

EULAR UPDATE 2017

BY

DR LOH YET LIN

CONSULTANT RHEUMATOLOGIST

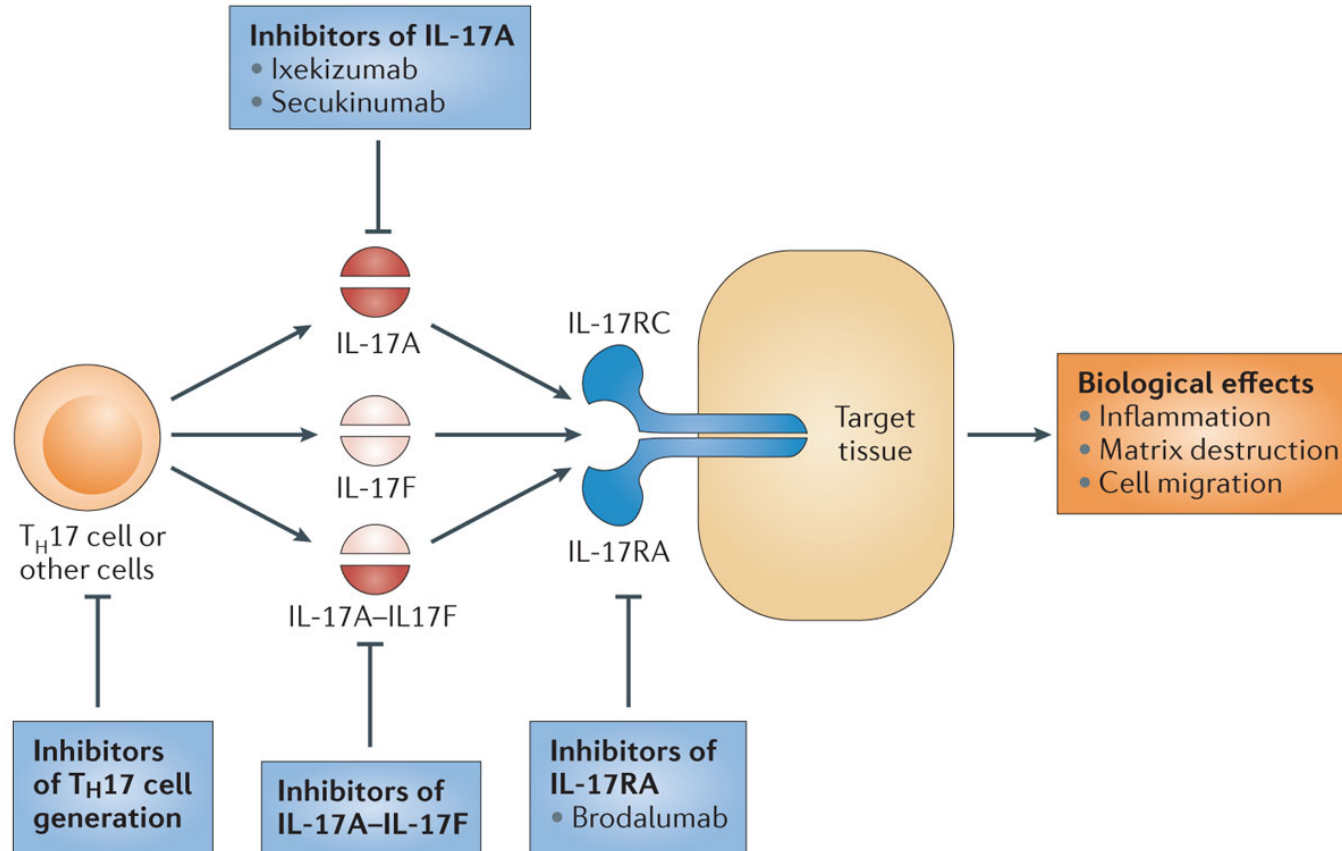
HOSPITAL SULTAN ISMAIL

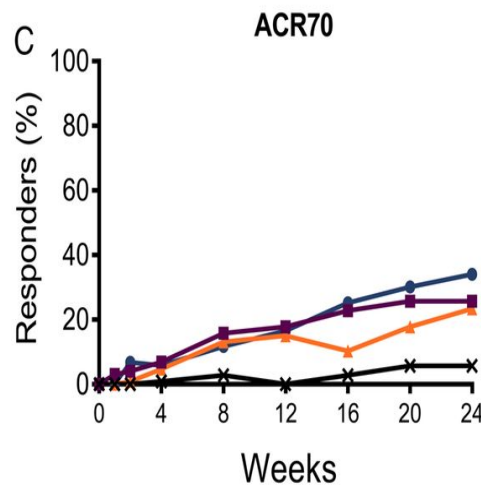
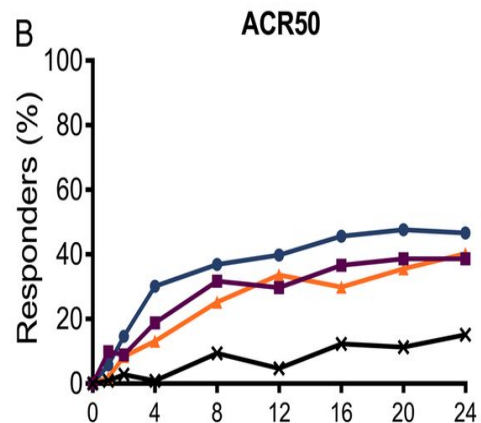
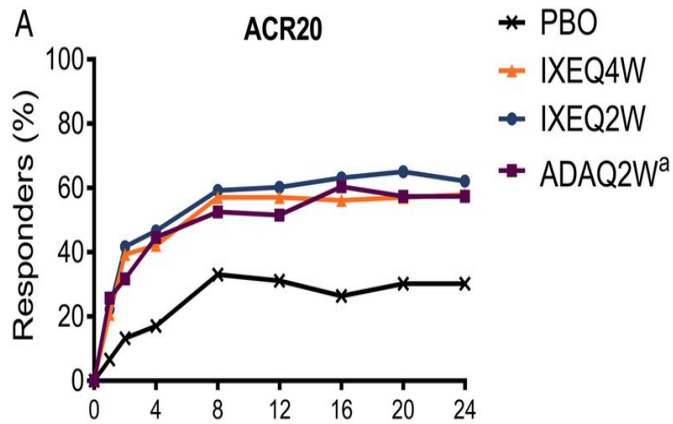
PSORIATIC ARTHRITIS

WHAT IS NEW ?

TREATMENT

IXEKIZUMAB : an anti-IL 17A antibody

