	≤0.95	83.9	94.0‡	96.9§	95.8§

Tolérance

AEs of special interest††, n (%)	36 (34.0)	52 (48.6)§	56 (54.9)†	45 (44.6)
Infection	27 (25.5)	30 (28.0)	24 (23.5)	26 (25.7)
Any candida infection	0	1 (0.9)	1 (1.0)	0
Active or reactivated tuberculosis	0	0	0	0
Injection site reactions	5 (4.7)	26 (24.3)**	27 (26.5)**	6 (5.9)
Hepatic event	7 (6.6)	5 (4.7)	9 (8.8)	13 (12.9)
Allergic reaction/hypersensitivity	3 (2.8)	2 (1.9)	5 (4.9)	5 (5.0)
Cytopenia (all types)	6 (5.7)	1 (0.9)	4 (3.9)	4 (4.0)
Neutropenia	0	0	1 (1.0)	0
Depression	0	2 (1.9)	1 (1.0)	1 (1.0)
Cerebrocardiovascular event	0	0	0	3 (3.0)
Malignancy	1 (0.9)	0	0	1 (1.0)

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The Efficacy and Safety of Clazakizumab, an Anti–Interleukin-6 Monoclonal Antibody, in a Phase IIb Study of Adults With Active Psoriatic Arthritis

Philip J. Mease,[1] Alice B. Gottlieb,[2] Alberto Berman,[3] Edit Drescher,[4] Jun Xing,[5] Robert Wong,[5] and Subhashis Banerjee[5]

Objective. **To evaluate the efficacy of clazakizumab, a monoclonal antibody with high affinity and specificity for the interleukin-6 (IL-6) cytokine, in psoriatic arthritis (PsA).**

Methods. **In this randomized, double-blind, placebo-controlled, dose-ranging study (ClinicalTrials.gov identifier: NCT01490450), patients with active PsA and an inadequate response to nonsteroidal antiinflammatory drugs were randomized (1:1:1:1) to receive subcutaneous placebo or clazakizumab 25 mg, 100 mg, or 200 mg every 4 weeks, with or without methotrexate. The primary end point was the response rate according to the American College of Rheumatology 20% criteria for improvement (ACR20) at week 16, with secondary efficacy end points at weeks 16 and 24.**

Results. **A total of 165 patients were randomized. At week 16, the ACR20 response rate was significantly higher with clazakizumab 100 mg versus placebo (52.4% versus 29.3%; $P = 0.039$). ACR20 response rates at week 16 were 46.3% with clazakizumab 25 mg ($P = 0.101$ versus placebo) and 39.0% with clazakizumab 200 mg ($P = 0.178$ versus placebo). ACR50/ACR70 response rates were numerically higher with clazakizumab versus placebo at weeks 16 and 24. Compared with placebo, clazakizumab treatment significantly improved musculoskeletal manifestations (joint signs and symptoms, enthesitis, and dactylitis), with minimal improvements in skin disease, without clear evidence of a dose response. Clazakizumab was well tolerated.**

Conclusion. **This is the first clinical trial of an IL-6–targeted therapy in PsA. Clazakizumab may be an effective treatment option for musculoskeletal aspects of PsA, but because of the lack of a dose response in this study, further studies are required to confirm the appropriate dose. The safety profile is consistent with the pharmacology of IL-6 blockade and prior clinical experience with this antibody in rheumatoid arthritis.**

Although the pathogenesis of psoriatic arthritis (PsA) is not fully understood, the pleiotropic inflammatory cytokine interleukin-6 (IL-6), which has a known role in synovitis, local and systemic inflammation, and the promotion of bone resorption in rheumatoid arthritis (RA) (1), may play a role. Serum levels of IL-6 are increased in patients with psoriasis, and the up-regulation of

ClinicalTrials.gov identifier: NCT01490450.
Supported by Bristol-Myers Squibb.

[1]Philip J. Mease, MD: Swedish Medical Center and University of Washington, Seattle; [2]Alice B. Gottlieb, MD, PhD: Tufts Medical Center and Tufts University School of Medicine, Boston, Massachusetts; [3]Alberto Berman, MD: Centro Médico Privado de Reumatología, Tucuman, Argentina; [4]Edit Drescher, MD: Csolnoky Ferenc Hospital, Veszprém, Hungary; [5]Jun Xing, PhD, Robert Wong, MD, Subhashis Banerjee, MD: Bristol-Myers Squibb, Princeton, New Jersey.

Dr. Mease has received consulting fees, speaking fees, and/or honoraria from AbbVie, Biogen Idec, Celgene, Crescendo, Genentech, Janssen, Lilly, Merck, Novartis, and UCB (less than $10,000 each) and from Amgen, Bristol-Myers Squibb, and Pfizer (more than $10,000 each) and research grants from AbbVie, Amgen, Biogen Idec, Bristol-Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB. Dr. Gottlieb has received consulting fees, speaking fees, and/or honoraria from Abbott/AbbVie, Actelion, Akros, Amgen, Astellas, Beiersdorf, Bristol-Myers Squibb, Canfite, Catabasis, Celgene, Centocor/Janssen, Coronado, CSL Behring Biotherapies for Life, DermiPsor, DUSA Pharmaceuticals, Genentech, GlaxoSmithKline, Incyte, Karyopharm Therapeutics, Lilly, Meiji Seika Pharma, Novartis, Novo Nordisk, Pfizer, Sanofi-Aventis, Teva Pharmaceuticals, UCB, Vertex, and XenoPort (less than $10,000 each) and research grants (to Tufts Medical Center) from Abbott/AbbVie, Amgen, Celgene, Centocor/Janssen, Daavlin, Lilly, Merck, Novartis, Pfizer, and XenoPort. Dr. Berman has received research grants from Bristol-Myers Squibb. Drs. Xing, Wong, and Banerjee own stock or stock options in Bristol-Myers Squibb.

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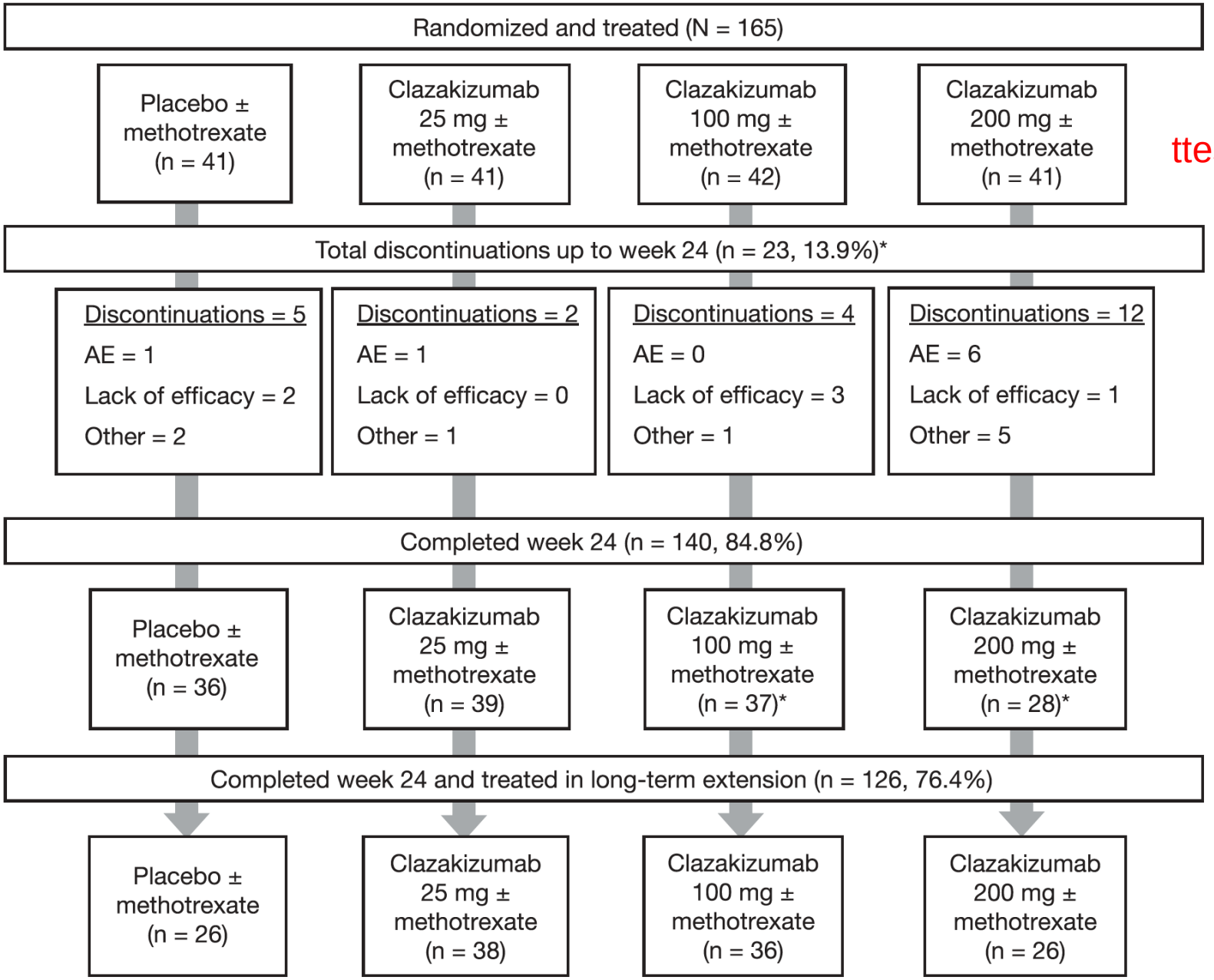
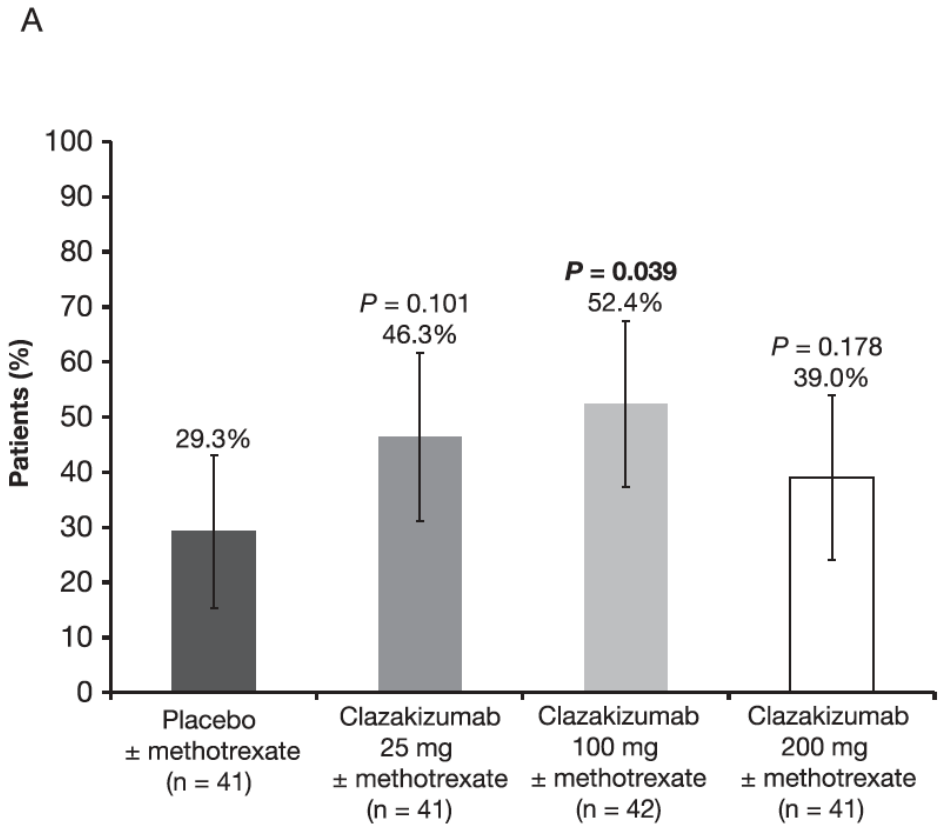
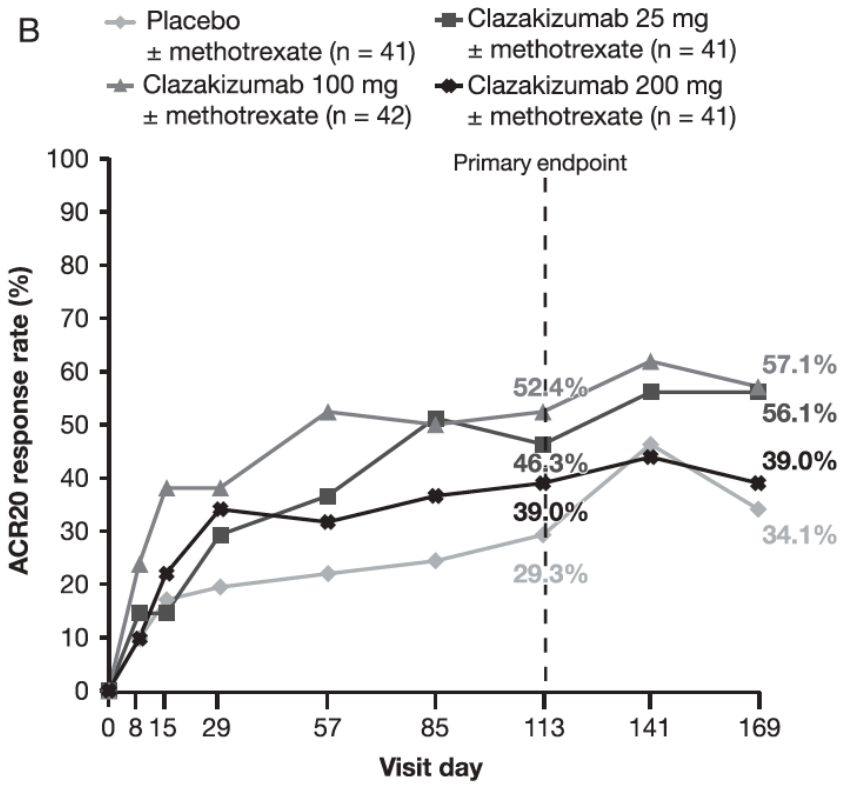


ttes/4s

The primary end point was the proportion of patients with a response according to the American College of Rheumatology 20% improvement criteria (ACR20) at 16 weeks





Pas d'effet dose

Skin disease. At week 24, PASI75 response rates were 12.2% for placebo, 19.5% for clazakizumab 25 mg, 28.6% for clazakizumab 100 mg, and 12.2% for clazakizumab 200 mg.

