



IL-17 inhibition in the management of SpA

Ennio G. Favalli



Department and Chair of Rheumatology
Gaetano Pini Institute
Milan

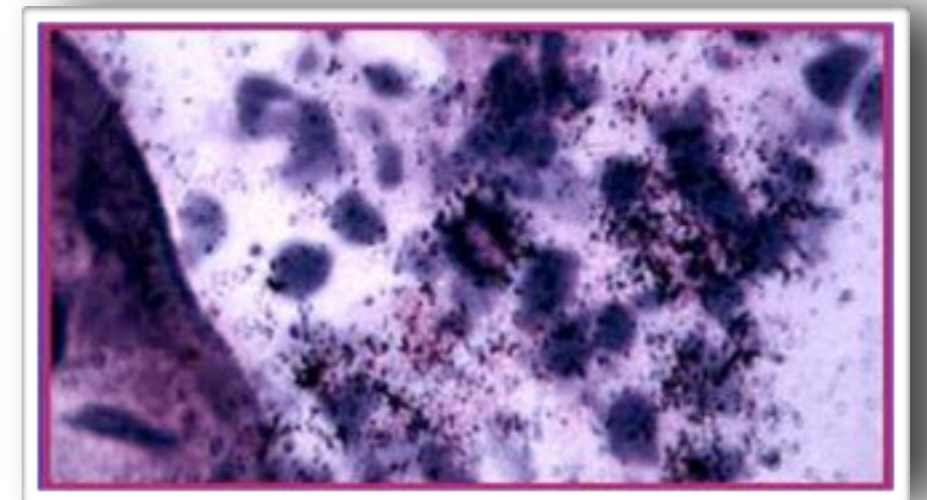


Financial Disclosure

- ◆ AbbVie
- ◆ Abiogen
- ◆ Alfa-Wassermann
- ◆ Bristol-Myers-Squibb
- ◆ Celgene
- ◆ Hoffmann-La Roche
- ◆ Janssen
- ◆ Merck-Sharp & Dohme
- ◆ Mundipharma
- ◆ Novartis
- ◆ Pfizer
- ◆ Samsung-Biogen
- ◆ Sandoz
- ◆ Sanofi
- ◆ UCB Pharma

Role of TNF α in SpA

- Higher compared with non-inflammatory back pain
 - Not correlated with other parameters of disease's activity ⁽¹⁾
- Serum levels of TNF- α in SpA patients
 - High expression of TNF- α in the sacroiliac joints (detection by biopsy). ⁽²⁾
 - High expression of TNF- α in the skin of psoriatic patients