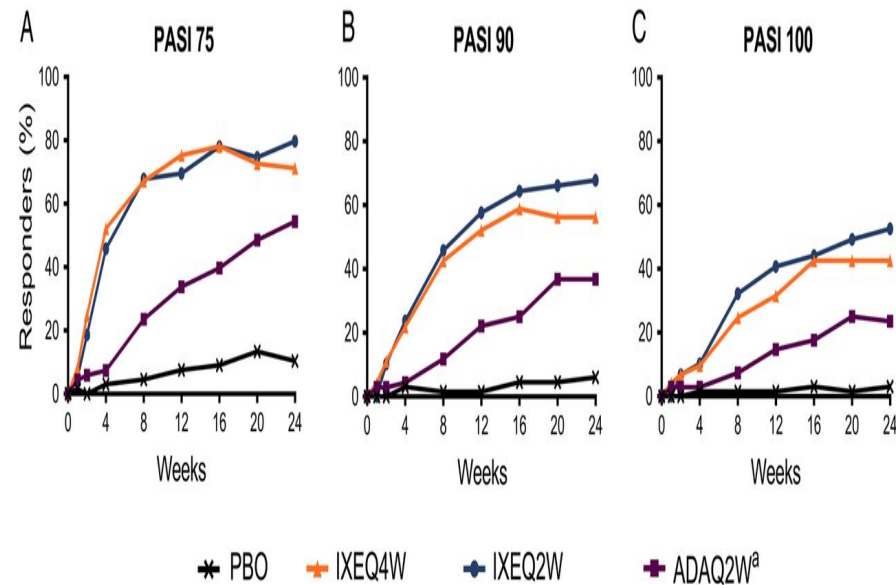




EXTENDED REPORT

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

Philip J Mease,¹ Désirée van der Heijde,² Christopher T Ritchlin,³ Masato Okada,⁴ Raquel S Cuchacovich,^{5,6} Catherine L Shuler,⁵ Chen-Yen Lin,⁵ Daniel K Braun,⁵ Chin H Lee,⁵ Dafna D Gladman,⁷ on behalf of the SPIRIT-P1 Study Group



Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial

Prof Peter Nash, Prof Bruce Kirkham, Masato Okada, Prof Proton Rahman, Prof Benard Combe, Prof Gerd-Ruediger Burmester,

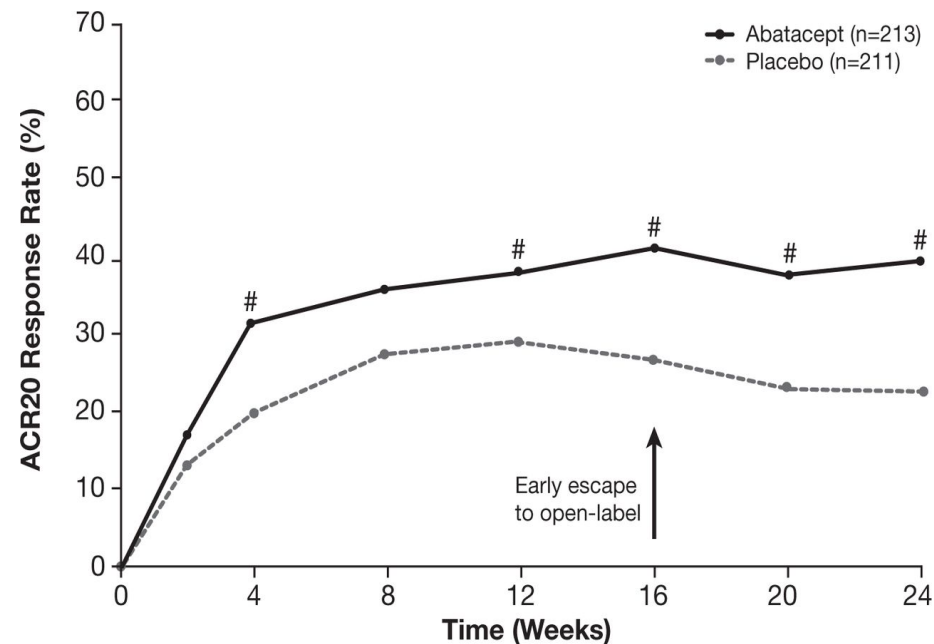
David H Adams, Lisa Kerr, Chin Lee, Catherine L Shuler, Prof Mark Genovese, on behalf of the SPIRIT-P2 Study Group

At week 24, a higher proportion of patients attained ACR-20 with ixekizumab every 4 weeks (65 [53%] patients; effect size vs placebo 33.8% [95% CI 22.4–45.2]; $p < 0.0001$) and ixekizumab every 2 weeks (59 [48%] patients; 28.5% [17.1–39.8]; $p < 0.0001$) than did patients with placebo (23 [20%] patients).