Table 3. Summary of safety at week 24 in the patients with psoriatic arthritis treated with placebo or clazakizumab*

	Placebo (n = 41)	Clazakizumab 25 mg (n = 41)	Clazakizumab 100 mg (n = 42)	Clazakizumab 200 mg (n = 41)
Deaths	0 (0)	0 (0)	0 (0)	0 (0)
SAEs	2 (4.9)	2 (4.9)	2 (4.8)	4 (9.8)
Related SAEs	0 (0)	0 (0)	0 (0)	1 (2.4)
Discontinuations due to SAEs	2 (4.9)†	0 (0)	0 (0)	1 (2.4)‡
AEs	27 (65.9)	30 (73.2)	32 (76.2)	34 (82.9)
Related AEs	9 (22.0)	18 (43.9)	18 (42.9)	26 (63.4)
Discontinuations due to AEs	3 (7.3)	1 (2.4)	2 (4.8)	7 (17.1)

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Ankylosing Spondylitis and Axial Spondyloarthritis

Joel D. Taurog, M.D., Avneesh Chhabra, M.D., and Robert A. Colbert, M.D., Ph.D.

N ENGL J MED 374;26 NEJM.ORG JUNE 30, 2016

REVIEWS

Genetics of ankylosing spondylitis—insights into pathogenesis

Matthew A. Brown, Tony Kenna and B. Paul Wordsworth

Brown, M. A. *et al. Nat. Rev. Rheumatol.* advance online publication 6 October 2015;

Recommandations ACR SA 2015

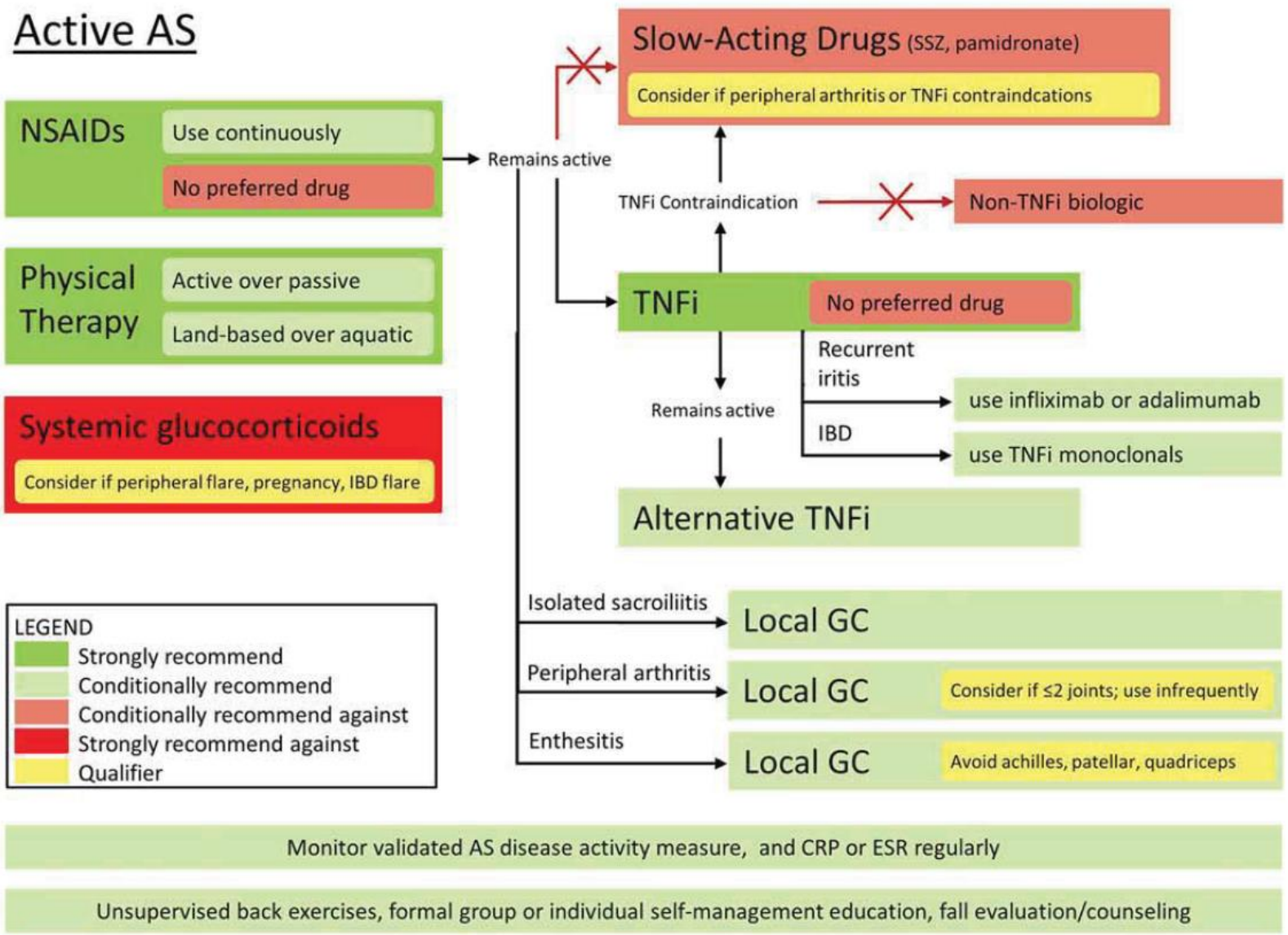
SPECIAL ARTICLE

American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis

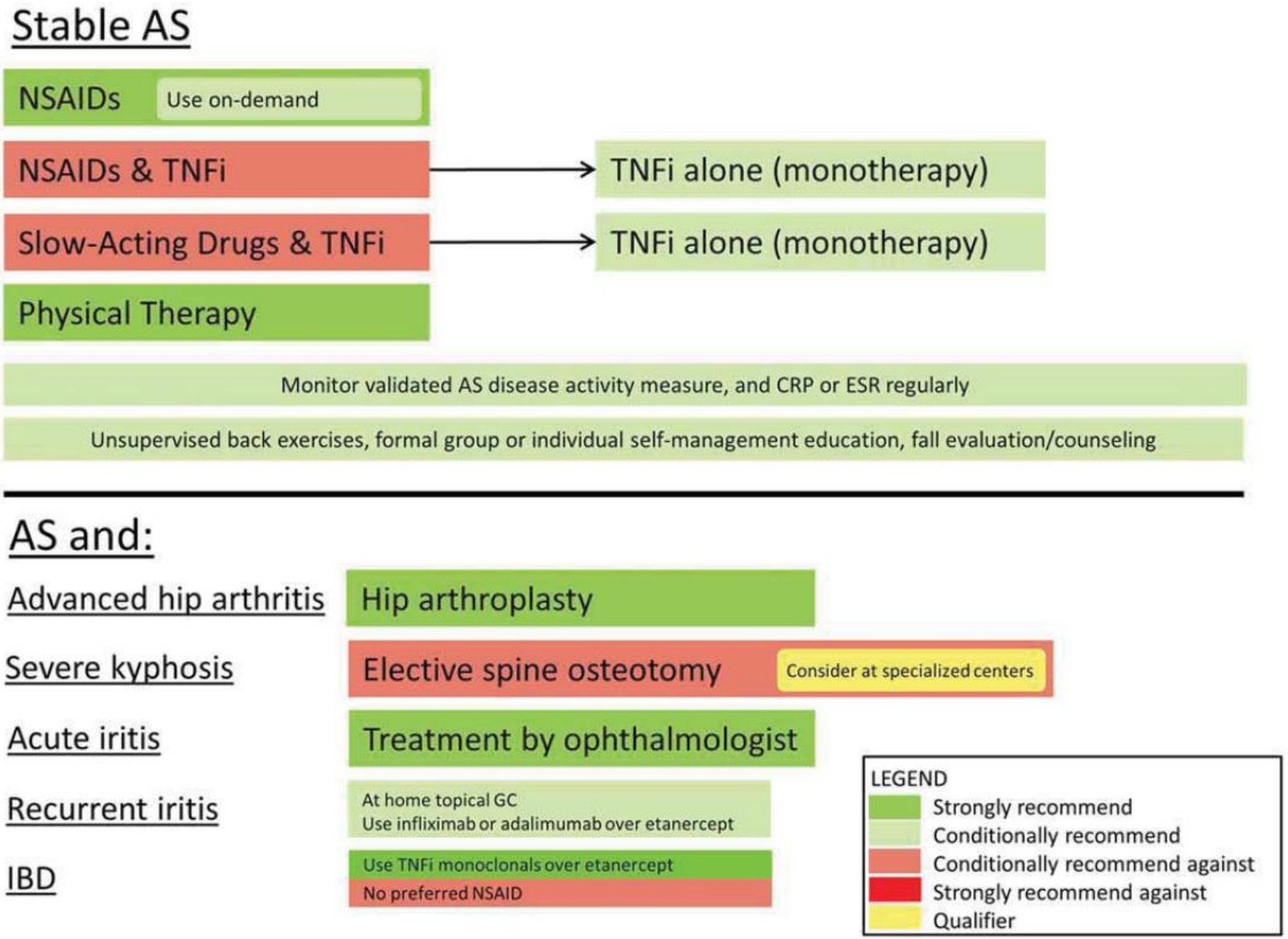
Michael M. Ward,[1] Atul Deodhar,[2] Elie A. Akl,[3] Andrew Lui,[4] Joerg Ermann,[5] Lianne S. Gensler,[4] Judith A. Smith,[6] David Borenstein,[7] Jayme Hiratzka,[2] Pamela F. Weiss,[8] Robert D. Inman,[9] Vikas Majithia,[10] Nigil Haroon,[9] Walter P. Maksymowych,[11] Janet Joyce,[12] Bruce M. Clark,[13] Robert A. Colbert,[1] Mark P. Figgie,[14] David S. Hallegua,[15] Pamela E. Prete,[16] James T. Rosenbaum,[17] Judith A. Stebulis,[18] Filip van den Bosch,[19] David T. Y. Yu,[20] Amy S. Miller,[12] John D. Reveille,[21] and Liron Caplan[22]

Submitted for publication December 16, 2014; accepte revised form July 21, 2015.

Recommandations ACR SA 2015



Recommandations ACR SA 2015



A Randomized, Double-Blind, Placebo-Controlled, Sixteen-Week Study of Subcutaneous Golimumab in Patients With Active Nonradiographic Axial Spondyloarthritis

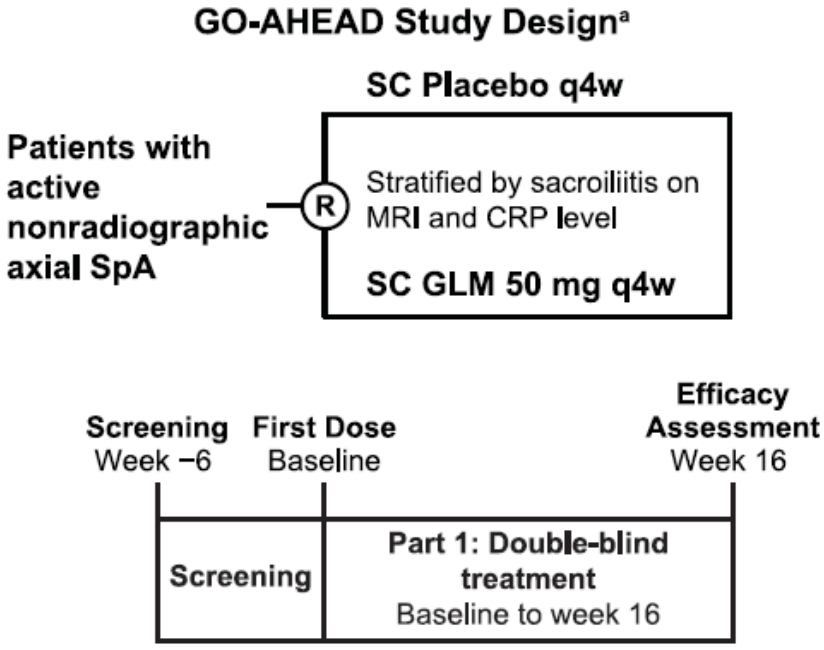
J. Sieper,[1] D. van der Heijde,[2] M. Dougados,[3] W. P. Maksymowych,[4] B. B. Scott,[5] J. A. Boice,[5] Y. Berd,[5] G. Bergman,[5] S. Curtis,[5] A. Tzontcheva,[5] S. Huyck,[5] and H. H. Weng[5]

- ERC GO-AHEAD : 2012-2014

SpA ASAS + < 5 ans, en échec au moins 1 AINS, BASDAI> 4 (exclu si SARx)

Golimumab 50mg versus PCB SC

- **ASAS 20 à la semaine 16,**
- BASDAI 50%,
- Evolution IRM SPARCC



CRP=C-reactive protein; GLM=golimumab; MRI=magnetic resonance imaging; q4w=every 4 weeks; R=randomization; SC=subcutaneous; SpA=spondyloarthritis.
[a]National Clinical Trial Registry Number: NCT01453725

ARTHRITIS & RHEUMATOLOGY
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AxSpA GLM/PCB : population Go HEAD