⁽¹⁾ Gratacos J, et al. Br J Rheumatol, 1994

⁽²⁾ Braun J, et al. Arthritis Rheum, 1995

Available anti-TNF agents for SpA

Etanercept



Infliximab



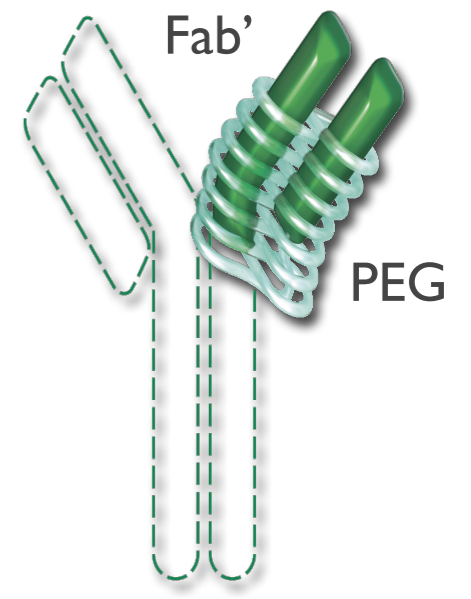
Adalimumab



Golimumab



Certolizumab



Chimeric

Humanized

Human

Recombinant
receptor/Fc
fusion protein

Monoclonal
antibodies

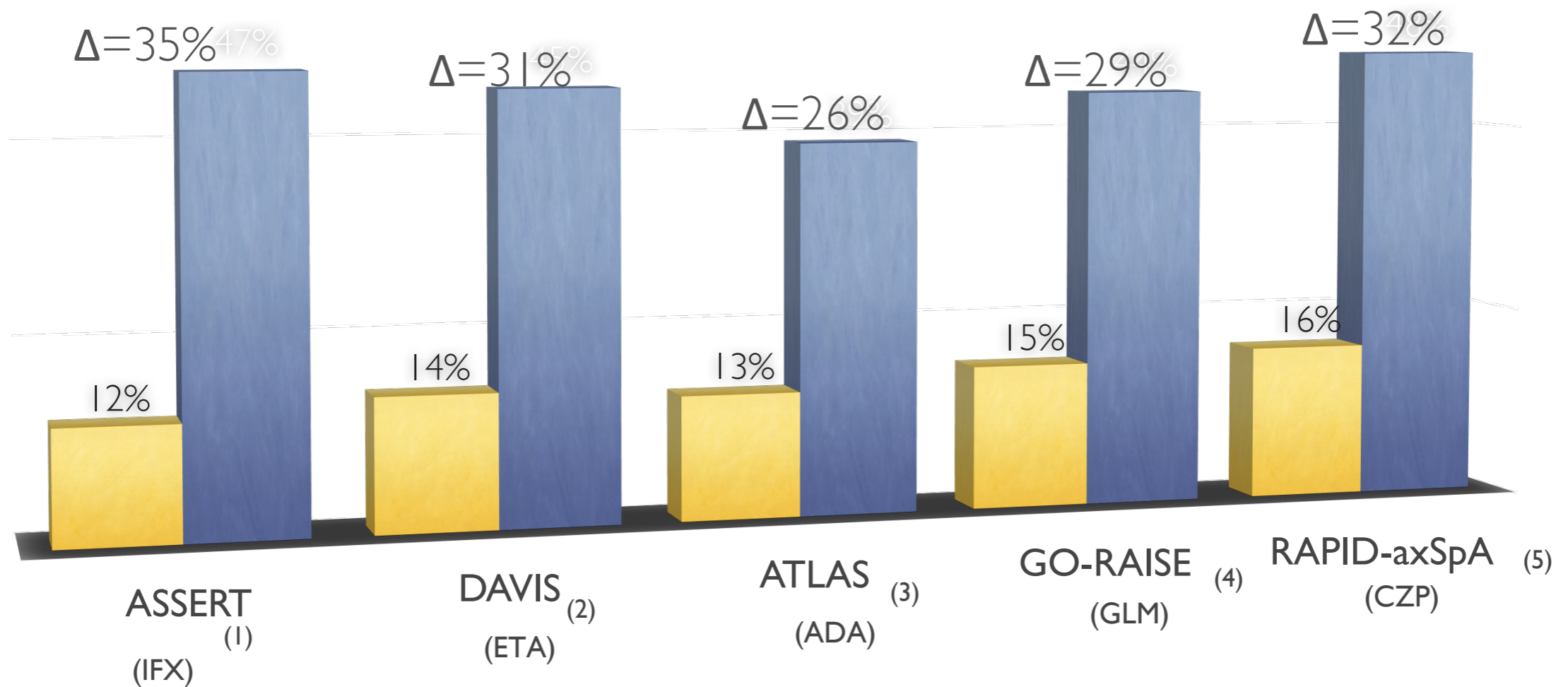
Pegylated FAB'
fragment

TNFis in axSpA: ASAS₄₀ response at 24 weeks

% of pts

■ Placebo ■ Anti-TNF

All values p<0.001 vs placebo



(1) van der Heijde D, et al., Arthritis Rheum 2005

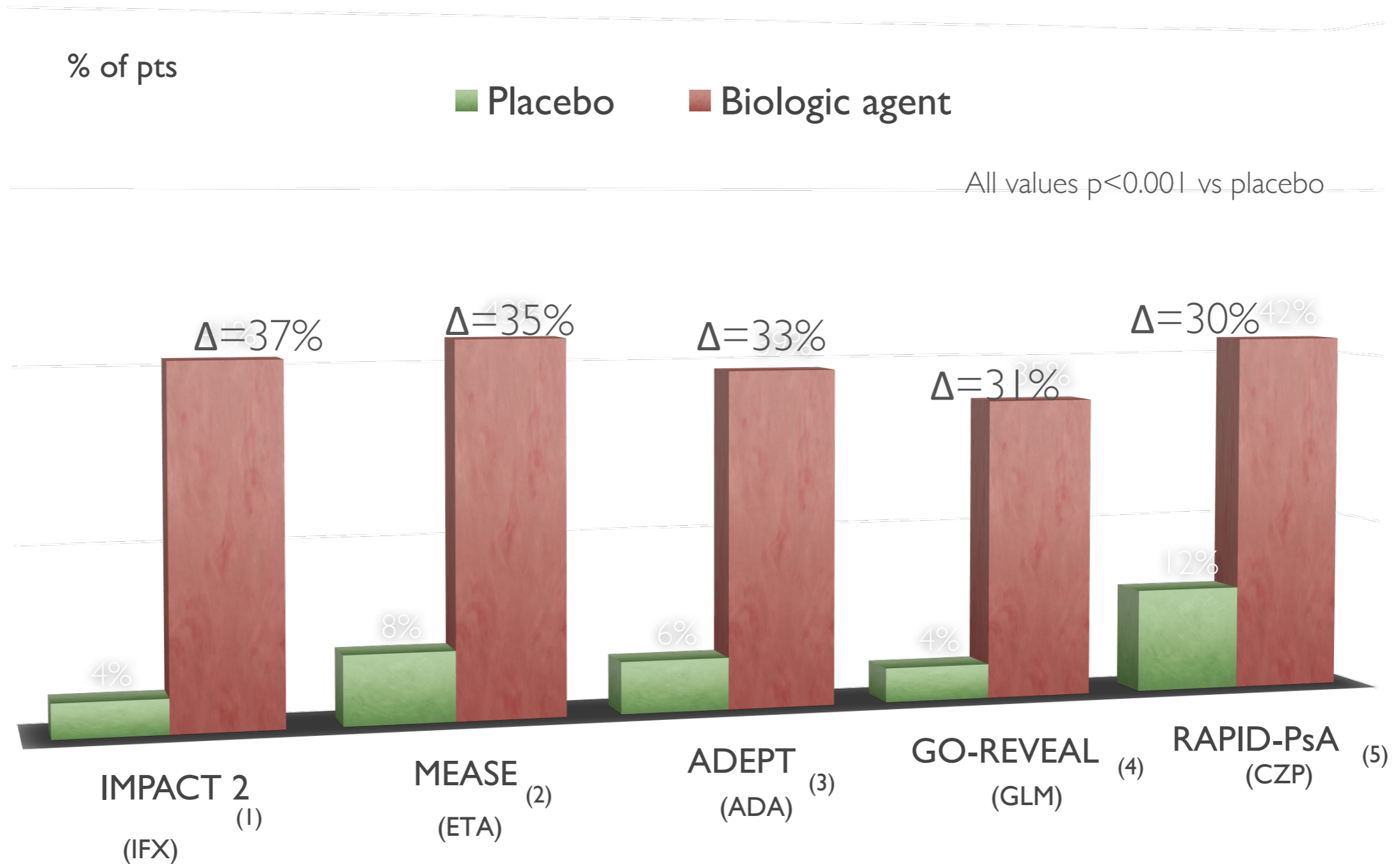
(2) Davis JC, et al. Arthritis Rheum 2003

(3) van der Heijde D, et al., Arthritis Rheum 2006

(4) Inman RD, et al., Arthritis Rheum 2008

(5) Landewè, R et al., Ann Rheum Dis 2014

TNFis in PsA: ACR₅₀ response at 24 weeks



(1) Antoni C, et al., Ann Rheum Dis 2005

(2) Mease PJ, et al. Arthritis Rheum 2004

(3) Mease PJ, et al. Arthritis Rheum 2005

(4) Kavanaugh A, et al., Arthritis Rheum 2009

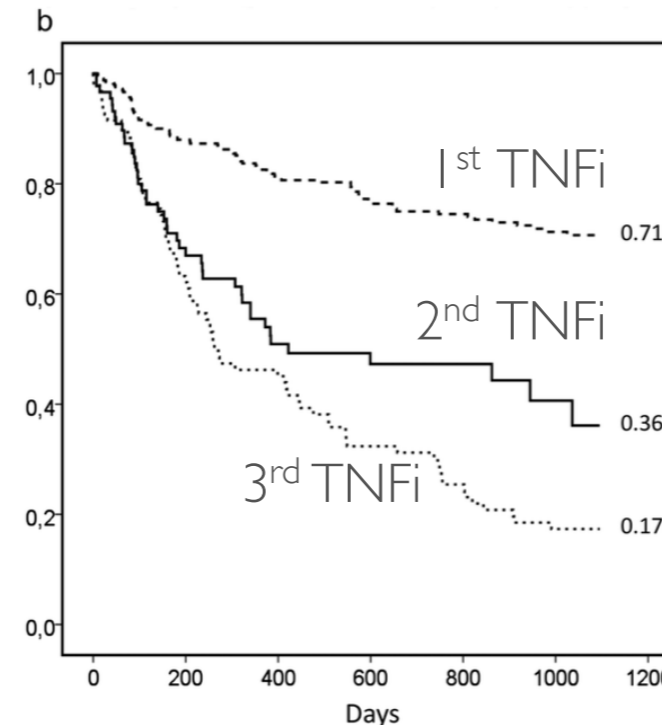
(5) Mease PJ, et al., Ann Rheum Dis 2014

Unmet needs in SpA treatment

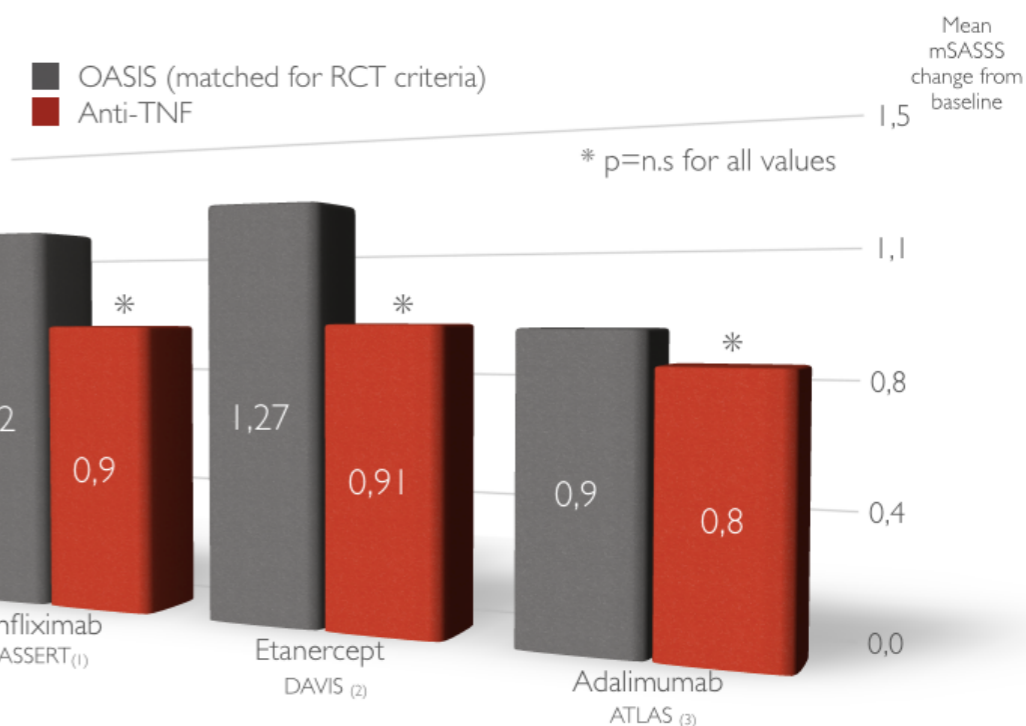
- Personalized therapy of bDMARD naïve patients