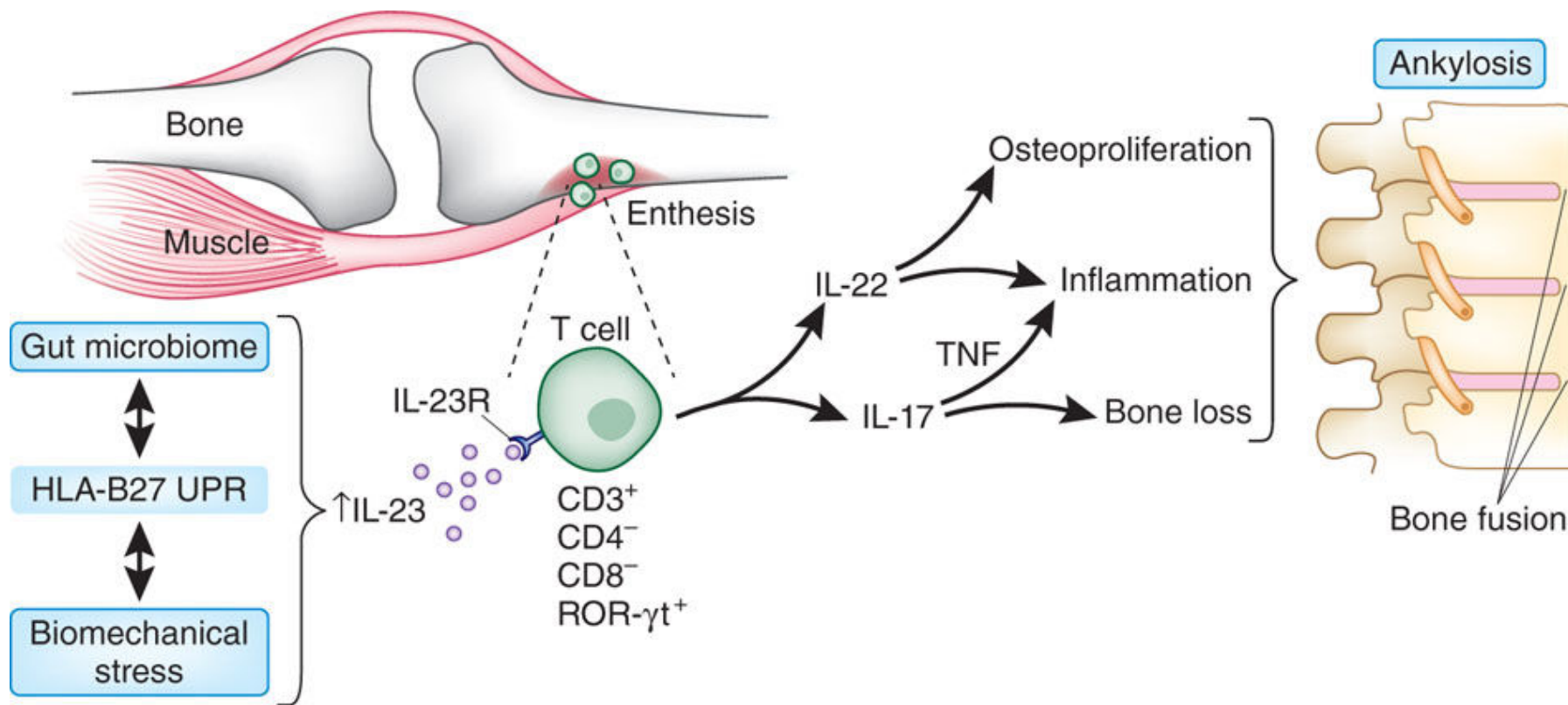
Extended report

Efficacy and safety of abatacept, a T-cell modulator, in a randomised, double-blind, placebo-controlled, phase III study in psoriatic arthritis

Philip J Mease, Alice B Gottlieb, Désirée van der Heijde, Oliver FitzGerald, Alyssa Johnsen, Marleen Nys, Subhashis Banerjee, Dafna D Gladman



BASIC IMMUNOLOGY



Various pathways may lead to elevated IL-23 expression, and Sherlock *et al.*⁷ now show that IL-23 can activate resident T cells within the enthesitis, the region in which tendons and ligaments insert into bone. These activated T cells can then promote local inflammation and bone remodeling through a variety of effector mediators, including IL-17 and IL-22. The net result of these actions is the typical ankylosed appearance of the spine. TNF, tumor necrosis factor; UPR, unfolded protein response.

IL-17 is produced by other cells and not just by T cells

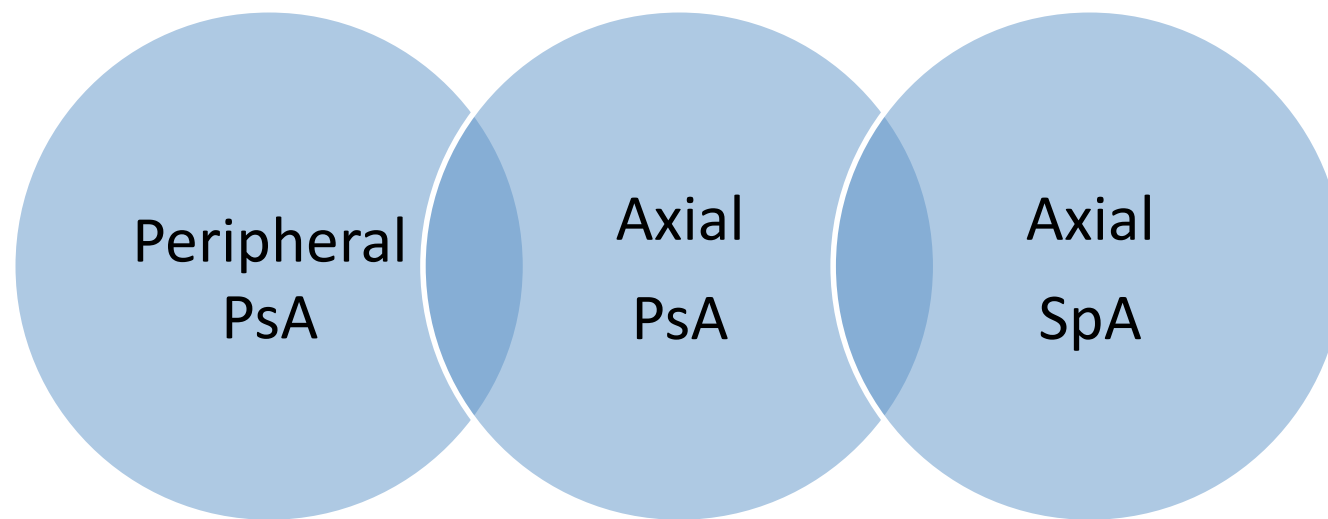
- $\gamma\delta$
- NK
- Neutrophil
- CD8