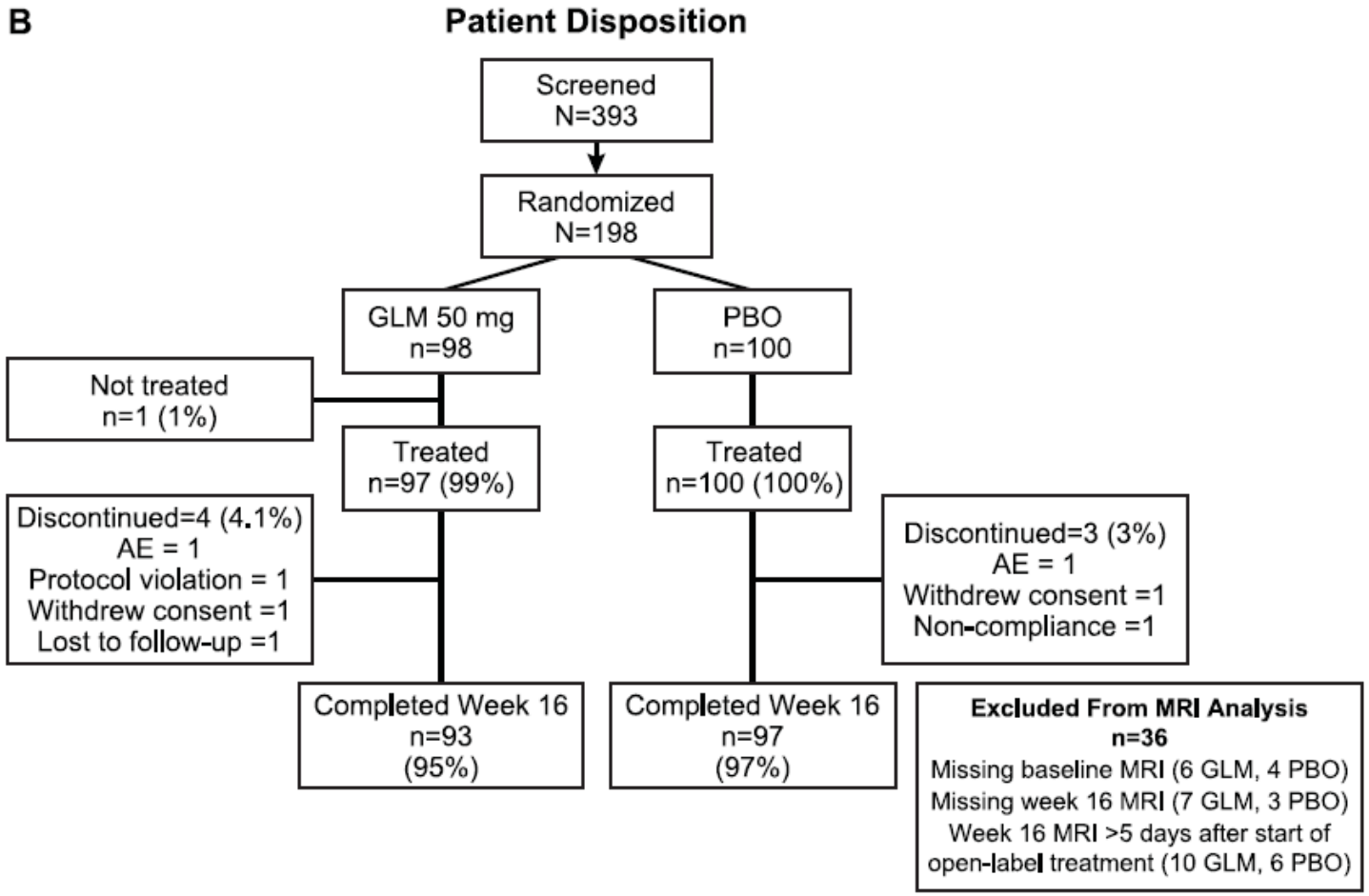

Figure 1. A, GO-AHEAD study design. B, Patient disposition. PBO = placebo; AE = adverse event.

ARTHRITIS & RHEUMATOLOGY
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AxSpA GLM/PCB : population Go HEAD

Table 1. Baseline characteristics of the 198 patients randomized to receive golimumab or placebo*

Characteristic	Golimumab (n = 98)	Placebo (n = 100)
Male sex	61 (62.2)	52 (52.0)
Age, mean ± SD years	30.7 ± 7.1	31.7 ± 7.2
White race	98 (100.0)	100 (100.0)
Geographic region		
Eastern Europe	52 (53.1)	53 (53.0)
Western Europe and US	46 (46.9)	47 (47.0)
BMI, mean ± SD kg/m^2	25.6 ± 4.7	25.1 ± 4.9
Disease duration since diagnosis		
1 year	67 (68.4)	65 (65.0)
1–2 years	20 (20.4)	19 (19.0)
3–5 years	11 (11.2)	16 (16.0)
BASDAI, mean ± SD (10-cm VAS)	6.6 ± 1.6	6.4 ± 1.5
BASFI, mean ± SD (10-cm VAS)	5.3 ± 2.4	4.8 ± 2.5
SPARCC SI MRI score, mean ± SD (range 0–72)†	9.9 ± 12.3	12.7 ± 15.4
MRI-positive for sacroiliitis‡	66 (67.3)	66 (66.0)
ASDAS, mean ± SD	3.6 ± 0.9	3.5 ± 0.8
CRP concentration, mean ± SD mg/dl	1.5 ± 2.9	1.3 ± 2.0
CRP > upper limit of normal	40 (40.8)	41 (41.0)
HLA–B27 positive	81 (82.7)	82 (82.0)

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AxSpA GLM/PCB : réponse semaine 16

Table 2. Efficacy assessments at 16 weeks in the full analysis set*

	Golimumab 50 mg			Placebo			Difference, golimumab vs. placebo	
	n	Baseline	Week 16	n	Baseline	Week 16	% (95% CI)	*P*
Responders, no. (%)								
BASDAI 50	97	–	57 (57.7)	100	–	30 (30.0)	28.0 (14.4, 40.6)	<0.0001†
ASAS partial remission	97	–	32 (33.0)	100	–	18 (18.0)	15.2 (3.2, 27.1)	0.0136†
SPARCC MRI SI score	74	9.9 ± 11.82	4.6 ± 7.92	87	12.7 ± 15.62	11.71 ± 14.79	−4.3	<0.0001‡
CRP, mg/dl	88	1.51 ± 2.94	0.43 ± 0.87	91	1.36 ± 2.08	1.06 ± 1.64	−0.64 (−0.98, −0.30)	0.0003§
BASDAI, 10-cm VAS	93	6.62 ± 1.57	2.93 ± 2.51	96	6.29 ± 1.45	4.68 ± 2.75	−2.00 (−2.68, −1.35)	<0.0001§
BASFI	93	5.26 ± 2.34	2.50 ± 2.53	97	4.70 ± 2.53	3.87 ± 2.83	−1.73 (−2.33, −1.13)	<0.0001
ASDAS	88	3.59 ± 0.94	1.87 ± 1.02	90	3.40 ± 0.78	2.80 ± 1.22	−1.05 (−1.37, −0.73)	<0.0001§
BASMI	94	2.4 ± 1.30	1.93 ± 1.18	100	2.51 ± 1.32	2.42 ± 1.39	−0.39 (−0.58, −0.20)	<0.0001§
MASES index score	92	3.2 ± 3.36	1.7 ± 2.95	97	3.2 ± 3.35	2.5 ± 3.18	−0.7 (−1.4, −0.1)	0.0302§
SF-36, physical summary scale	91	32.85 ± 8.08	43.43 ± 10.21	96	34.97 ± 8.68	38.33 ± 9.65	6.56 (4.28, 8.83)	<0.0001§
SF-36, mental summary scale	91	41.10 ± 11.94	47.06 ± 11.08	96	41.55 ± 11.14	43.08 ± 11.84	4.24 (1.42, 7.07)	0.0034§
EQ-5D index score	94	0.41 ± 0.32	0.68 ± 0.28	100	0.44 ± 0.33	0.54 ± 0.31	0.15 (0.08, 0.22)	<0.0001§
ASQoL questionnaire score	94	11.1 ± 4.45	5.6 ± 5.16	100	10.2 ± 4.57	8.6 ± 5.09	−3.5 (−4.7, −2.2)	<0.0001§
Total back pain, 10-cm VAS	93	6.98 ± 1.78	2.77 ± 2.78	97	6.61 ± 1.67	4.74 ± 3.17	−2.13 (−2.94, −1.32)	<0.0001§

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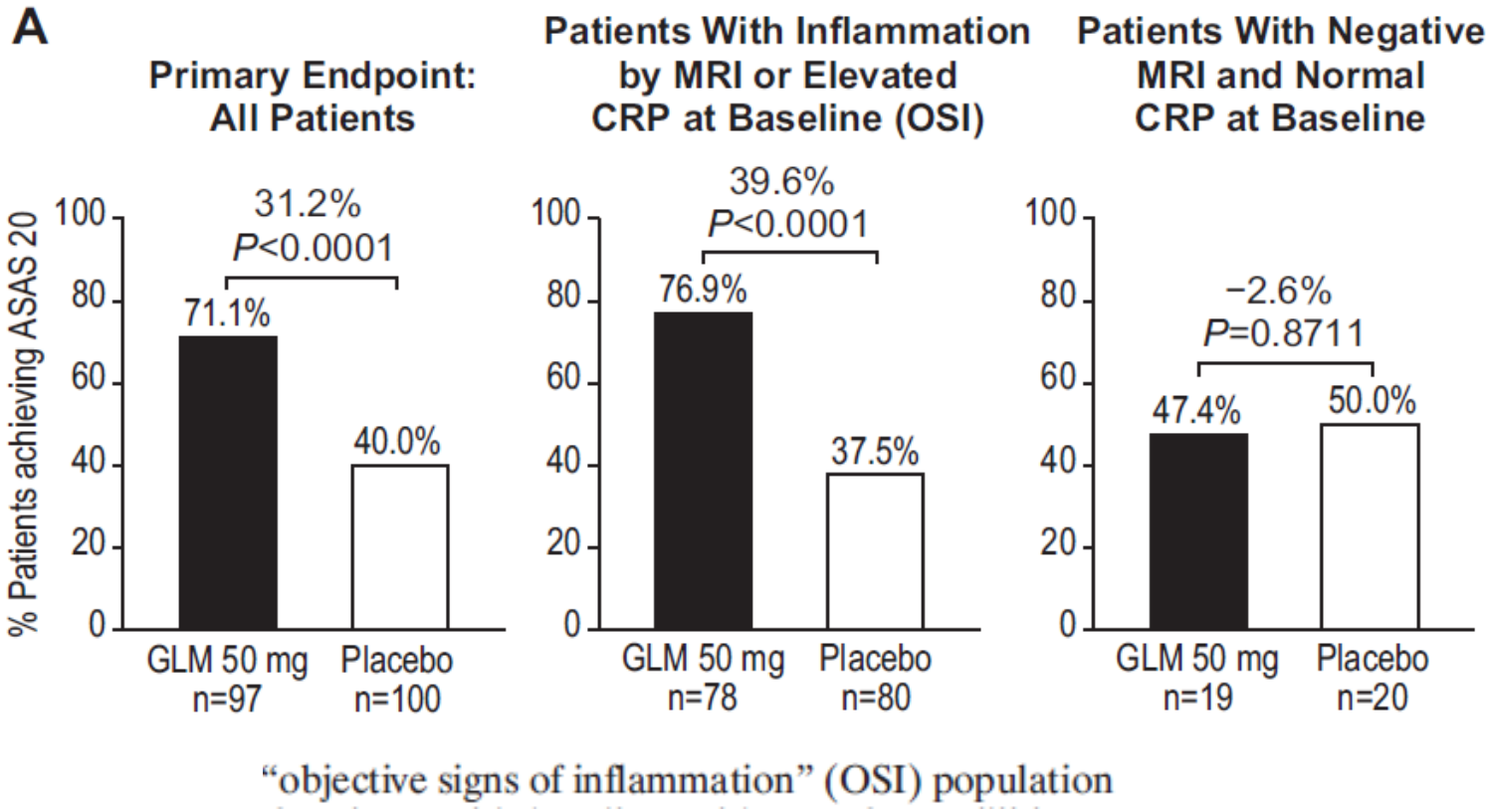
AxSpA GLM PCB : réponse ASAS 20



"objective signs of inflammation" (OSI) population

ASAS 20 : 71% vs 40%

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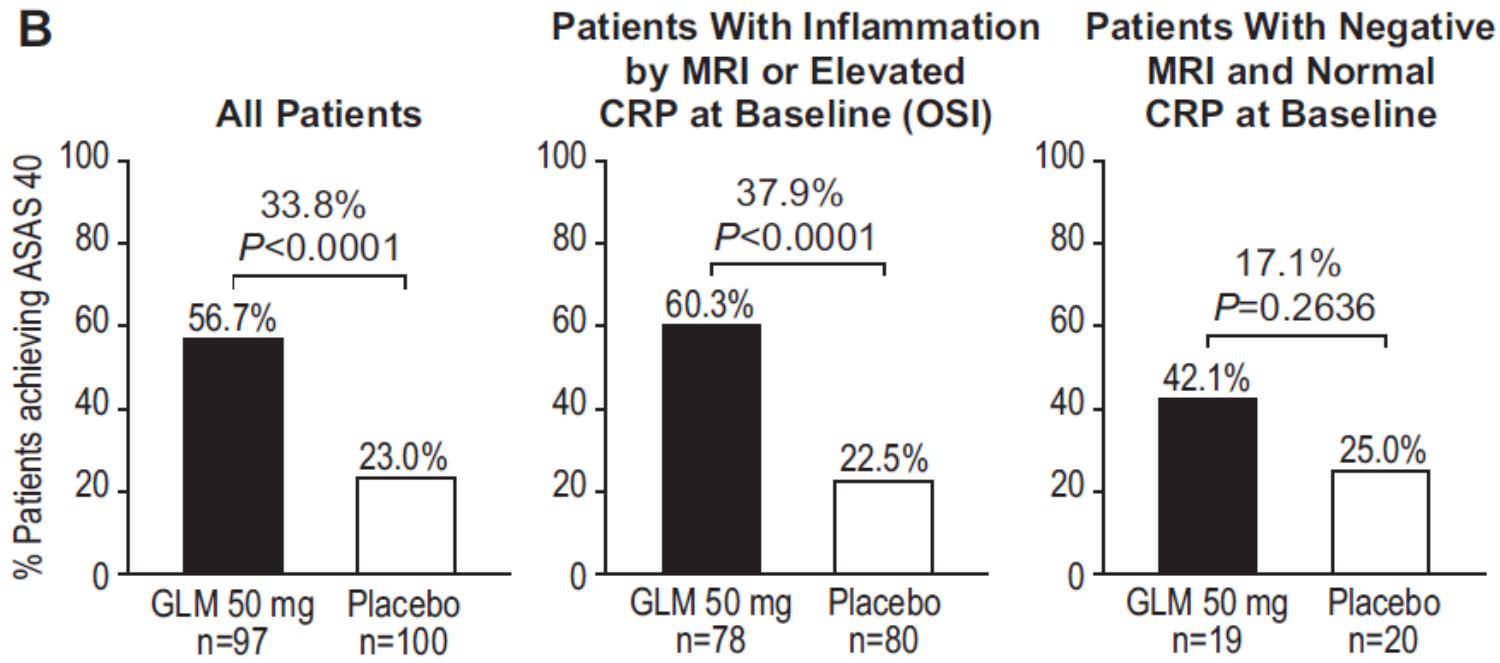
AxSpA GLM PCB : réponse ASAS 40



"objective signs of inflammation" (OSI) population

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AxSpA GLM PCB : réponse ASDAS et BASDAI