- Treatment of anti-TNF insufficient responders

- Treatment of **damage progression** in axial disease



Fagerli KM, et al. Ann Rheum Dis 2013



⁽¹⁾ van der Heijde D, et al., Arthritis Rheum 2008
⁽²⁾ van der Heijde D, et al., Arthritis Rheum 2008
⁽³⁾ van der Heijde D, et al., Arthritis Res Ther 2009



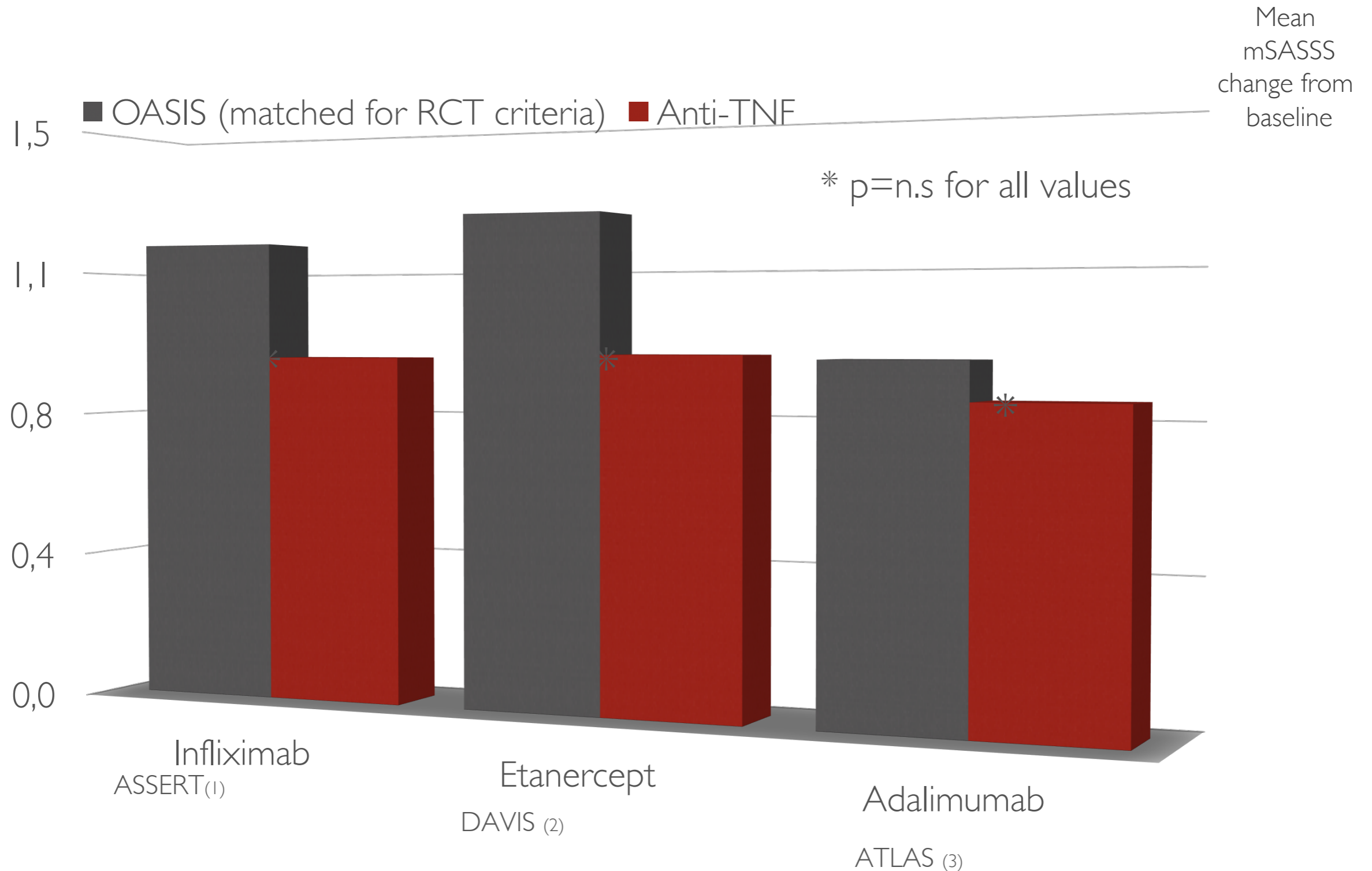
Transgenic mice expressing human tumour necrosis factor: a predictive genetic model of arthritis

Jeanne Keffer, Lesley Probert, Haris Cazlaris,
Spiros Georgopoulos, Evangelos Kaslaris¹,
Dimitris Kioussis² and George Kollias

EMBO J 1991

- Transgenic mice carrying 3'-modified hTNF trans-genes shows deregulated patterns of expression and develop **chronic inflammatory arthritis**
- These rodents develop a **synovial-associated pathology** with pannus formation that is more reminiscent of **rheumatoid arthritis than spondyloarthropathy**

Radiographic progression in historic AS cohort OASIS and in anti-TNF treated patients



(1) van der Heijde D, et al., Arthritis Rheum 2008

(2) van der Heijde D, et al., Arthritis Rheum 2008

(3) van der Heijde D, et al., Arthritis Res Ther 2009



REVIEWS

The IL-23–IL-17 axis in inflammatory arthritis

Erik Lubberts

Nat Rev Rheumatol 2014



The interleukin-23/interleukin-17 immune axis as a promising new target in the treatment of spondyloarthritis

Curr Opin Rheumatol 2014

Nataliya Yeremenko^{a,b}, Jacqueline E. Paramarta^a, and Dominique Baeten^{a,b}



The Bench-to-Bedside Story of IL-17 and the Therapeutic Efficacy of its Targeting in Spondyloarthritis