STRATEGY

EXTENDED REPORT

Axial Disease in Psoriatic Arthritis study: defining the clinical and radiographic phenotype of psoriatic spondyloarthritis

Deepak R Jadon,^{1,2} Raj Sengupta,¹ Alison Nightingale,³ Mark Lindsay,³ Eleanor Korendowych,¹ Graham Robinson,¹ Amelia Jobling,⁴ Gavin Shaddick,⁴ Jing Bi,⁵ Robert Winchester,⁵ Jon T Giles,⁵ Neil J McHugh^{1,3}



Less HLA B27

**Less sacroiliitis
More silent disease**

more radiographic damage

Jadon DR, et al. Ann Rheum Dis 2017;76:701–707

Definition of Remission

Minimal Disease Activity

5/7 of the following criteria:

- Tender joint count ≤ 1
- Swollen joint count ≤ 1
- PASI ≤ 1 or BSA $\leq 3\%$
- Patient pain VAS ≤ 15
- Patient global activity VAS ≤ 20
- HAQ ≤ 0.5
- Tender entheseal points ≤ 1

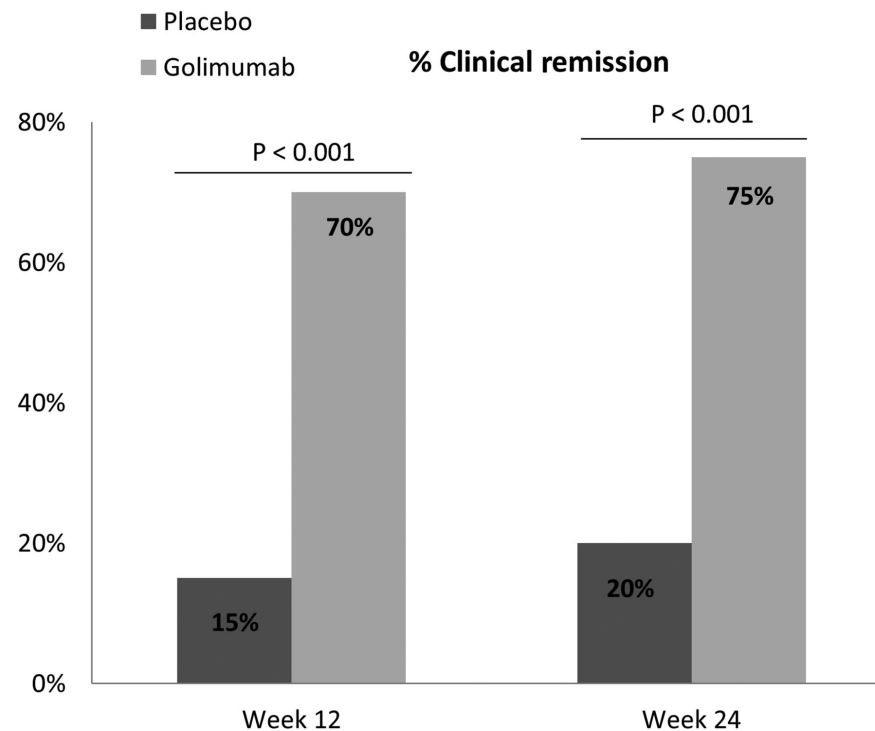
Ideas and questions post-TICOPA

- Better outcome at week 48 but also more side effects
- No detectable difference in radiographic disease progression
- No difference between the subforms but underpowered
- One strategy for all – to be further defined
- Currently little evidence for cost - effectiveness