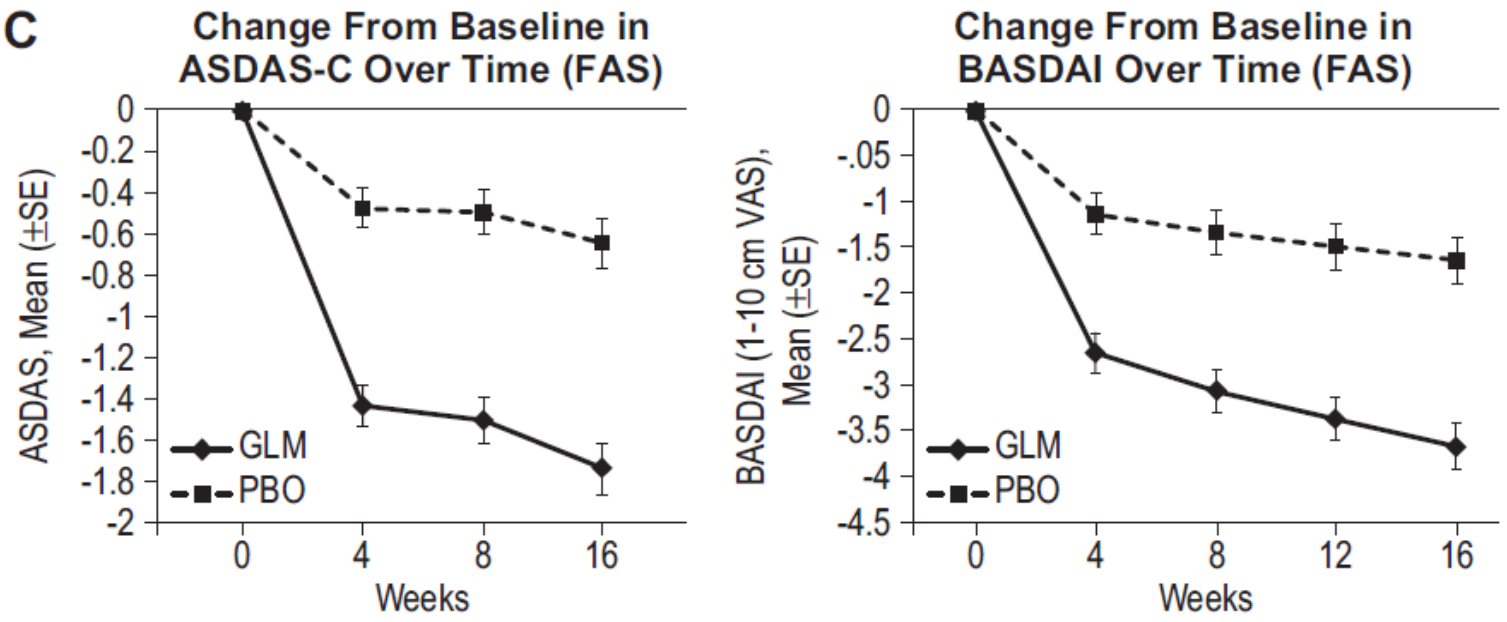

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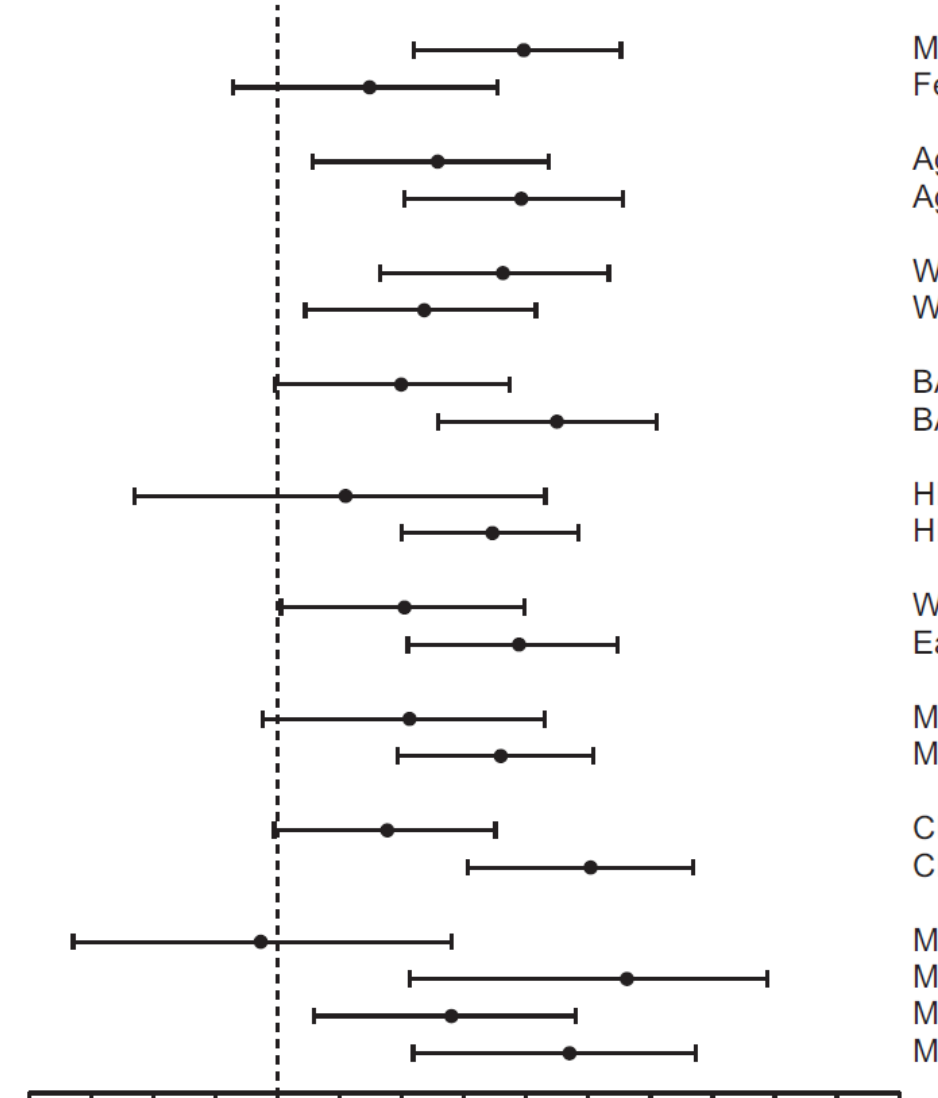
Table 3. Adverse events (AEs) in the patients during 16 weeks of treatment*

	Golimumab (n = 97)	Placebo (n = 100)
Any AE	40 (41.2)	47 (47.0)
AE related to study medication†	13 (13.4)	17 (17.0)
Serious AE	1 (1.0)	2 (2.0)
Female partner reported fetal death	1 (1.0)	0
Cholelithiasis	0	1 (1.0)
Back pain	0	1 (1.0)
AE leading to early withdrawal‡	2 (2.1)	1 (1.0)
Specific AEs of interest		
Serious infections	0	0
Active tuberculosis	0	0
Malignancies	0	0
Serious systemic hypersensitivity	0	0
Deaths	0	0

* Values are the number (%).
† As determined by the investigator.
‡ Study medication withdrawn.

AxSpA GLM PCB : estimation de la réponse ASAS 20 en fonction …



Male (n=61,52)
Female (n=36,48)

Age: >30 years (n=41,55)
Age: ≤30 years (n=56,45)

Weight ≤ Median (n=45,56)
Weight > Median (n=52,44)

BASDAI score ≤ Median (n=43,55)
BASDAI score > Median (n=54,45)

HLA-B27 negative (n=16,18)
HLA-B27 positive (n=81,82)

Western Europe and US (n=45,47)
Eastern Europe (n=52,53)

MRI (-) (n=32,34)
MRI (+) (n=65,66)

CRP ≤ (n=58,59)
CRP > ULN (n=39,41)

MRI (-) and CRP ≤ ULN (n=19,20)
MRI (-) and CRP > ULN (n=13,14)
MRI (+) and CRP ≤ ULN (n=39,39)
MRI (+) and CRP > ULN (n=26,27)

ARTHRITIS & RHEUMATOLOGY
Vol. 67, No. 10, October 2015, pp 2702–2712

A Randomized, Double-Blind, Placebo-Controlled, Sixteen-Week Study of Subcutaneous Golimumab in Patients With Active Nonradiographic Axial Spondyloarthritis

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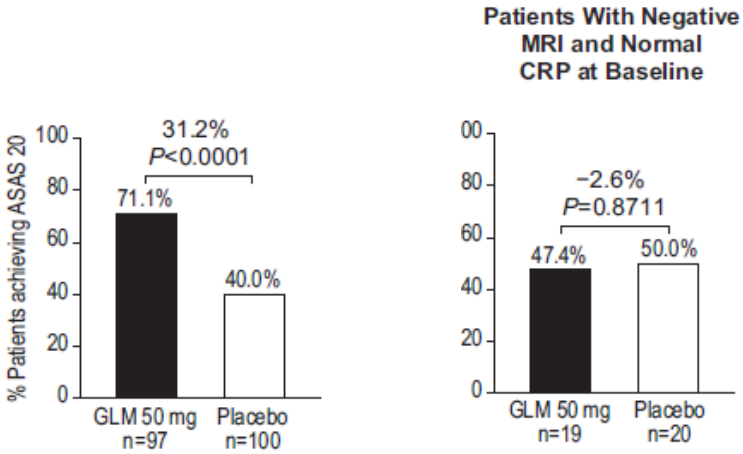

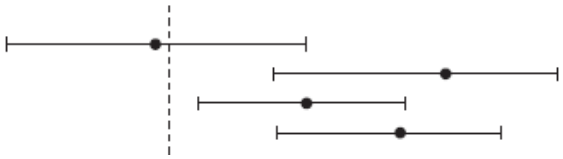

MRI (-) and CRP ≤ ULN (n=19,20)
MRI (-) and CRP > ULN (n=13,14)
MRI (+) and CRP ≤ ULN (n=39,39)
MRI (+) and CRP > ULN (n=26,27)

ARTHRITIS & RHEUMATOLOGY
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ORIGINAL ARTICLE

Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis

Dominique Baeten, M.D., Joachim Sieper, M.D., Jürgen Braun, M.D., Xenofon Baraliakos, M.D., Maxime Dougados, M.D., Paul Emery, F.R.C.P., Atul Deodhar, M.D., Brian Porter, M.D., Ph.D., M.P.H., Ruvie Martin, Ph.D., Mats Andersson, M.Sc., Shephard Mpofu, M.D., and Hanno B. Richards, M.D., for the MEASURE 1 and MEASURE 2 Study Groups*

secukinumab AC humain monoclonal inhibe les effets de IL-17A.

- ERC,sponsorisée, multicentrique, phase 3, **Measure 1** (2 ans et 3 ans d'extension- début 2011), **Measure 2** (5 ans, début 2012) : résultats S16 et S 52

- SA NY+ > 18 ans , en échec AINS pleine dose, BASDAI> 4 et Douleur ax>4
- Echec de DMARD et d' un anti TNF alpha autorisé (max 1)
- Exclusion si autre bioDMARDS , ankylose complète, infection active

A l'essai sécukinumab (différentes doses) versus placebo : évaluation S16

- **ASAS 20 à la semaine 16,**
- deltaBASDAI,ASAS40, ASAS 5/6, CRP

The MEASURE Clinical Trial Program:
Assessment of Secukinumab in AS

2013				2014				2015				2016			
Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4

MEASURE 1 (CAIN457F2305) – N = 371
i.v. loading (10 mg/kg) S0 S2 S4 →
s.c. maintenance dosing (75 or 150 mg)/ 4s

Extension Study

MEASURE 2 (CAIN457F2310) – N = 219
s.c. loading (75 or 150 mg) → s.c. maintenance dosing (75 or 150 mg)
Pre-filled syringe

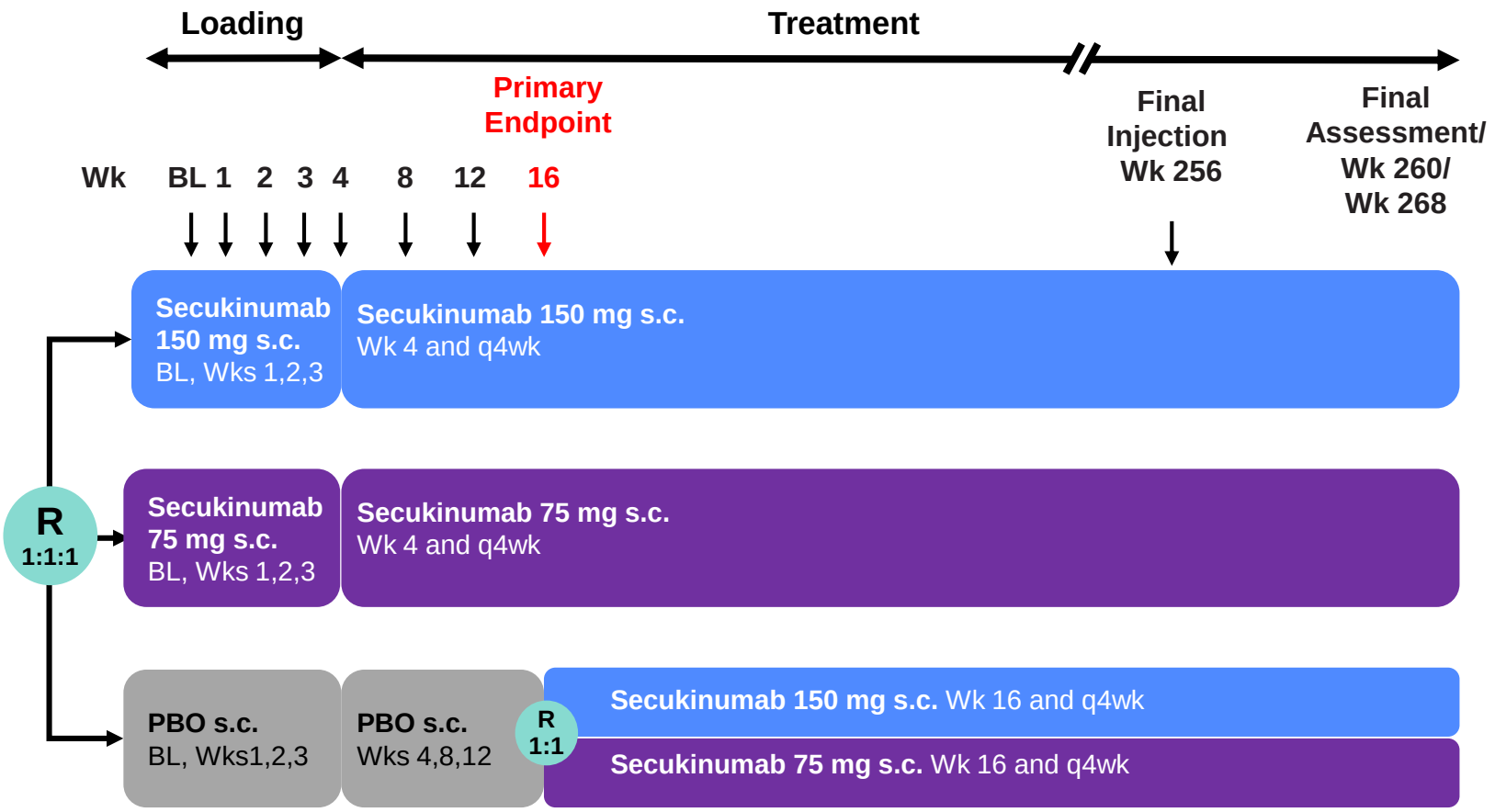
Inclusion criteria:

- AS diagnosed by prior documented radiological evidence fulfilling modified New York criteria
- Inadequate response to, or intolerance of, NSAIDs
- TNF-naive or inadequate response to, or intolerance of, not more than 1 TNF inhibitor
- BASDAI ≥ 4 (0–10 scale)
- Back pain VAS > 40 (0–100 mm scale)

[a]Estimated enrollment. [b]Not yet recruiting
MEASURE 1 is a 2-year study with 3 year extension study; MEASURE 2 is a 5 year study; MEASURE 3 is a 3 year study; MEASURE 4 is a 2 year study.
The primary endpoint for all studies is at Week 16.
AS, ankylosing spondylitis; i.v., intravenous; s.c., subcutaneous; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; NSAID, nonsteroidal antiinflammatory drug; VAS, visual analog scale

Clinicaltrials.gov: NCT01358175 (MEASURE 1); NCT01649275 (MEASURE 2); NCT02008916 (MEASURE 3); NCT02159053 (MEASURE 4).