Judith A. Smith¹

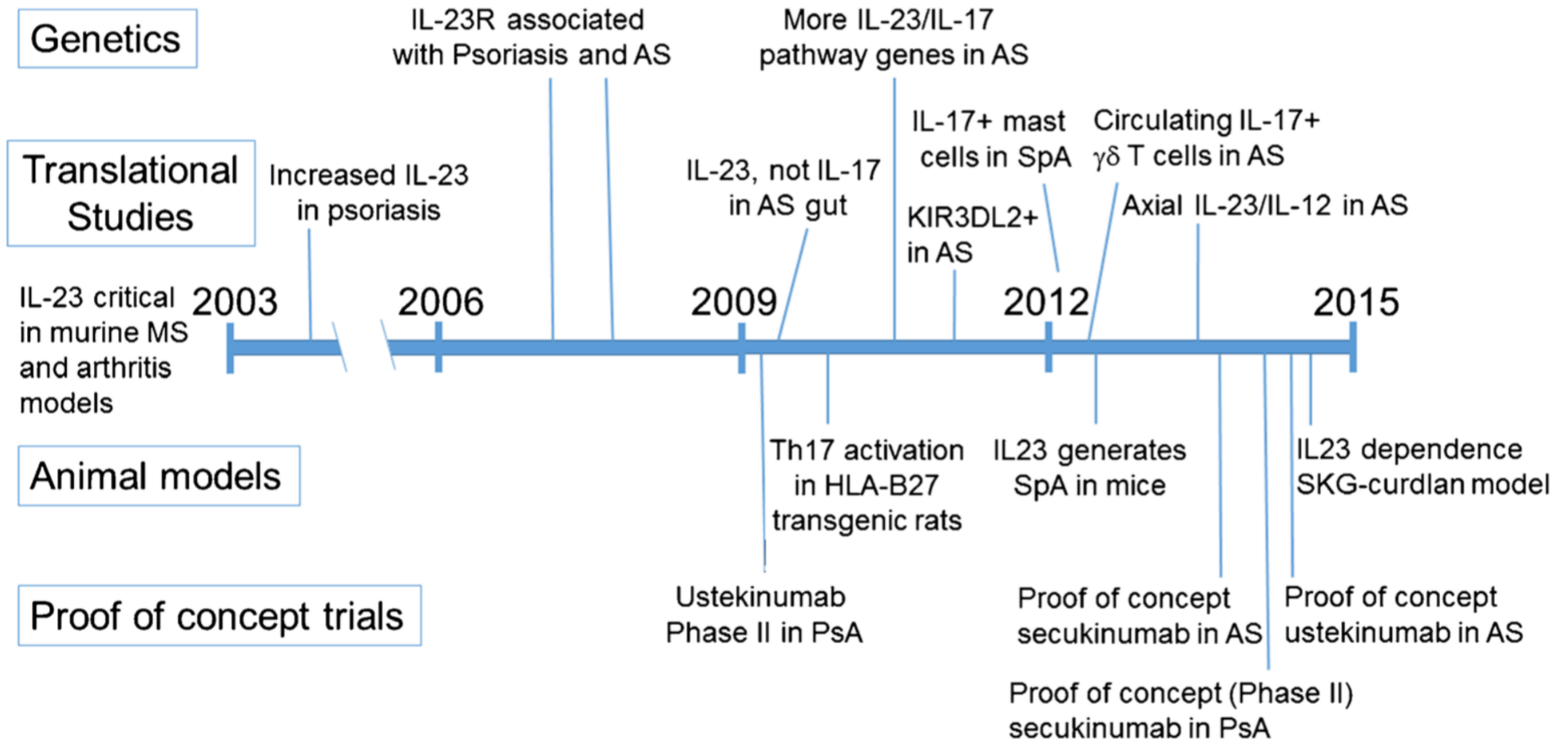
Curr Rheumatol Rep 2016



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Curr Rheumatol Rep 2016

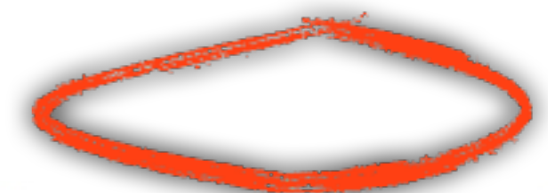
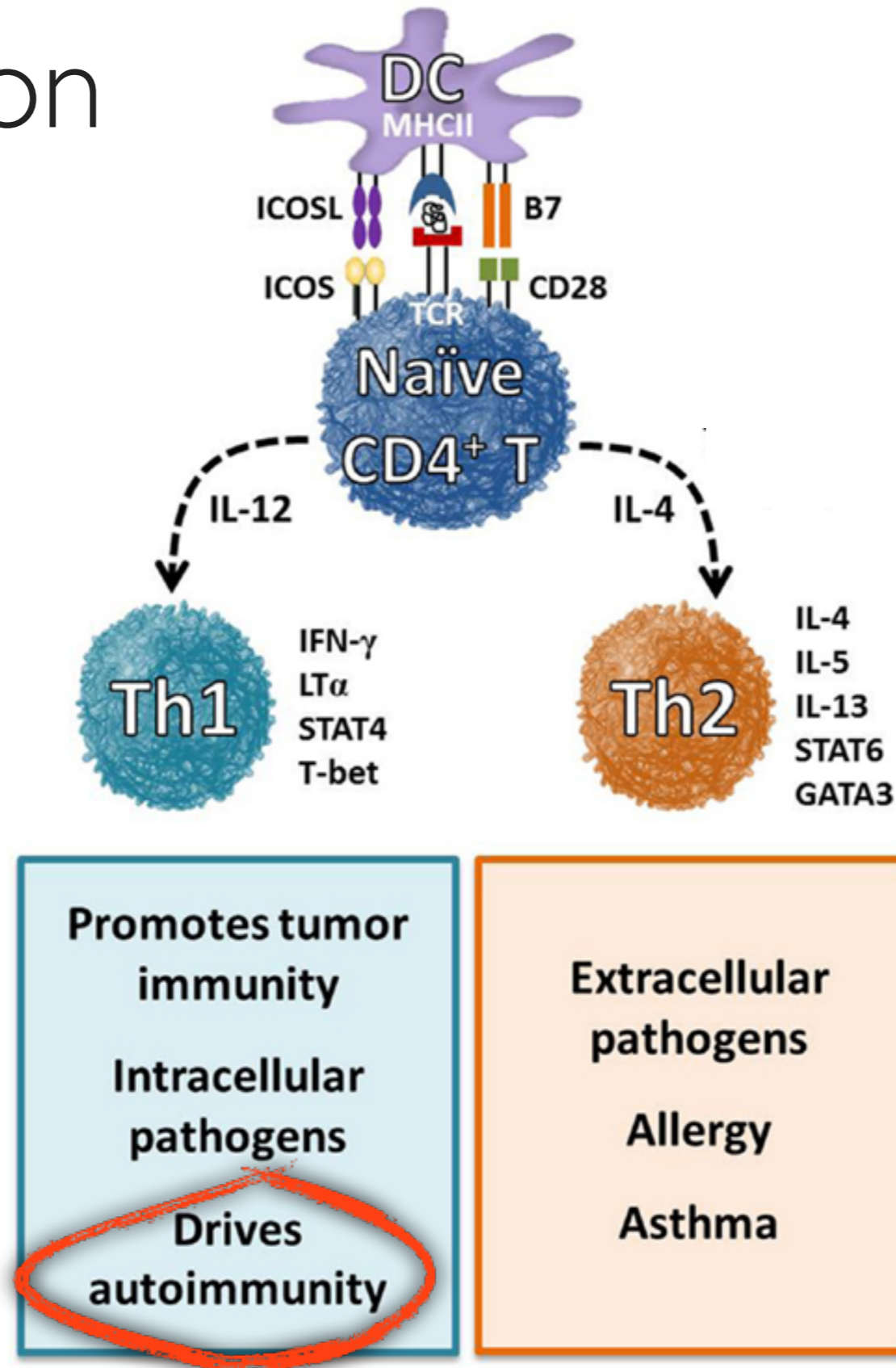