EXTENDED REPORT

Anti-TNF-induced remission in very early peripheral spondyloarthritis: the CRESPA study

Philippe Carron,¹ Gaëlle Varkas,^{1,2} Heleen Cypers,^{1,2} Liesbet Van Praet,¹ Dirk Elewaut,^{1,2} Filip Van den Bosch,¹ on behalf of the CRESPA investigator group



Primary outcome: percentage of patients in clinical remission after 12 and 24 weeks in the placebo and golimumab group, respectively.
Philippe Carron et al. Ann Rheum Dis 2017;76:1389-1395

Residual disease activity in psoriatic arthritis : discordance between the rheumatologist's opinion and minimal disease activity measurement

- cross-sectional study included 250 PsA patients
- Rheumatologists to refer those patients whom they considered sufficiently treated
- **One-third of the PsA** patients with acceptable disease state according to the treating rheumatologist did not fulfil the MDA criteria
- Had residual disease activity on both subjective and objective disease activity measurements

The Development of Psoriatic Arthritis in Patients With Psoriasis Is Preceded by a Period of Nonspecific Musculoskeletal Symptoms A Prospective Cohort Study

Lihi Eder,¹ Ari Polachek,² Cheryl F. Rosen,³ Vinod Chandran,³ Richard Cook,⁴ and Dafna D. Gladman³

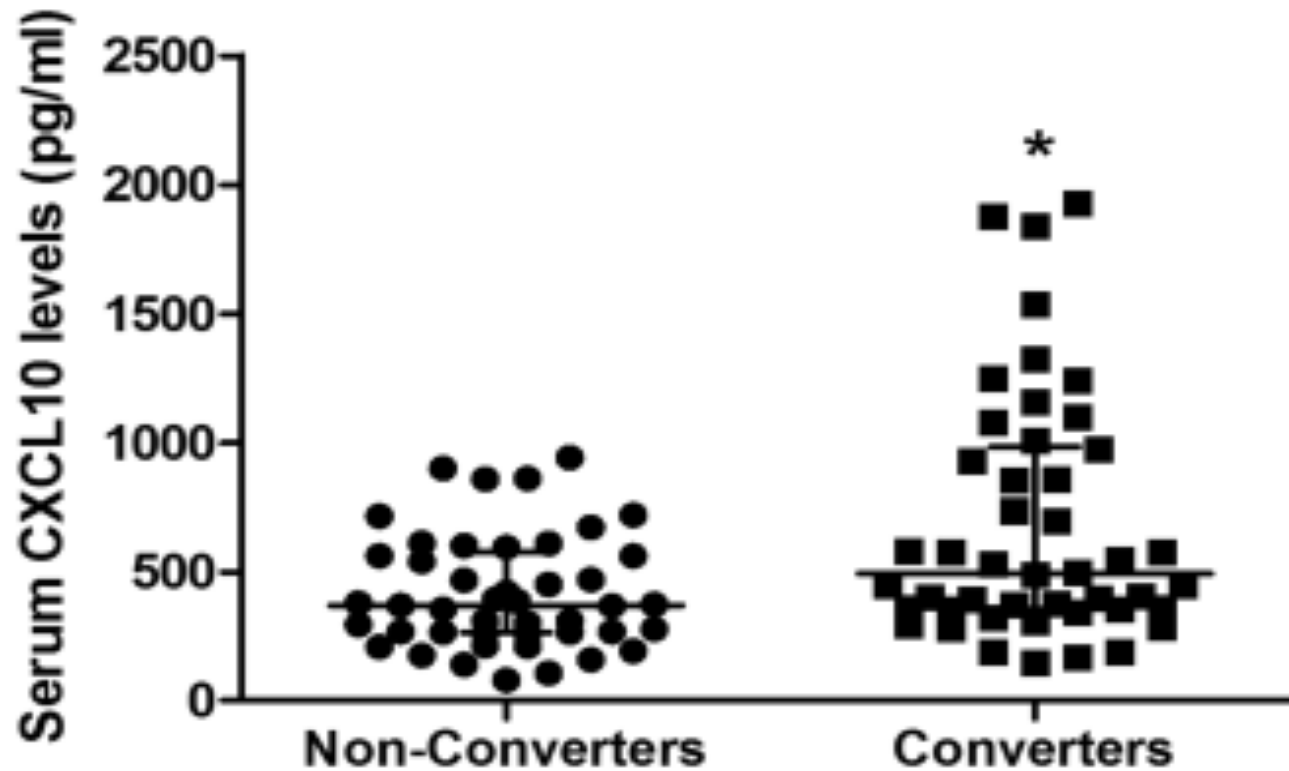
- 57/410 developed PsA over 8 years
- Baseline
 1. Arthralgia
 2. Heel pain
 3. High fatigue
 4. High stiffness
- Intercurrent
 1. Increase in pain
 2. Increase in stiffness
 3. Increase in fatigue