Measure 2 : dessin de l'étude



Randomization was stratified according to whether subjects were anti–TNF-naïve or anti–TNF-IR.
BL, baseline; q4wk, every 4 weeks; R, randomization; Wk, Week
Baeten D, et al. *N Engl J Med.* 2015;373:2534–48

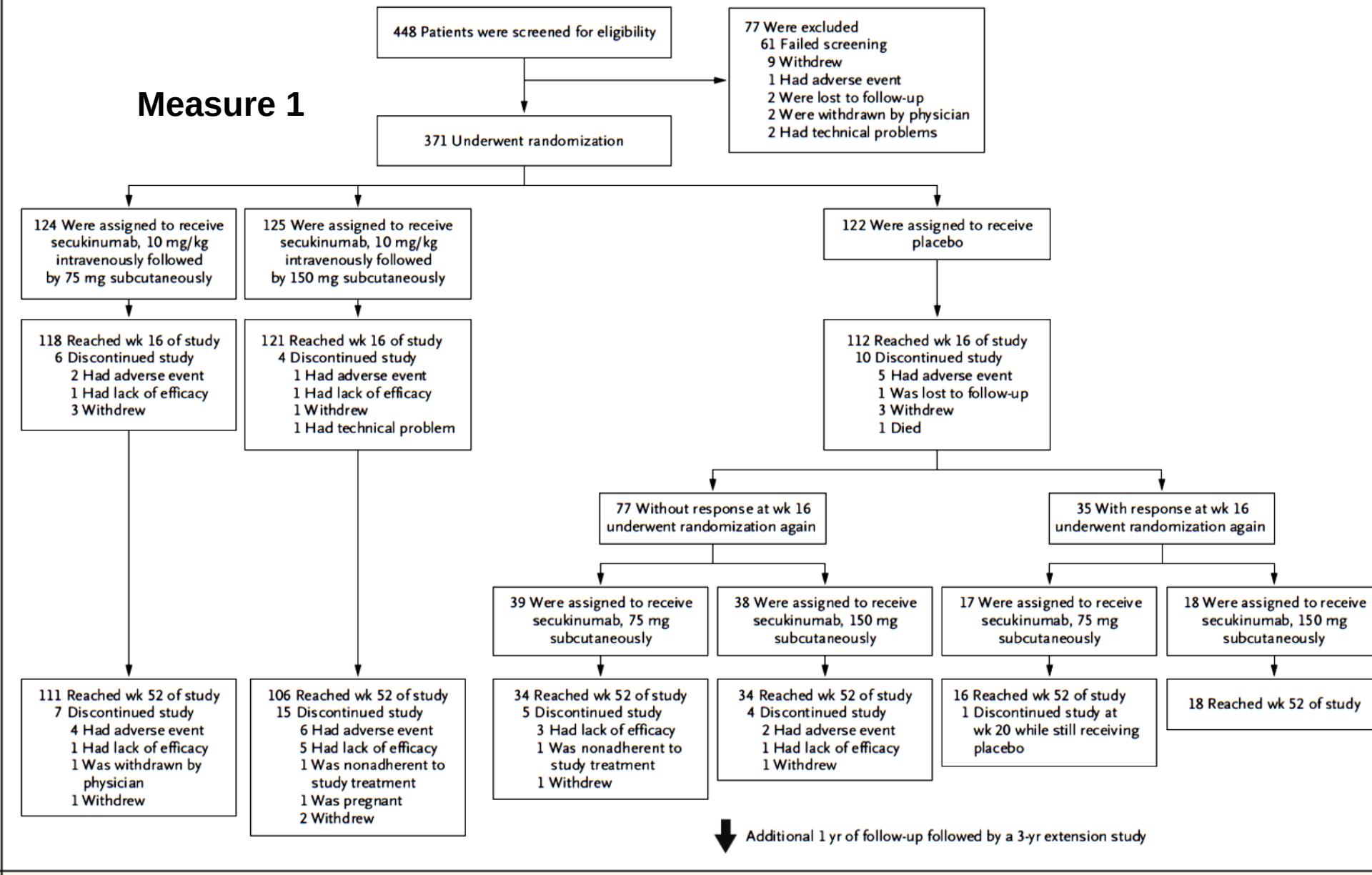


Figure 1. Numbers of Patients in MEASURE 1 Who Were Screened, Underwent Randomization, and Completed 52 Weeks of the Study.

In MEASURE 1, the secukinumab groups received intravenous secukinumab at a dose of 10 mg per kilogram of body weight at baseline, week 2, and week 4, followed by subcutaneous secukinumab at a dose of 150 mg or 75 mg, starting at week 8 and then every 4 weeks. The placebo group received intravenous placebo at baseline, week 2, and week 4, followed by subcutaneous placebo every 4 weeks starting at week 8. Patients initially assigned to receive placebo were randomly reassigned at week 16 to receive secukinumab, with active treatment starting either at week 16 (for those without a response to placebo) or at week 24 (for those with a response to placebo). Analyses of primary and secondary efficacy end points at week 16 included all patients according to the assigned study treatment at baseline.

Measure 2

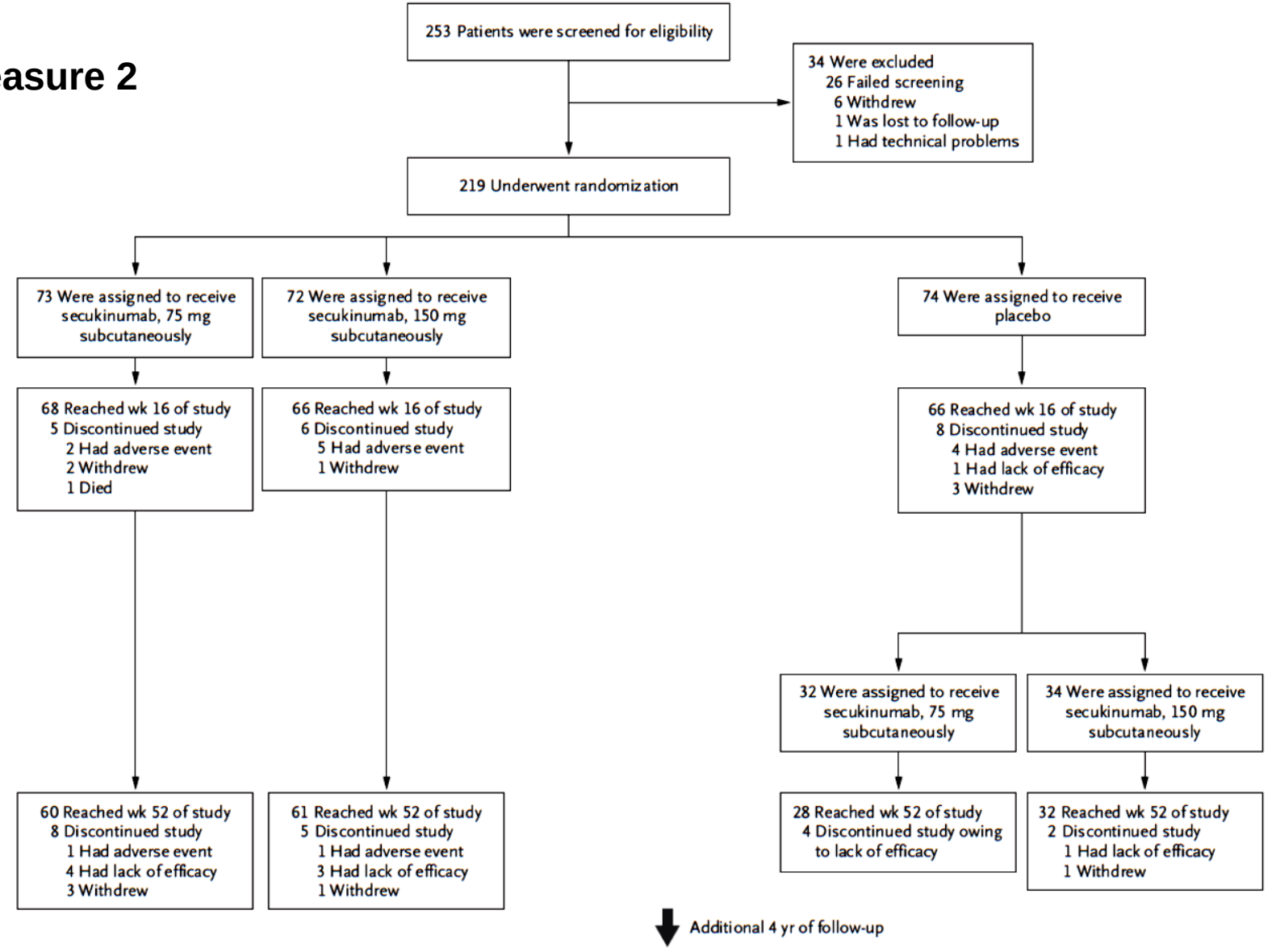


Figure 2. Numbers of Patients in MEASURE 2 Who Were Screened, Underwent Randomization, and Completed 52 Weeks of the Study.

In MEASURE 2, the patients received subcutaneous secukinumab, at a dose of 150 mg or 75 mg, or placebo at baseline; at weeks 1, 2, and 3; and every 4 weeks thereafter. Patients initially assigned to receive placebo were randomly reassigned at week 16 to receive secukinumab. Analyses of primary and secondary efficacy end points at week 16 included all patients according to the assigned study treatment at baseline.

Measure 1 et 2 : population

Table 1. Demographic and Baseline Characteristics of the Patients in MEASURE 1 and MEASURE 2 (Full Analysis Set).*

Characteristic	MEASURE 1			MEASURE 2		
	Secukinumab, 150 mg SC (N=125)	Secukinumab, 75 mg SC (N=124)	Placebo (N=122)	Secukinumab, 150 mg SC (N=72)	Secukinumab, 75 mg SC (N=73)	Placebo (N=74)
Age — yr	40.1±11.6	42.3±13.2	43.1±12.4	41.9±12.5	44.4±13.1	43.6±13.2
Male sex — no. (%)	84 (67)	88 (71)	85 (70)	46 (64)	51 (70)	56 (76)
Weight — kg	74.7±16.2	77.7±19.6	76.7±14.4	82.3±18.0	81.5±17.4	80.3±15.2
Race — no. (%)†						
White	69 (55)	76 (61)	81 (66)	69 (96)	70 (96)	70 (95)
Asian	21 (17)	23 (19)	19 (16)	2 (3)	3 (4)	4 (5)
Other	35 (28)	25 (20)	22 (18)	1 (1)	0	0
Time since diagnosis of ankylosing spondylitis — yr	6.5±6.9	7.9±9.7	8.3±8.9	7.0±8.2	5.3±7.4	6.4±8.9
Positive for HLA-B27 — no. (%)	86 (69)	99 (80)	90 (74)	57 (79)	53 (73)	58 (78)
Previous disorders — no. (%)						
Psoriasis	8 (6)	4 (3)	7 (6)	6 (8)	6 (8)	8 (11)
Inflammatory bowel disease	2 (2)	6 (5)	2 (2)	3 (4)	0	2 (3)
Uveitis	15 (12)	25 (20)	22 (18)	11 (15)	10 (14)	13 (18)
No previous anti-TNF therapy — no. (%)	92 (74)	90 (73)	89 (73)	44 (61)	45 (62)	45 (61)
Medication use — no. (%)						
Methotrexate	17 (14)	22 (18)	16 (13)	8 (11)	9 (12)	9 (12)
Sulfasalazine	42 (34)	40 (32)	42 (34)	10 (14)	12 (16)	9 (12)
Glucocorticoid	19 (15)	15 (12)	16 (13)	4 (6)	7 (10)	7 (9)
Median hsCRP (range) — mg/liter	7.4 (0.2–147.7)	9.2 (0.4–139.7)	7.9 (0.2–146.8)	7.5 (0.4–237.0)	5.7 (0.5–86.2)	8.3 (0.5–84.6)
BASDAI, total score	6.4±1.6	6.1±1.4	6.5±1.5	6.6±1.5	6.6±1.3	6.8±1.3
Total score for back pain (0–100 mm scale)‡	64.0±18.6	61.7±18.9	66.7±16.5	66.2±16.7	65.1±17.7	69.2±18.8
Patient's global assessment of disease activity (0–100 mm scale)§	64.0±19.4	60.5±18.3	66.3±18.6	67.5±16.8	64.6±17.9	70.5±15.8

Measure 1 et 2 : résultats à 16 semaines

Table 2. Efficacy End Points at Week 16 in the MEASURE 1 and MEASURE 2 Studies (Full Analysis Set).*

End Point	MEASURE 1			MEASURE 2		
	Secukinumab, 150 mg SC (N=125)	Secukinumab, 75 mg SC (N=124)	Placebo (N=122)	Secukinumab, 150 mg SC (N=72)	Secukinumab, 75 mg SC (N=73)	Placebo (N=74)
ASAS20 response — no. (%)†	76 (61)‡	74 (60)‡	35 (29)	44 (61)‡	30 (41)	21 (28)
ASAS40 response — no. (%)§	52 (42)‡	41 (33)‡	16 (13)	26 (36)‡	19 (26)	8 (11)
hsCRP, ratio of postbaseline level to baseline level	0.40±1.09‡	0.45±1.09‡	0.97±1.10	0.55±1.10‡	0.61±1.10	1.13±1.11
ASAS5/6 response — no. (%)¶	61 (49)‡	56 (45)‡	16 (13)	31 (43)‡	25 (34)	6 (8)
BASDAI score, mean change from baseline	−2.32±0.17‡	−2.34±0.18‡	−0.59±0.18	−2.19±0.25‡	−1.92±0.25	−0.85±0.25
SF-36 physical-component summary score, mean change from baseline‖	5.57±0.59‡	5.64±0.60‡	0.96±0.61	6.06±0.78‡	4.77±0.80	1.92±0.79
ASQoL score, mean change from baseline**	−3.58±0.42‡	−3.61±0.42‡	−1.04±0.44	−4.00±0.53††	−3.33±0.54	−1.37±0.53
ASAS partial remission — no. (%)‡‡	19 (15) ††	20 (16) ††	4 (3)	10 (14)	11 (15)	3 (4)

* In MEASURE 1, subcutaneous doses of secukinumab were preceded by an intravenous loading dose of 10 mg per kilogram of body weight. Plus–minus values are least-squares mean (±SE) changes from baseline. A prespecified hierarchical testing strategy was used to account for multiple testing in the overall study population. Missing data for binary variables were imputed as nonresponses. Missing data for continuous variables were imputed with the use of mixed-model repeated-measures analysis.