Talk composition

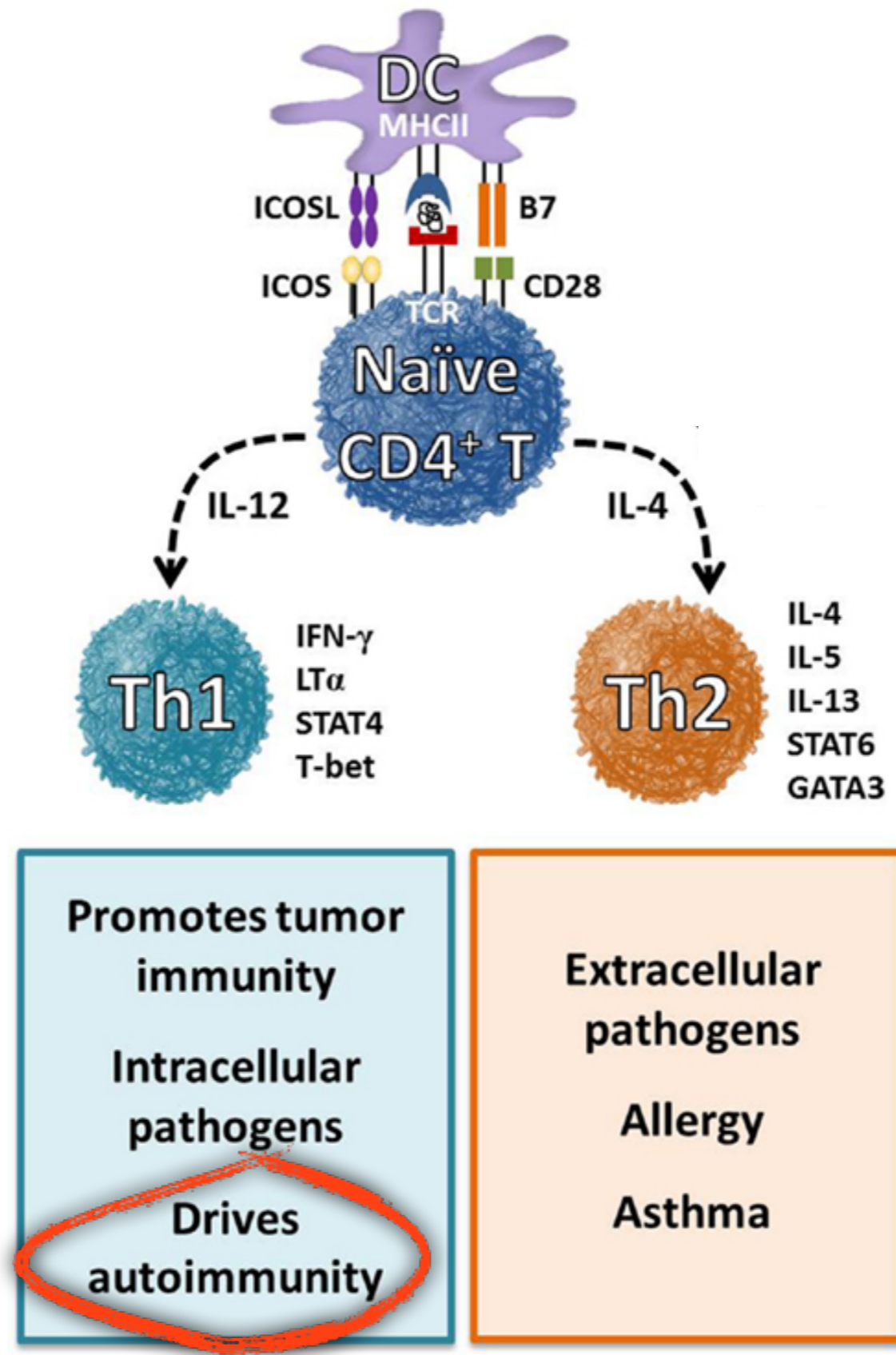
- ☑ IL-17, immunity and inflammation



CD4⁺ T-cell differentiation



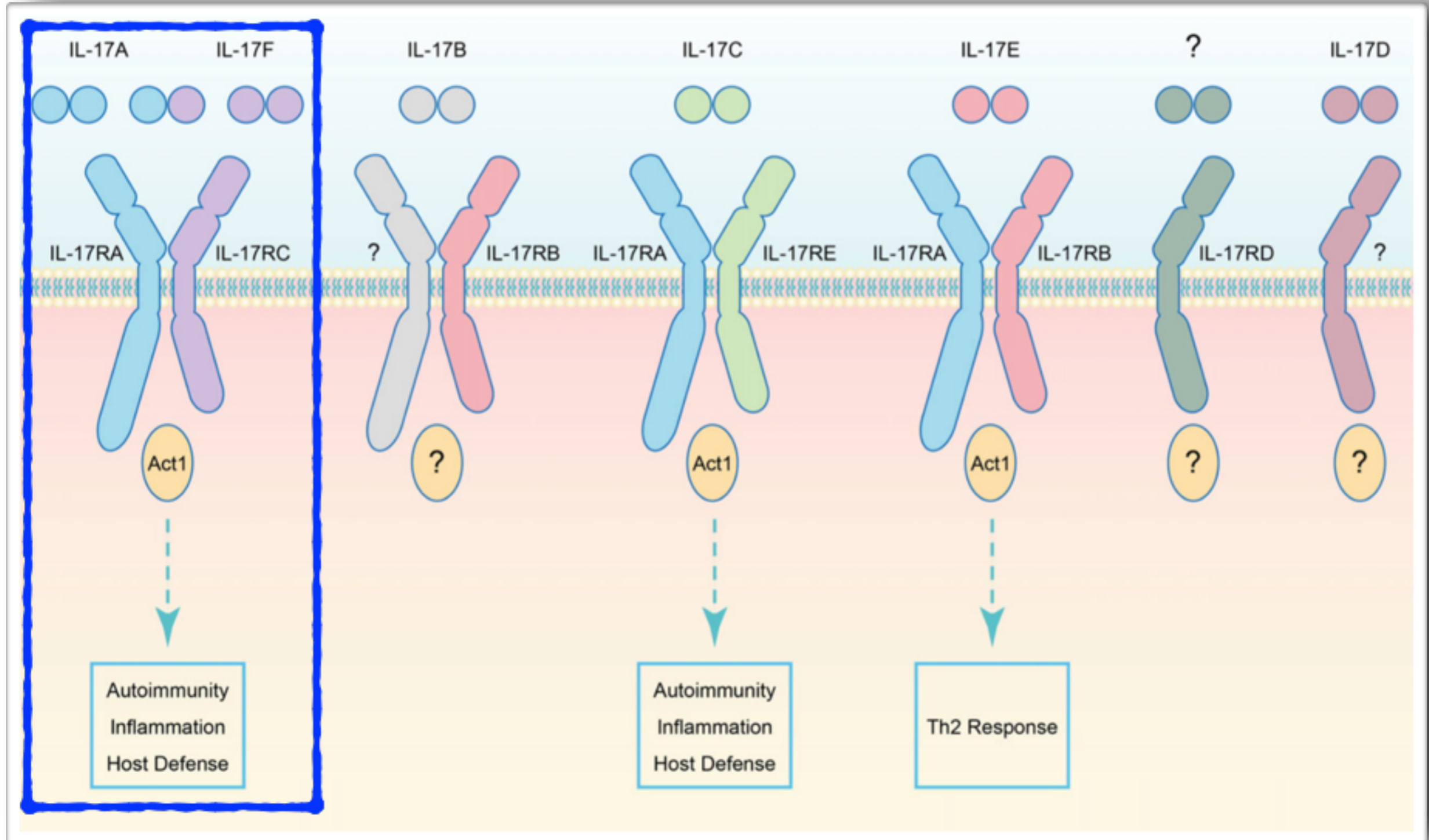
CD4⁺ T-cell differentiation



IL-17 family cytokines mediated signaling in the pathogenesis of inflammatory diseases