Performance of screening tools for PsA: a cross-sectional study in primary care

- Psoriasis Epidemiology Screening Tool (PEST), Psoriatic Arthritis Screening and Evaluation (PASE) and Early Arthritis for Psoriatic Patients (EARP) questionnaires
- PEST most favourable trade-off between sensitivity and specificity
- Prevalence of psoriasis and PsA low in primary care
- Screening only psoriasis patients with musculoskeletal complaints may be a better allocation of resources

CXCL10 Is a Possible Biomarker for the Development of Psoriatic Arthritis Among Patients With Psoriasis

Fatima Abji,¹ Remy A. Pollock,¹ Kun Liang,² Vinod Chandran,³ and Dafna D. Gladman³



CONCERNS

Suicidal ideation

- Warning for apremilast
- Development of brodalumab halted
- Overall mortality and cause-specific mortality risk were not elevated among patients with PsA except for suicide deaths

Ogdie et al. Rheumatology 2017;56(6):907-911

- The risk of depression, but not suicidal ideation or suicide attempt, was significantly increased in patients with psoriasis, PsA and AS

Wu et al. J Eur Acad Dermatol Venereol 2017 E-pub

Cardiovascular risk

- Overall mortality and cause-specific mortality risk were not elevated among patients with PsA except for suicide deaths
Ogdie et al. Rheumatology 2017;56(6):907-911
- Increased prevalence of coronary plaque in patients with psoriatic arthritis without prior diagnosis of coronary artery disease
Shen et al. ARD 2017 E-pub
- Patients with PsA had a small but significant increase in death due to diseases of the circulatory system compared with the general population
Juneblad et al. J Rheumatology 2016;43(12):2155-2161

Interventions

- Gastric bypass was associated with a significantly reduced risk and improved prognosis of psoriasis and PsA, whereas gastric banding was not
- This finding may be caused by the postoperative differences in nutrient intake and/or weight loss as well as differences in the secretion of hormones that potentially modulate inflammation

Enberg et al. JAMA Surgery 2017;152(4):344-349

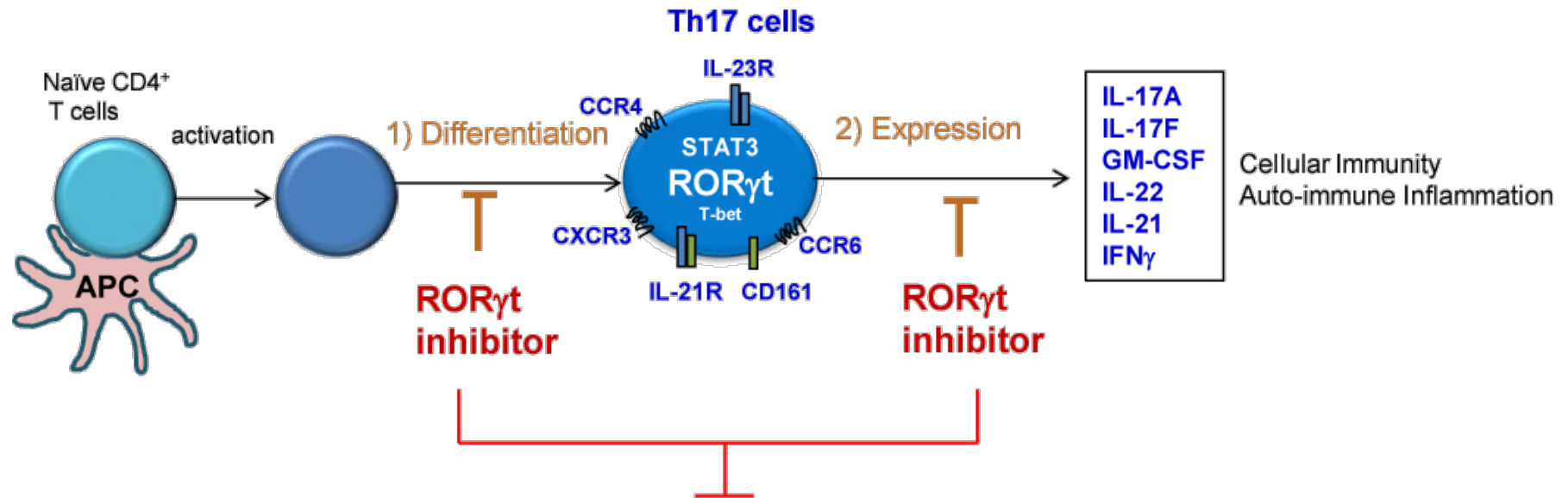
- Obesity associated with higher disease activity and seemed to diminish response and adherence to TNFIs in PsA (DANBIO & ICEBIO)