† ASAS20 response indicates improvement of at least 20% and absolute improvement of at least 1 unit (on a 10-unit scale) in at least three of the four main Assessment of Spondyloarthritis International Society domains, with no worsening by 20% or more in the remaining domain.

‡ P<0.001 for the comparison with placebo.

§ ASAS40 response indicates improvement of at least 40% and absolute improvement of at least 2 units (on a 10-unit scale) in at least three of the four main ASAS domains, with no worsening in the remaining domain.

¶ ASAS5/6 response indicates 20% or more improvement in five of the six ASAS response criteria.

‖ Scores on the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) range from 0 (maximum disability) to 100 (no disability) for individual domains, with a normative composite summary score of 50.

** Scores on the Ankylosing Spondylitis Quality of Life (ASQoL) scale range from 0 (best quality) to 18 (poorest quality).

†† P<0.01 for the comparison with placebo.

‡‡ ASAS partial remission indicates a score of 2 units or less (on a scale from 0 to 10) in each of the four core ASAS domains.

Measure 1 et 2 : résultats à 16 semaines

Table 2. Efficacy End Points at Week 16 in the MEASURE 1 and MEASURE 2 Studies (Full Analysis Set).*

End Point	MEASURE 1			MEASURE 2		
	Secukinumab, 150 mg SC (N=125)	Secukinumab, 75 mg SC (N=124)	Placebo (N=122)	Secukinumab, 150 mg SC (N=72)	Secukinumab, 75 mg SC (N=73)	Placebo (N=74)
ASAS20 response — no. (%)†	76 (61)‡	74 (60)‡	35 (29)	44 (61)‡	30 (41)	21 (28)
ASAS40 response — no. (%)§	52 (42)‡	41 (33)‡	16 (13)	26 (36)‡	19 (26)	8 (11)
hsCRP, ratio of postbaseline level to baseline level	0.40±1.09‡	0.45±1.09‡	0.97±1.10	0.55±1.10‡	0.61±1.10	1.13±1.11
ASAS5/6 response — no. (%)¶	61 (49)‡	56 (45)‡	16 (13)	31 (43)‡	25 (34)	6 (8)
BASDAI score, mean change from baseline	−2.32±0.17‡	−2.34±0.18‡	−0.59±0.18	−2.19±0.25‡	−1.92±0.25	−0.85±0.25
SF-36 physical-component summary score, mean change from baseline‖	5.57±0.59‡	5.64±0.60‡	0.96±0.61	6.06±0.78‡	4.77±0.80	1.92±0.79
ASQoL score, mean change from baseline**	−3.58±0.42‡	−3.61±0.42‡	−1.04±0.44	−4.00±0.53††	−3.33±0.54	−1.37±0.53
ASAS partial remission — no. (%)‡‡	19 (15) ††	20 (16) ††	4 (3)	10 (14)	11 (15)	3 (4)

* In MEASURE 1, subcutaneous doses of secukinumab were preceded by an intravenous loading dose of 10 mg per kilogram of body weight. Plus–minus values are least-squares mean (±SE) changes from baseline. A prespecified hierarchical testing strategy was used to account for multiple testing in the overall study population. Missing data for binary variables were imputed as nonresponses. Missing data for continuous variables were imputed with the use of mixed-model repeated-measures analysis.

† ASAS20 response indicates improvement of at least 20% and absolute improvement of at least 1 unit (on a 10-unit scale) in at least three of the four main Assessment of Spondyloarthritis International Society domains, with no worsening by 20% or more in the remaining domain.

‡ P<0.001 for the comparison with placebo.

§ ASAS40 response indicates improvement of at least 40% and absolute improvement of at least 2 units (on a 10-unit scale) in at least three of the four main ASAS domains, with no worsening in the remaining domain.

¶ ASAS5/6 response indicates 20% or more improvement in five of the six ASAS response criteria.

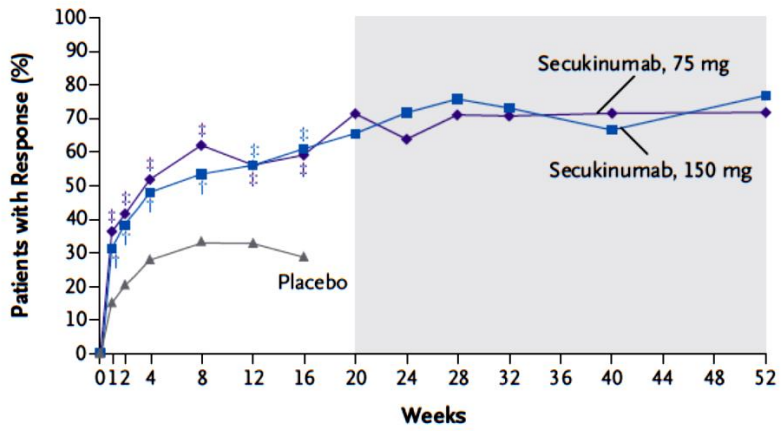
‖ Scores on the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) range from 0 (maximum disability) to 100 (no disability) for individual domains, with a normative composite summary score of 50.

** Scores on the Ankylosing Spondylitis Quality of Life (ASQoL) scale range from 0 (best quality) to 18 (poorest quality).

†† P<0.01 for the comparison with placebo.

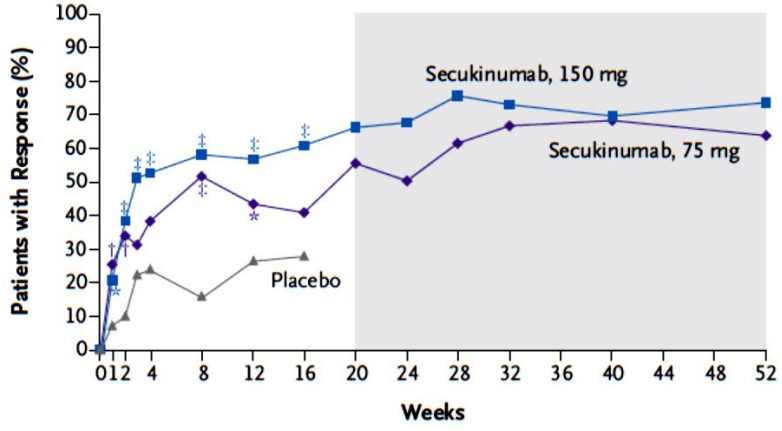
‡‡ ASAS partial remission indicates a score of 2 units or less (on a scale from 0 to 10) in each of the four core ASAS domains.

A MEASURE 1, ASAS20 Response



No. of Patients											
Secukinumab, 150 mg	125	125	125	125	125	120	113	110	116	111	103
Secukinumab, 75 mg	124	124	124	124	124	116	113	111	112	112	108
Placebo	122	122	122	122	122						

C MEASURE 2, ASAS20 Response



No. of Patients											
Secukinumab, 150 mg	72	72	72	72	72	65	65	62	63	63	61
Secukinumab, 75 mg	73	73	73	73	73	68	67	68	66	64	61
Placebo	74	74	74	74	74						

Résultats ASAS 20 au cours du temps (52 semaines)

Dose 150 mg
ASAS 20 : 61% vs 29%

Measure 1 et 2 : résultats à 16 semaines

Table 2. Efficacy End Points at Week 16 in the MEASURE 1 and MEASURE 2 Studies (Full Analysis Set).*

End Point	MEASURE 1			MEASURE 2		
	Secukinumab, 150 mg SC (N=125)	Secukinumab, 75 mg SC (N=124)	Placebo (N=122)	Secukinumab, 150 mg SC (N=72)	Secukinumab, 75 mg SC (N=73)	Placebo (N=74)
ASAS20 response — no. (%)†	76 (61)‡	74 (60)‡	35 (29)	44 (61)‡	30 (41)	21 (28)
ASAS40 response — no. (%)§	52 (42)‡	41 (33)‡	16 (13)	26 (36)‡	19 (26)	8 (11)
hsCRP, ratio of postbaseline level to baseline level	0.40±1.09‡	0.45±1.09‡	0.97±1.10	0.55±1.10‡	0.61±1.10	1.13±1.11
ASAS5/6 response — no. (%)¶	61 (49)‡	56 (45)‡	16 (13)	31 (43)‡	25 (34)	6 (8)
BASDAI score, mean change from baseline	−2.32±0.17‡	−2.34±0.18‡	−0.59±0.18	−2.19±0.25‡	−1.92±0.25	−0.85±0.25
SF-36 physical-component summary score, mean change from baseline‖	5.57±0.59‡	5.64±0.60‡	0.96±0.61	6.06±0.78‡	4.77±0.80	1.92±0.79
ASQoL score, mean change from baseline**	−3.58±0.42‡	−3.61±0.42‡	−1.04±0.44	−4.00±0.53††	−3.33±0.54	−1.37±0.53
ASAS partial remission — no. (%)‡‡	19 (15) ††	20 (16) ††	4 (3)	10 (14)	11 (15)	3 (4)

* In MEASURE 1, subcutaneous doses of secukinumab were preceded by an intravenous loading dose of 10 mg per kilogram of body weight. Plus–minus values are least-squares mean (±SE) changes from baseline. A prespecified hierarchical testing strategy was used to account for multiple testing in the overall study population. Missing data for binary variables were imputed as nonresponses. Missing data for continuous variables were imputed with the use of mixed-model repeated-measures analysis.

† ASAS20 response indicates improvement of at least 20% and absolute improvement of at least 1 unit (on a 10-unit scale) in at least three of the four main Assessment of Spondyloarthritis International Society domains, with no worsening by 20% or more in the remaining domain.

‡ P<0.001 for the comparison with placebo.

§ ASAS40 response indicates improvement of at least 40% and absolute improvement of at least 2 units (on a 10-unit scale) in at least three of the four main ASAS domains, with no worsening in the remaining domain.

¶ ASAS5/6 response indicates 20% or more improvement in five of the six ASAS response criteria.

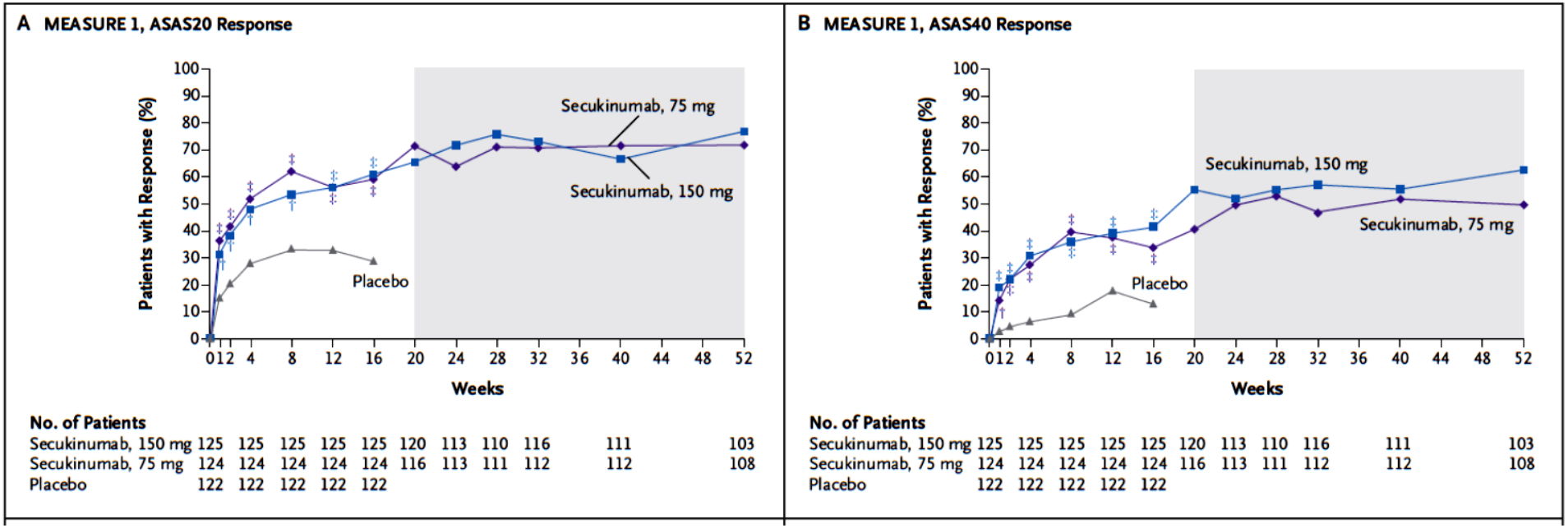
‖ Scores on the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) range from 0 (maximum disability) to 100 (no disability) for individual domains, with a normative composite summary score of 50.

** Scores on the Ankylosing Spondylitis Quality of Life (ASQoL) scale range from 0 (best quality) to 18 (poorest quality).

†† P<0.01 for the comparison with placebo.

‡‡ ASAS partial remission indicates a score of 2 units or less (on a scale from 0 to 10) in each of the four core ASAS domains.