Xinyang Song, Youcun Qian *

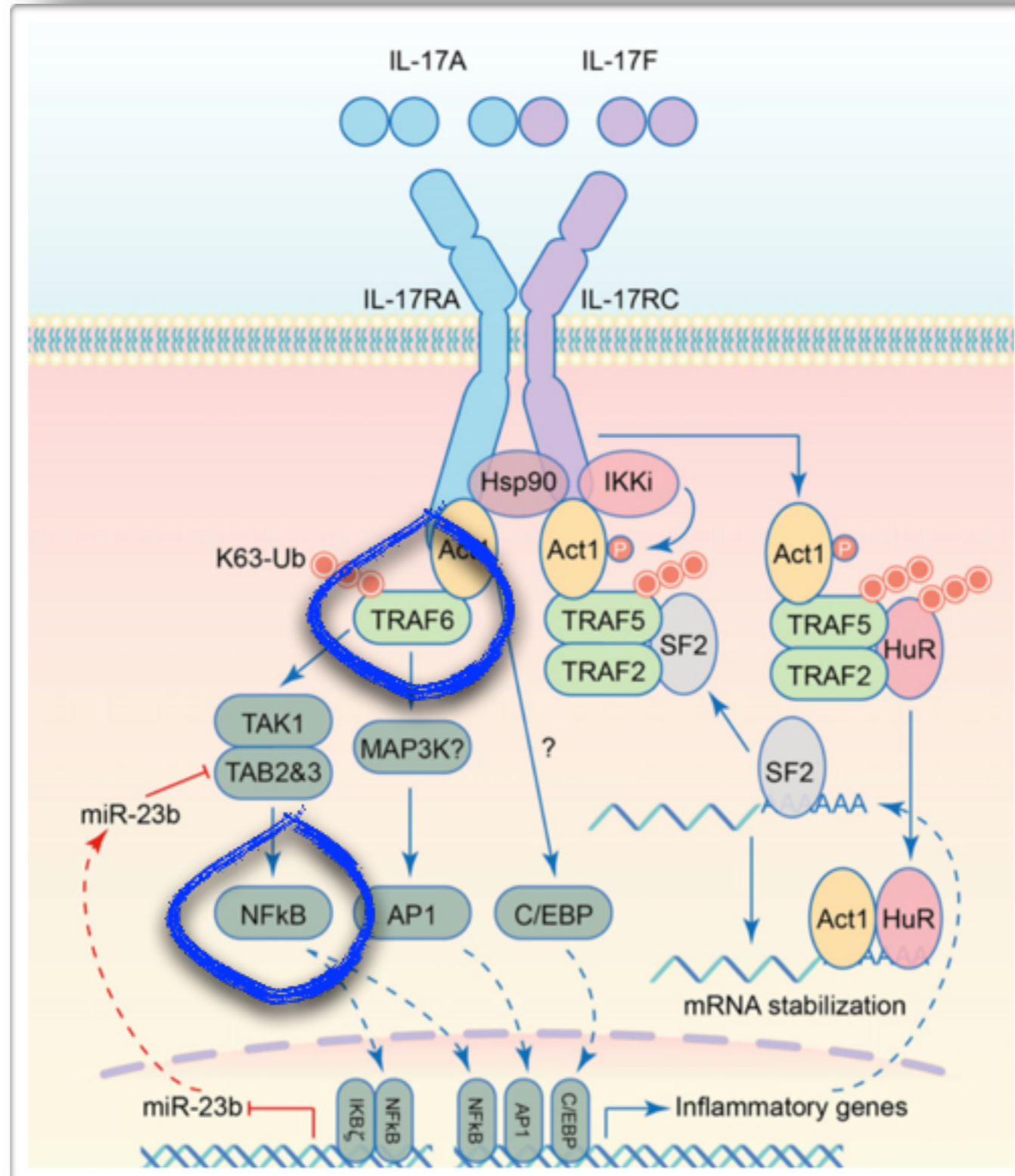
Cellular Signaling 2013

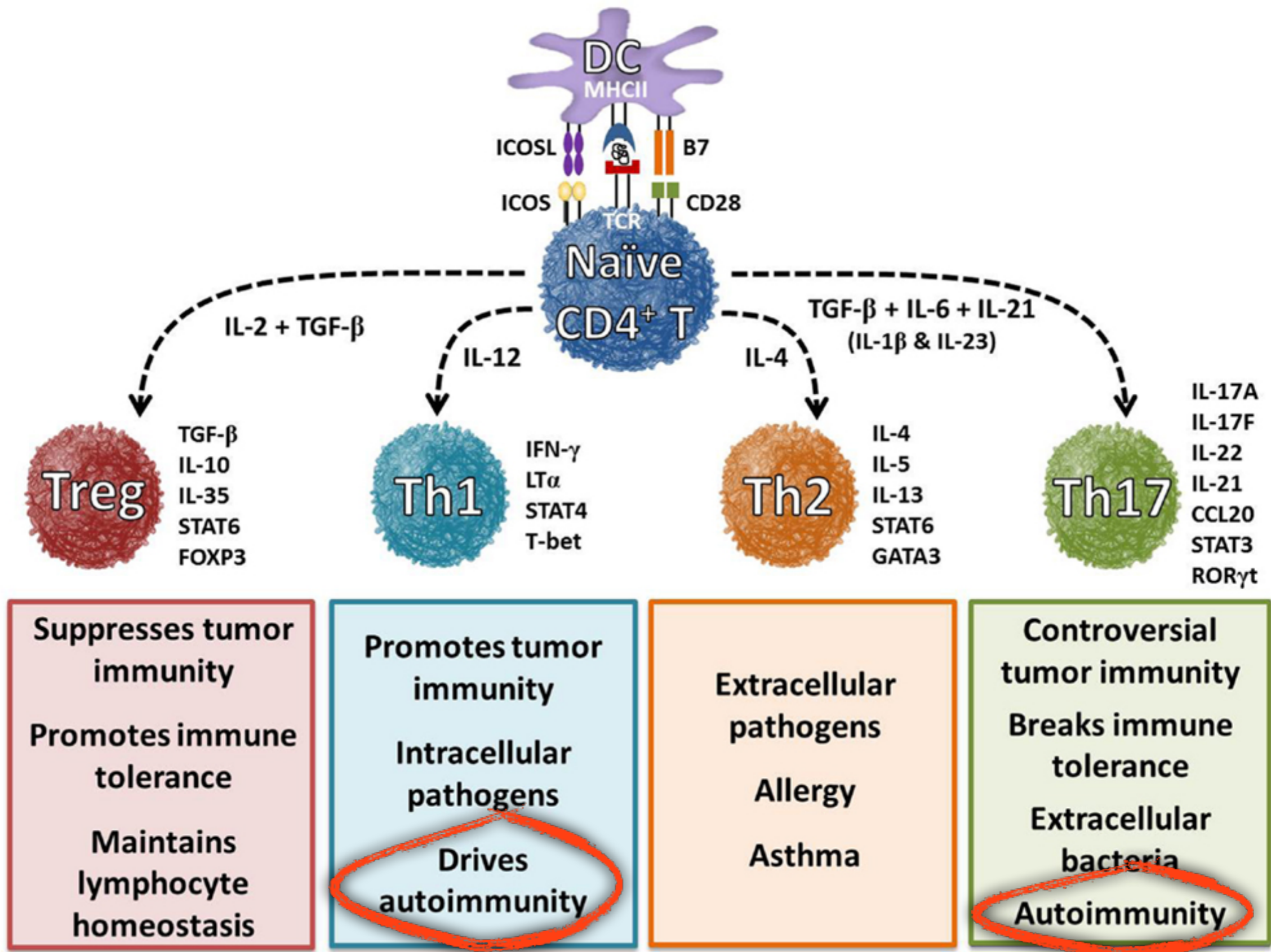


IL-17 family cytokines mediated signaling in the pathogenesis of inflammatory diseases

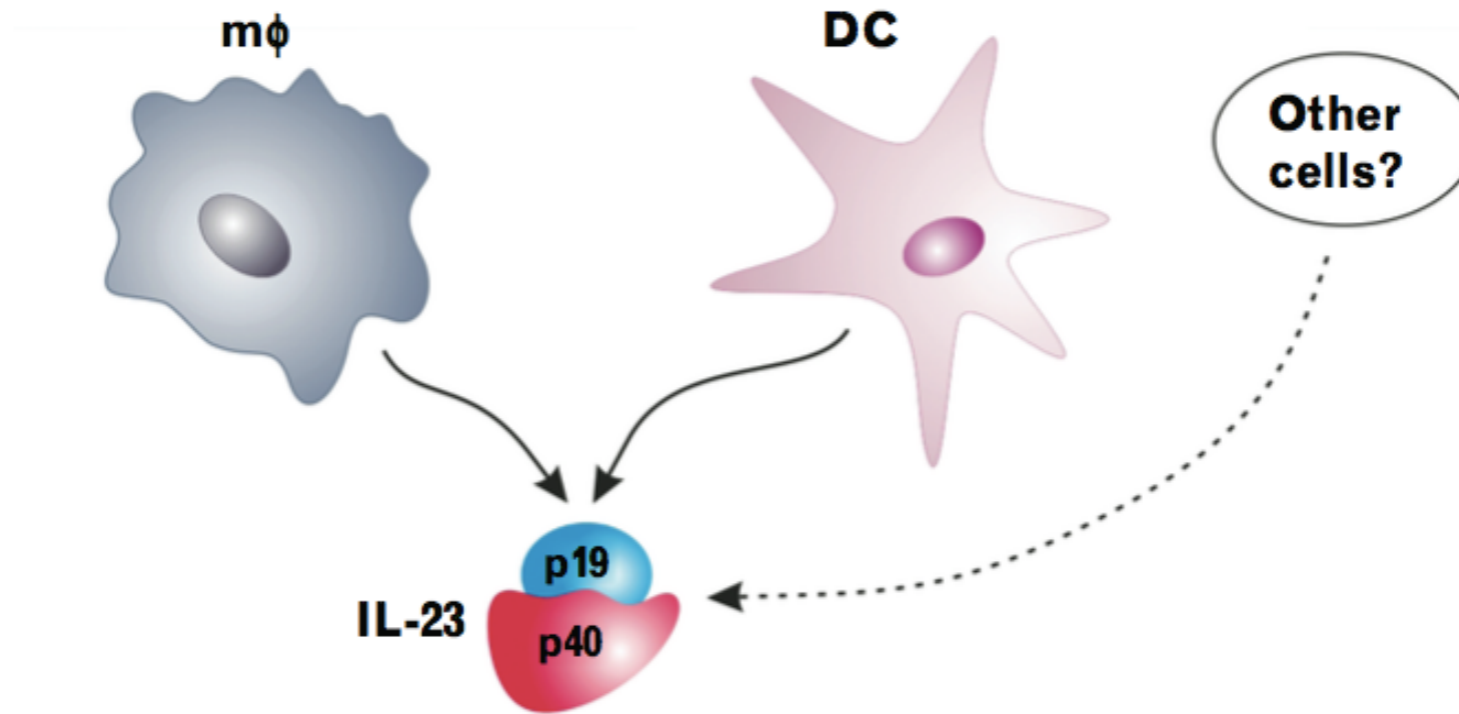
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Cellular Signaling 2013