Cancer risk in patients with spondyloarthritis treated with TNF inhibitors: a collaborative study from the ARTIS and DANBIO registers

- 8703 (ARTIS=5448, DANBIO=3255) patients with SpA initiating a first TNFi 2001-2011 – a TNFi-naive SpA cohort (n=28,164) and a Swedish age-matched and sex-matched general population comparator cohort (n=131687)
- 1188 cancers among the TNFi-naive patients with SpA
- RR of cancer overall was 1.1 (95% CI 0.7 to 1.0)
- Based on 157 cancers among TNFi with SpA, RR versus TNFi-naïve was 0.8 (95% CI 0.7 to 1.0)
- Results were similar for AS and PsA when analysed separately

FUTURE

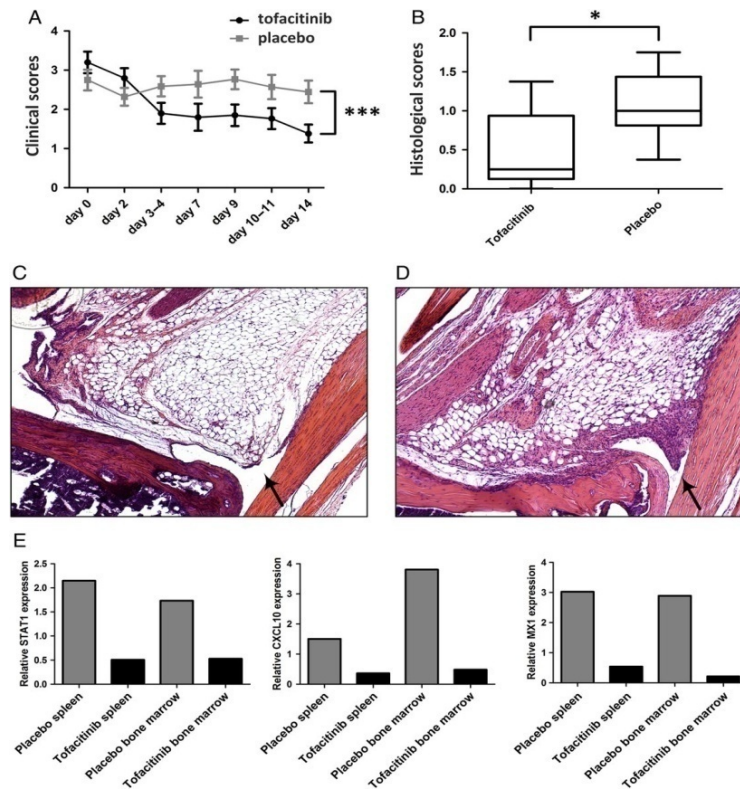
New Attractive Targets



- Psoriasis
- Rheumatoid Arthritis
- Psoriatic Arthritis
- Multiple Sclerosis
- IBD
- Ankylosing spondylitis
- COPD
- Glomerulonephritis
- Autoimmune Myocarditis
- Hashimoto Thyroiditis
- Dry Eye
- Uveitis
- Behcet's disease
- Certain types of cancers
- Sjögren's syndrome

A20 inhibition of STAT1 expression in myeloid cells: a novel endogenous regulatory mechanism preventing development of enthesitis

Katelijne De Wilde, Anne Martens et al



Thank you