Measure 1 : réponse ASAS 20 et 40



SCK 150 mg/PCB
ASAS 20 : 61% vs 29%
ASAS 40 : 42% vs 13%

Measure 1 et 2 : résultats à 16 semaines

Table 2. Efficacy End Points at Week 16 in the MEASURE 1 and MEASURE 2 Studies (Full Analysis Set).*

End Point	MEASURE 1			MEASURE 2		
	Secukinumab, 150 mg SC (N=125)	Secukinumab, 75 mg SC (N=124)	Placebo (N=122)	Secukinumab, 150 mg SC (N=72)	Secukinumab, 75 mg SC (N=73)	Placebo (N=74)
ASAS20 response — no. (%)†	76 (61)‡	74 (60)‡	35 (29)	44 (61)‡	30 (41)	21 (28)
ASAS40 response — no. (%)§	52 (42)‡	41 (33)‡	16 (13)	26 (36)‡	19 (26)	8 (11)
hsCRP, ratio of postbaseline level to baseline level	0.40±1.09‡	0.45±1.09‡	0.97±1.10	0.55±1.10‡	0.61±1.10	1.13±1.11
ASAS5/6 response — no. (%)¶	61 (49)‡	56 (45)‡	16 (13)	31 (43)‡	25 (34)	6 (8)
BASDAI score, mean change from baseline	−2.32±0.17‡	−2.34±0.18‡	−0.59±0.18	−2.19±0.25‡	−1.92±0.25	−0.85±0.25
SF-36 physical-component summary score, mean change from baseline‖	5.57±0.59‡	5.64±0.60‡	0.96±0.61	6.06±0.78‡	4.77±0.80	1.92±0.79
ASQoL score, mean change from baseline**	−3.58±0.42‡	−3.61±0.42‡	−1.04±0.44	−4.00±0.53††	−3.33±0.54	−1.37±0.53
ASAS partial remission — no. (%)‡‡	19 (15) ††	20 (16) ††	4 (3)	10 (14)	11 (15)	3 (4)

* In MEASURE 1, subcutaneous doses of secukinumab were preceded by an intravenous loading dose of 10 mg per kilogram of body weight. Plus–minus values are least-squares mean (±SE) changes from baseline. A prespecified hierarchical testing strategy was used to account for multiple testing in the overall study population. Missing data for binary variables were imputed as nonresponses. Missing data for continuous variables were imputed with the use of mixed-model repeated-measures analysis.

† ASAS20 response indicates improvement of at least 20% and absolute improvement of at least 1 unit (on a 10-unit scale) in at least three of the four main Assessment of Spondyloarthritis International Society domains, with no worsening by 20% or more in the remaining domain.

‡ P<0.001 for the comparison with placebo.

§ ASAS40 response indicates improvement of at least 40% and absolute improvement of at least 2 units (on a 10-unit scale) in at least three of the four main ASAS domains, with no worsening in the remaining domain.

¶ ASAS5/6 response indicates 20% or more improvement in five of the six ASAS response criteria.

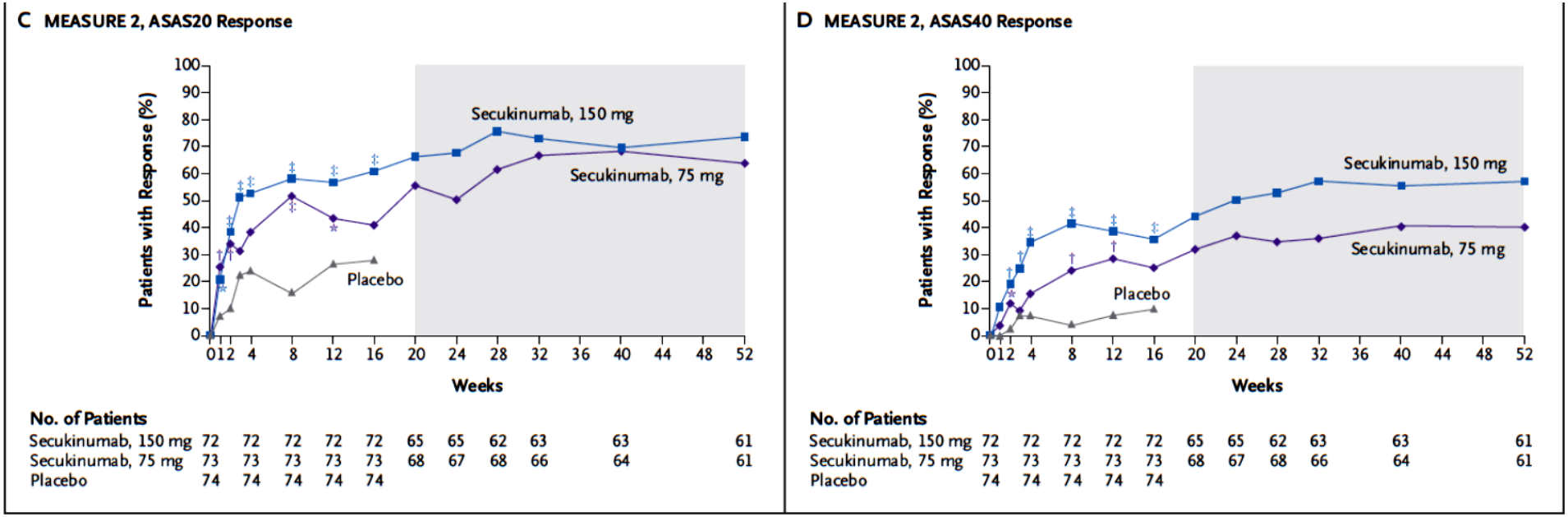
‖ Scores on the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) range from 0 (maximum disability) to 100 (no disability) for individual domains, with a normative composite summary score of 50.

** Scores on the Ankylosing Spondylitis Quality of Life (ASQoL) scale range from 0 (best quality) to 18 (poorest quality).

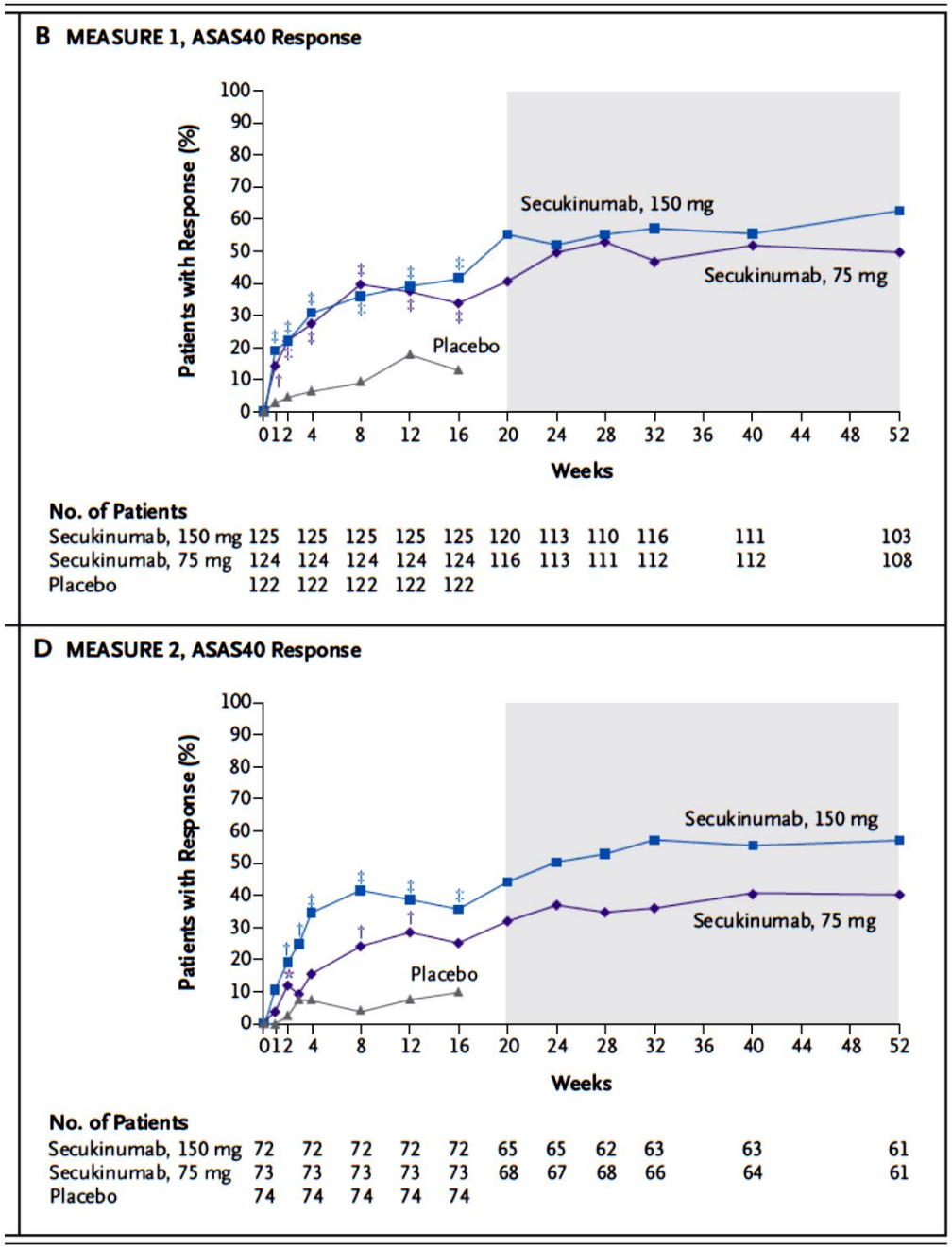
†† P<0.01 for the comparison with placebo.

‡‡ ASAS partial remission indicates a score of 2 units or less (on a scale from 0 to 10) in each of the four core ASAS domains.

Measure 2 : réponse ASAS 20 et 40



SCK 150 mg/PCB
ASAS 20 : 61% vs 28%
ASAS 40 : 36% vs 11%



Résultats ASAS 40 au cours du temps (52 semaines)

SCK 150 /75 mg
Maintien de la réponse
86% et 83% des malades restent sous taitement

Measure 1 et 2 : effets secondaires

Table 3. Safety Profile during the 16-Week, Placebo-Controlled Induction Period of the MEASURE 1 and MEASURE 2 Studies.*

Variable	MEASURE 1		MEASURE 2	
	Secukinumab, Pooled Data (N=249)	Placebo (N=122)	Secukinumab, Pooled Data (N=145)	Placebo (N=74)
Exposure to study treatment — days	113.2±13.2	109.2±22.7	110.1±15.8	107.6±22.4
Any adverse event — no. of patients (%)	170 (68)	68 (56)	89 (61)	47 (64)
Death — no. of patients (%)	0	1 (<1)†	1 (<1)‡	0
Serious adverse event — no. of patients (%)‡	5 (2)	5 (4)	8 (6)	3 (4)
Discontinuation of study treatment because of any adverse event — no. of patients (%)	3 (1)	5 (4)	7 (5)	4 (5)
Infection or infestation — no. of patients (%)§	75 (30)	15 (12)	46 (32)	20 (27)
Common adverse events — no. of patients (%)¶				
Nasopharyngitis	30 (12)	9 (7)	14 (10)	3 (4)
Dyslipidemia	24 (10)	6 (5)	2 (1)	1 (1)
Headache	20 (8)	7 (6)	6 (4)	6 (8)
Adverse events of special interest — no. of patients (%)				
Candida infection	1 (<1)	0	1 (<1)	0
Crohn's disease	1 (<1)	0	1 (<1)	0
Major adverse cardiac event, adjudicated	0	0	1 (<1)‡	0
Neutropenia, grade 3 or 4	0	0	0	0

Measure 1 et 2 : effets secondaires

Table 3. Safety Profile during the 16-Week, Placebo-Controlled Induction Period of the MEASURE 1 and MEASURE 2 Studies.*

Variable	MEASURE 1		MEASURE 2	
	Secukinumab, Pooled Data (N=249)	Placebo (N=122)	Secukinumab, Pooled Data (N=145)	Placebo (N=74)
Exposure to study treatment — days	113.2±13.2	109.2±22.7	110.1±15.8	107.6±22.4
Any adverse event — no. of patients (%)	170 (68)	68 (56)	89 (61)	47 (64)
Death — no. of patients (%)	0	1 (<1)†	1 (<1)‡	0
Serious adverse event — no. of patients (%)‡	5 (2)	5 (4)	8 (6)	3 (4)
Discontinuation of study treatment because of any adverse event — no. of patients (%)	3 (1)	5 (4)	7 (5)	4 (5)
Infection or infestation — no. of patients (%)§	75 (30)	15 (12)	46 (32)	20 (27)
Common adverse events — no. of patients (%)¶				
Nasopharyngitis	30 (12)	9 (7)	14 (10)	3 (4)
Dyslipidemia	24 (10)	6 (5)	2 (1)	1 (1)
Headache	20 (8)	7 (6)	6 (4)	6 (8)
Adverse events of special interest — no. of patients (%)				
Candida infection	1 (<1)	0	1 (<1)	0
Crohn's disease	1 (<1)	0	1 (<1)	0
Major adverse cardiac event, adjudicated	0	0	1 (<1)‡	0
Neutropenia, grade 3 or 4	0	0	0	0

Measure 1 et 2 : effets secondaires

Table 3. Safety Profile during the 16-Week, Placebo-Controlled Induction Period of the MEASURE 1 and MEASURE 2 Studies.*

Variable	MEASURE 1		MEASURE 2	
	Secukinumab, Pooled Data (N=249)	Placebo (N=122)	Secukinumab, Pooled Data (N=145)	Placebo (N=74)
Exposure to study treatment — days	113.2±13.2	109.2±22.7	110.1±15.8	107.6±22.4
Any adverse event — no. of patients (%)	170 (68)	68 (56)	89 (61)	47 (64)
Death — no. of patients (%)	0	1 (<1)†	1 (<1)‡	0
Serious adverse event — no. of patients (%)‡	5 (2)	5 (4)	8 (6)	3 (4)
Discontinuation of study treatment because of any adverse event — no. of patients (%)	3 (1)	5 (4)	7 (5)	4 (5)
Infection or infestation — no. of patients (%)§				
Common adverse events — no. of patients (%)¶				
Nasopharyngitis	30 (12)	9 (7)	14 (10)	3 (4)
Dyslipidemia	24 (10)	6 (5)	2 (1)	1 (1)
Headache	20 (8)	7 (6)	6 (4)	6 (8)
Adverse events of special interest — no. of patients (%)				
Candida infection	1 (<1)	0	1 (<1)	0
Crohn's disease	1 (<1)	0	1 (<1)	0
Major adverse cardiac event, adjudicated	0	0	1 (<1)‡	0
Neutropenia, grade 3 or 4	0	0	0	0

Sur-risque d'infection 30/32% vs 12/27%

Measure 1 et 2 : effets secondaires

Table 3. Safety Profile during the 16-Week, Placebo-Controlled Induction Period of the MEASURE 1 and MEASURE 2 Studies.*