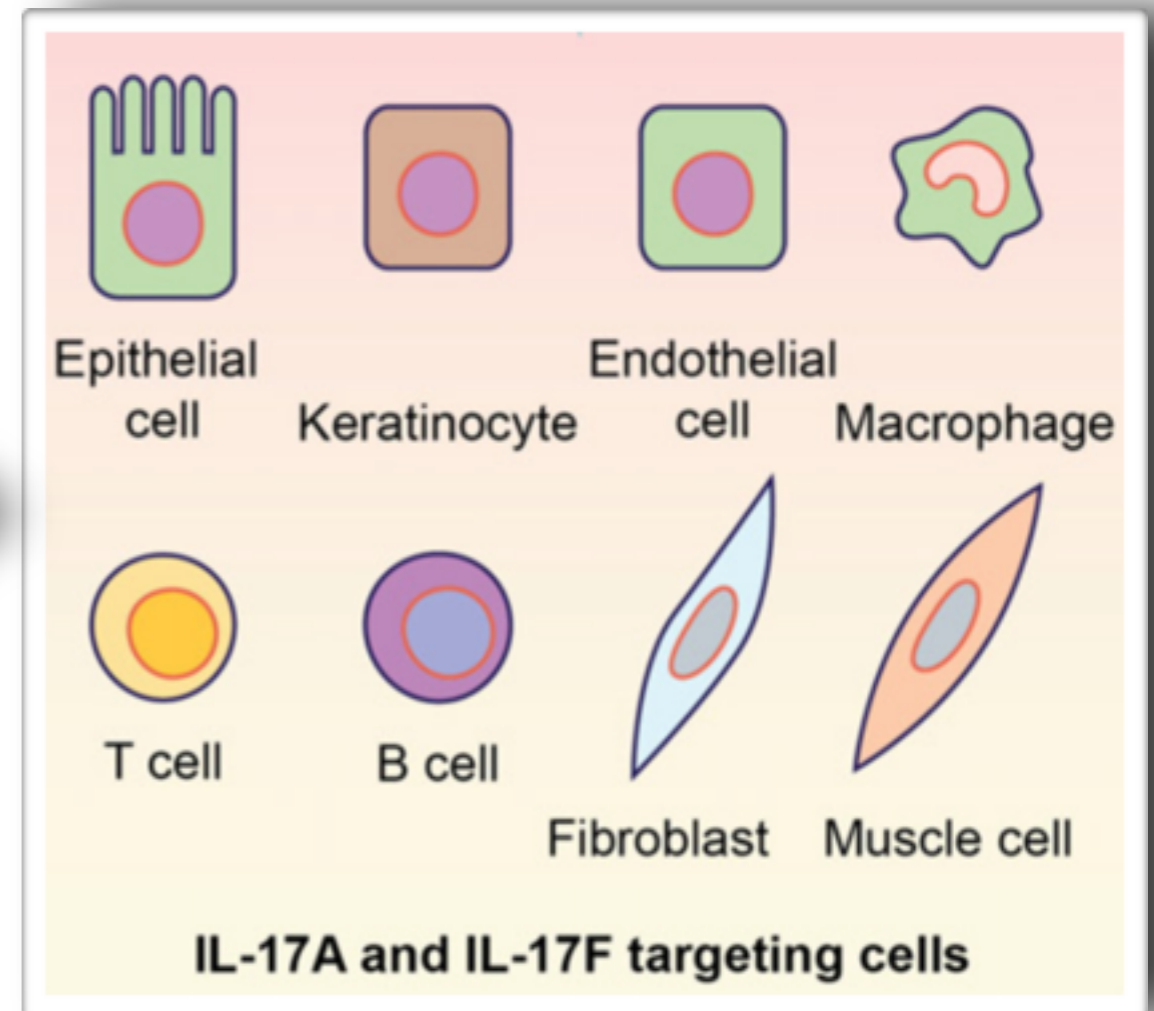
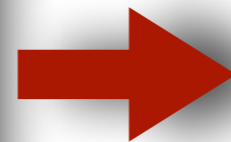
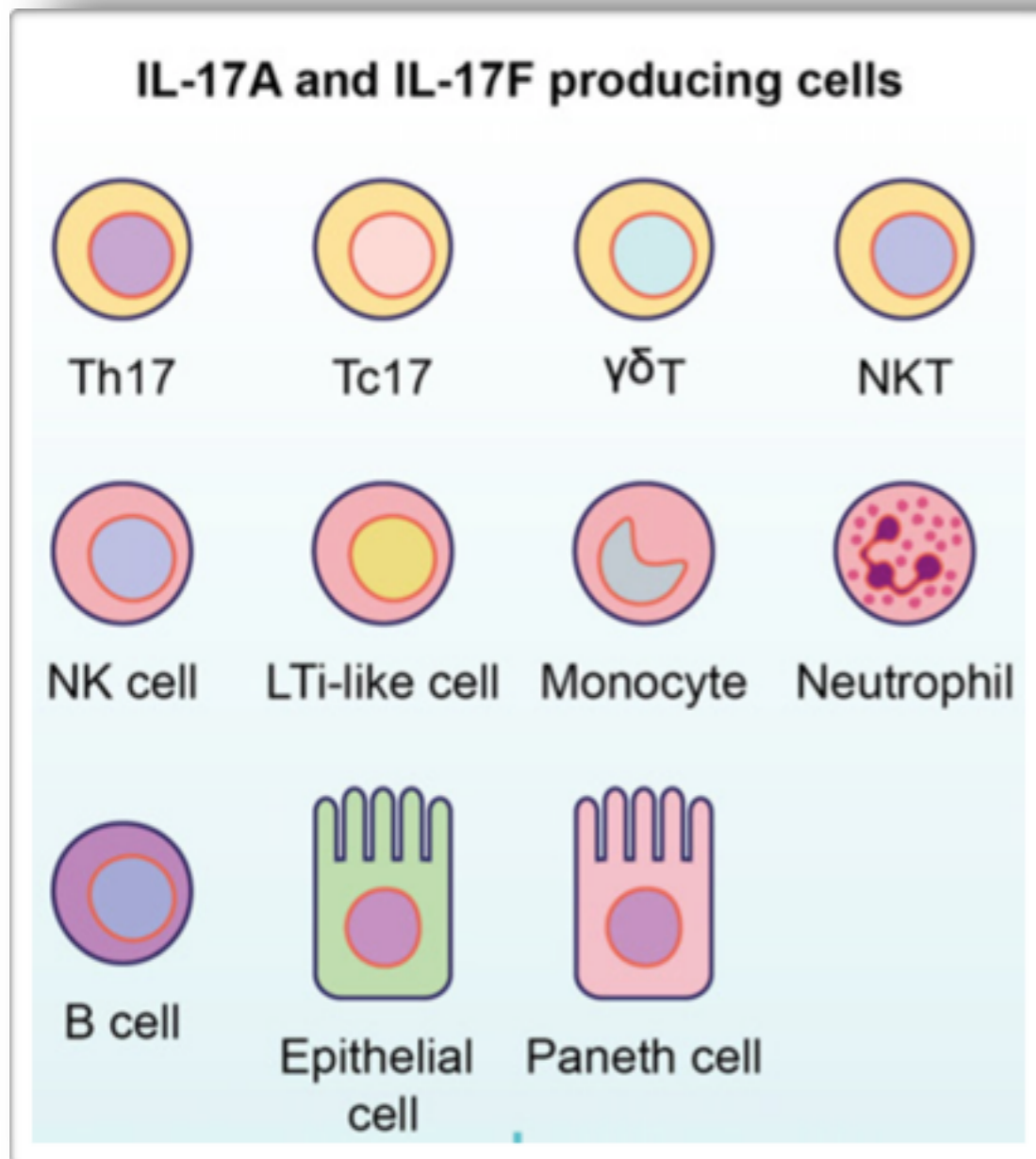