Variable	MEASURE 1		MEASURE 2	
	Secukinumab, Pooled Data (N=249)	Placebo (N=122)	Secukinumab, Pooled Data (N=145)	Placebo (N=74)
Exposure to study treatment — days	113.2±13.2	109.2±22.7	110.1±15.8	107.6±22.4
Any adverse event — no. of patients (%)	170 (68)	68 (56)	89 (61)	47 (64)
Death — no. of patients (%)	0	1 (<1)†	1 (<1)‡	0
Serious adverse event — no. of patients (%)‡	5 (2)	5 (4)	8 (6)	3 (4)
Discontinuation of study treatment because of any adverse event — no. of patients (%)	3 (1)	5 (4)	7 (5)	4 (5)
Infection or infestation — no. of patients (%)§	Sur-risque d'infection 30/32% vs 12/27%			
Common adverse events — no. of patients (%)¶				
Nasopharyngitis	30 (12)	9 (7)	14 (10)	3 (4)
Dyslipidemia	24 (10)	6 (5)	2 (1)	1 (1)
Headache	20 (8)	7 (6)	6 (4)	6 (8)
Adverse events of special interest — no. of patients (%)				
Candida infection	1 (<1)	0	1 (<1)	0
Crohn's disease	1 (<1)	0	1 (<1)	0
Major adverse cardiac event, adjudicated	0	0	1 (<1)‡	0
Neutropenia, grade 3 or 4	0	0	0	0

Measure 1 et 2 : effets secondaires

Table 3. Safety Profile during the 16-Week, Placebo-Controlled Induction Period of the MEASURE 1 and MEASURE 2 Studies.*

Variable	MEASURE 1		MEASURE 2	
	Secukinumab, Pooled Data (N=249)	Placebo (N=122)	Secukinumab, Pooled Data (N=145)	Placebo (N=74)
Exposure to study treatment — days	113.2±13.2	109.2±22.7	110.1±15.8	107.6±22.4
Any adverse event — no. of patients (%)	170 (68)	68 (56)	89 (61)	47 (64)
Death — no. of patients (%)	0	1 (<1)†	1 (<1)‡	0
Serious adverse event — no. of patients (%)‡	5 (2)	5 (4)	8 (6)	3 (4)
Discontinuation of study treatment because of any adverse event — no. of patients (%)	3 (1)	5 (4)	7 (5)	4 (5)
Infection or infestation — no. of patients (%)§	75 (30)	15 (12)	46 (32)	20 (27)
Common adverse events — no. of patients (%)¶				
Nasopharyngitis	30 (12)	9 (7)	14 (10)	3 (4)
Dyslipidemia	24 (10)	6 (5)	2 (1)	1 (1)
Headache	20 (8)	7 (6)	6 (4)	6 (8)
Adverse events of special interest — no. of patients (%)				
Candida infection	1 (<1)	0	1 (<1)	0
Crohn's disease	1 (<1)	0	1 (<1)	0
Major adverse cardiac event, adjudicated	0	0	1 (<1)‡	0
Neutropenia, grade 3 or 4	0	0	0	0

Measure 1 et 2 : sécurité d'emploi

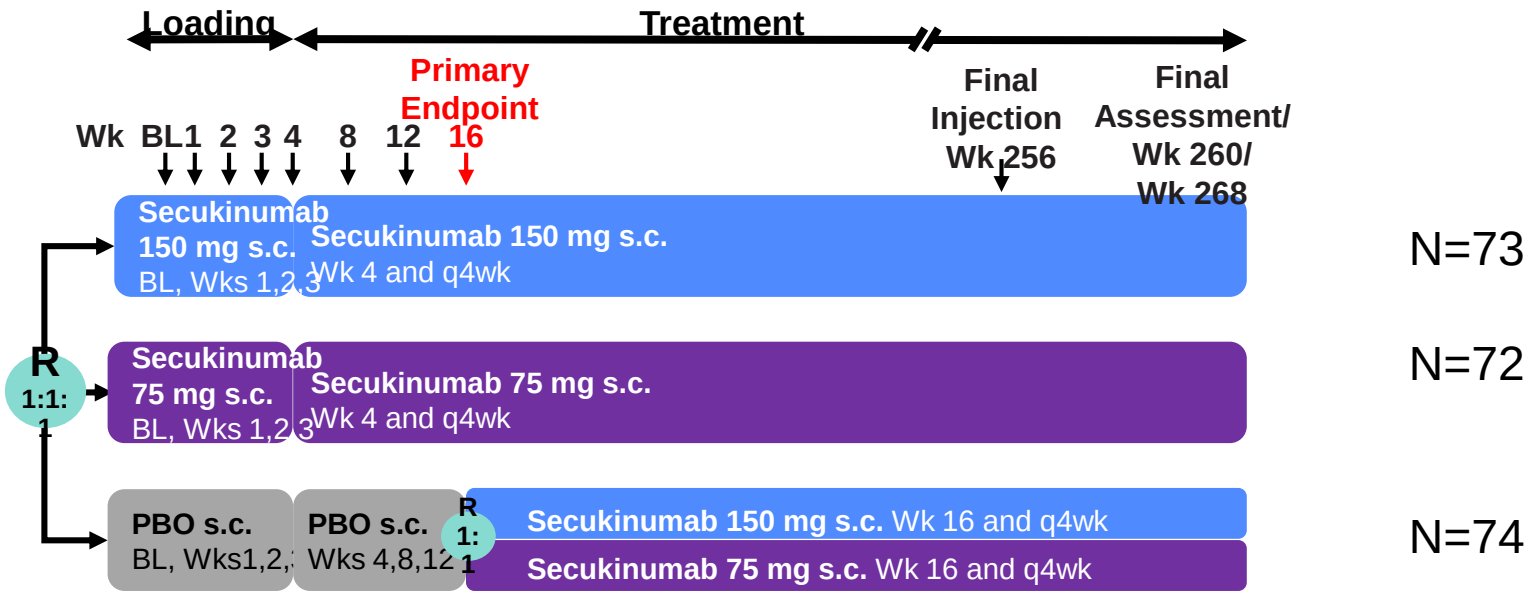
Table 4. Safety Profile during the Entire Safety Reporting Period in the MEASURE 1 and MEASURE 2 Studies.*

Variable	MEASURE 1	MEASURE 2	MEASURE 1 and MEASURE 2
	Any Secukinumab, Pooled Data (N=360)	Any Secukinumab, Pooled Data (N=211)	Any Secukinumab, Pooled Data (N=571)
Exposure to study treatment — days	451.7±146.5	425.8±135.1	442.1±142.8
Any adverse event — no. of patients (no. of cases/100 patient-yr)	291 (203.2)	175 (212.9)	466 (206.8)
Death — no. of patients (no. of cases/100 patient-yr)†	0	1‡	1‡
Serious adverse event — no. of patients (no. of cases/100 patient-yr)§	35 (8.3)	17 (7.1)	52 (7.9)
Discontinuation of study treatment due to adverse event — no. of patients (no. of cases/100 patient-yr)†¶	15	9	24
Infection or infestation — no. of patients (no. of cases/100 patient-yr)	187 (66.1)	111 (73.7)	298 (68.8)
Common adverse events — no. of patients (no. of cases/100 patient-yr)‖			
Nasopharyngitis	72 (18.8)	35 (16.3)	107 (17.9)
Headache	39 (9.6)	14 (6.0)	53 (8.3)
Diarrhea	39 (9.4)	14 (5.9)	53 (8.1)
Upper respiratory tract infection	35 (8.4)	17 (7.3)	52 (8.0)
Adverse events of special interest — no. of patients (no. of cases/100 patient-yr)			
Candida infection	3 (0.7)	3 (1.2)	6 (0.9)
Crohn's disease	3 (0.7)	2 (0.8)	5 (0.7)
Major adverse cardiac event, adjudicated	2 (0.5)	1 (0.4)	3 (0.4)
Neutropenia, grade 3 or 4	4 (0.9)	1 (0.4)	5 (0.7)

CONCISE REPORT

Secukinumab efficacy in anti-TNF-naive 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



1 anti TNF autorisé

Sieper J, *et al*. *Ann Rheum Dis* 2016;**0**:1–5.

Measure 2 : population

Table 1. Demographic and Baseline Characteristics of the I

Characteristic	MEASURE 2		
	Secukinumab, 150 mg SC (N=72)	Secukinumab, 75 mg SC (N=73)	Placebo (N=74)
Age — yr	41.9±12.5	44.4±13.1	43.6±13.2
Male sex — no. (%)	46 (64)	51 (70)	56 (76)
Weight — kg	82.3±18.0	81.5±17.4	80.3±15.2
Race — no. (%)†			
White	69 (96)	70 (96)	70 (95)
Asian	2 (3)	3 (4)	4 (5)
Other	1 (1)	0	0
Time since diagnosis of ankylosing spondylitis — yr	7.0±8.2	5.3±7.4	6.4±8.9
Positive for HLA-B27 — no. (%)	57 (79)	53 (73)	58 (78)
Previous disorders — no. (%)			
Psoriasis	6 (8)	6 (8)	8 (11)
Inflammatory bowel disease	3 (4)	0	2 (3)
Uveitis	11 (15)	10 (14)	13 (18)
No previous anti-TNF therapy — no. (%)	44 (61)	45 (62)	45 (61)
Medication use — no. (%)			
Methotrexate	8 (11)	9 (12)	9 (12)
Sulfasalazine	10 (14)	12 (16)	9 (12)
Glucocorticoid	4 (6)	7 (10)	7 (9)
Median hsCRP (range) — mg/liter	7.5 (0.4–237.0)	5.7 (0.5–86.2)	8.3 (0.5–84.6)
BASDAI, total score	6.6±1.5	6.6±1.3	6.8±1.3
Total score for back pain (0–100 mm scale)‡	66.2±16.7	65.1±17.7	69.2±18.8
Patient's global assessment of disease activity (0–100 mm scale)§	67.5±16.8	64.6±17.9	70.5±15.8

Sieper J, *et al. Ann Rheum Dis* 2016;**0**:1–5.

Measure 2 : population TNF naïf / TNF IR

Table 1 Demographic and baseline characteristics

	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)
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)

Sieper J, *et al*. *Ann Rheum Dis* 2016;**0**:1–5.

Measure 2 : résultats ASAS20 à 16 semaines

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

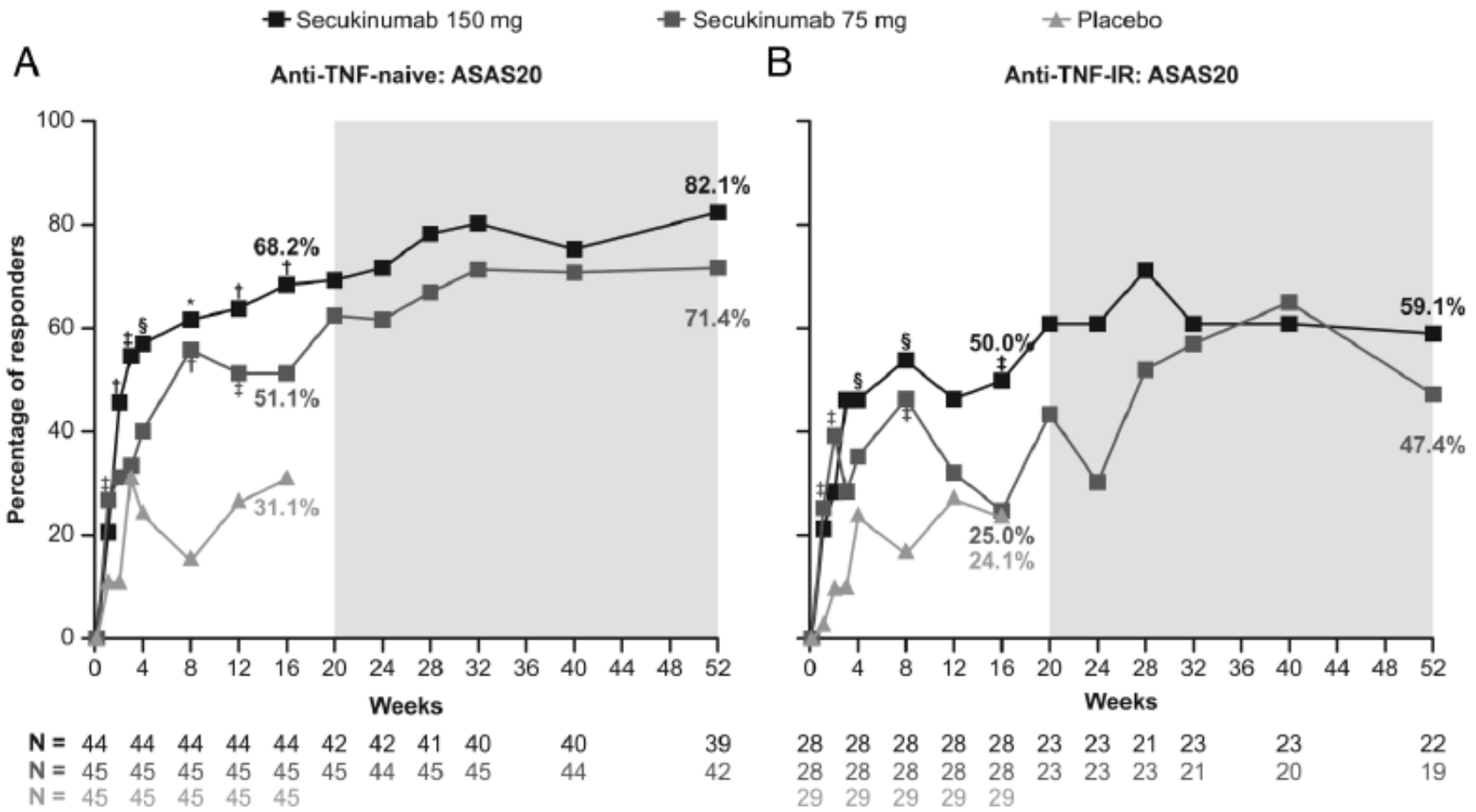
	Anti-TNF-naive			Anti-TNF-IR		
	Secukinumab s.c.			Secukinumab s.c.		
	150 mg (N=44)	75 mg (N=45)	Placebo (N=45)	150 mg (N=28)	75 mg (N=28)	Placebo (N=29)
ASAS20, n (%) responders¶	30 (68.2)†	23 (51.1)	14 (31.1)	14 (50.0)‡	7 (25.0)	7 (24.1)
ASAS40, n (%) responders**	19 (43.2)‡	14 (31.1)	8 (17.8)	7 (25.0)§	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

Measure 2 : résultats ASAS20 à 16 semaines

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

Measure 2 : résultats ASAS20 (TNF naifs/ TNFIR)



Réponse si naïfs anti TNF 68%
Réponse si TNF IR 50%

Sieper J, *et al. Ann Rheum Dis* 2016;**0**:1–5.

CONCISE REPORT

Secukinumab efficacy in anti-TNF-naive 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

Réponse ASAS 20 à S16 :

- **si naïfs anti TNF 68%**
- **si TNF IR 50%**

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.

Sieper J, *et al*. *Ann Rheum Dis* 2016;**0**:1–5.