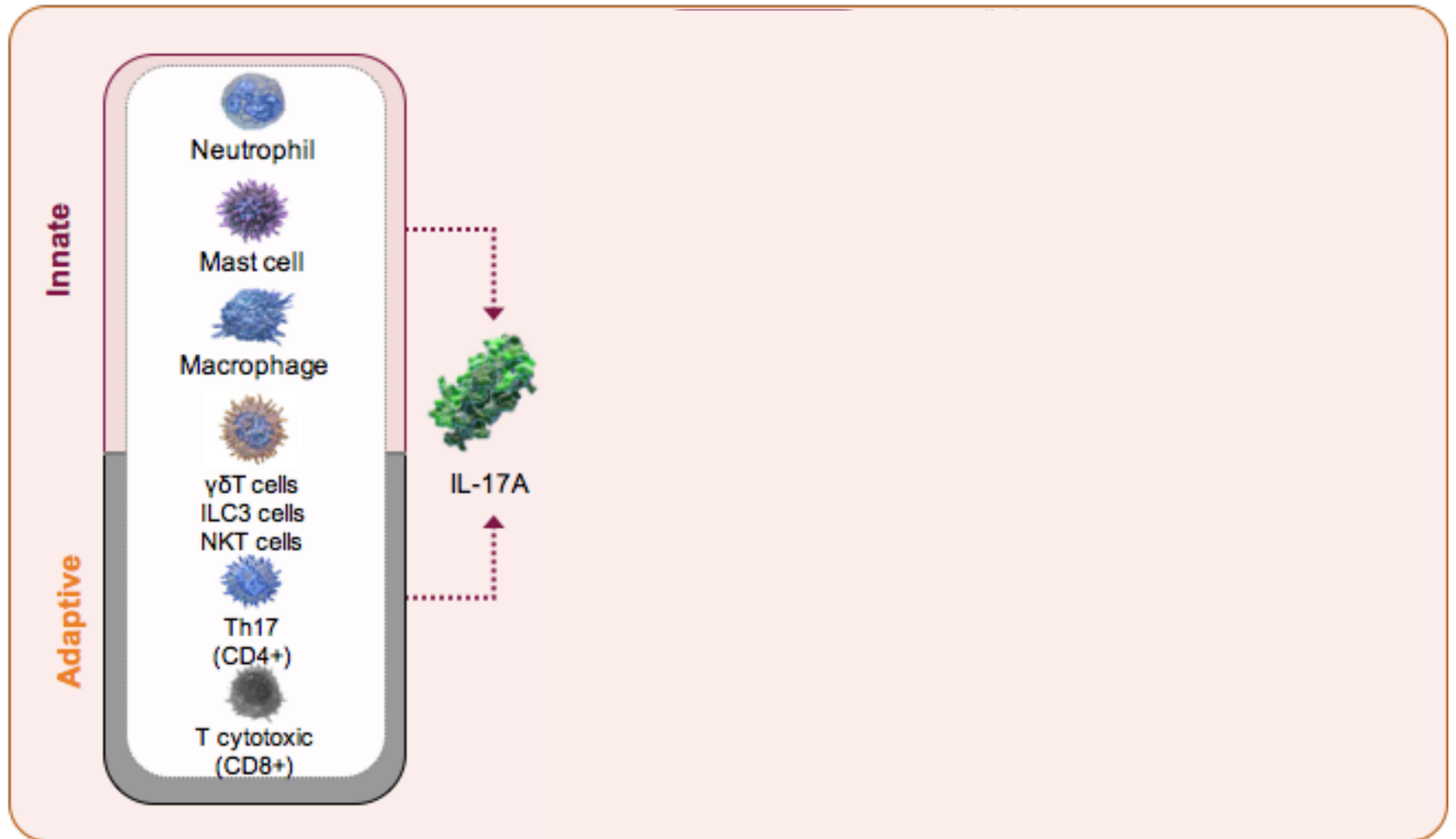
The IL-23/IL-17 pathway



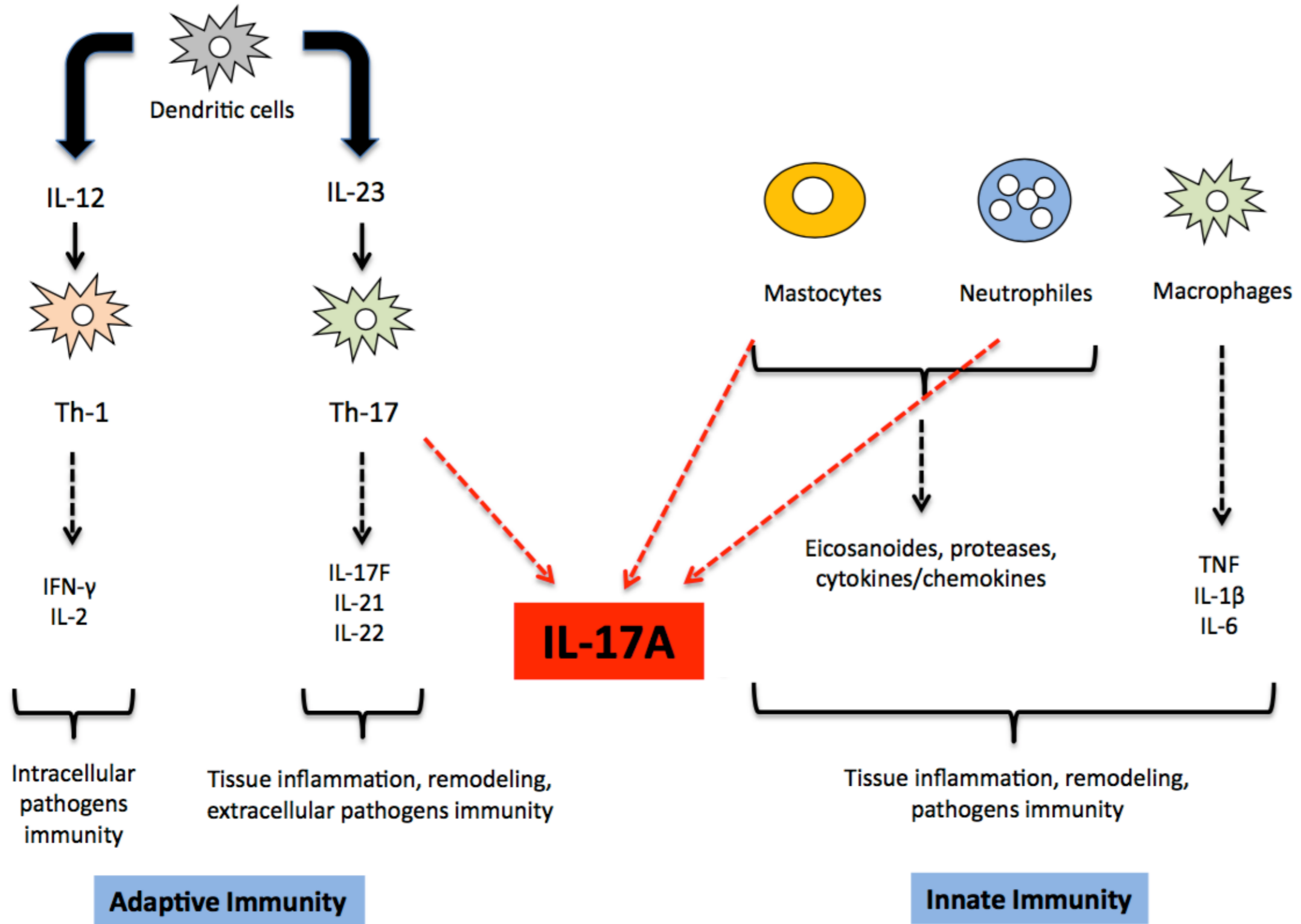
Cellular sources of IL-17A/F



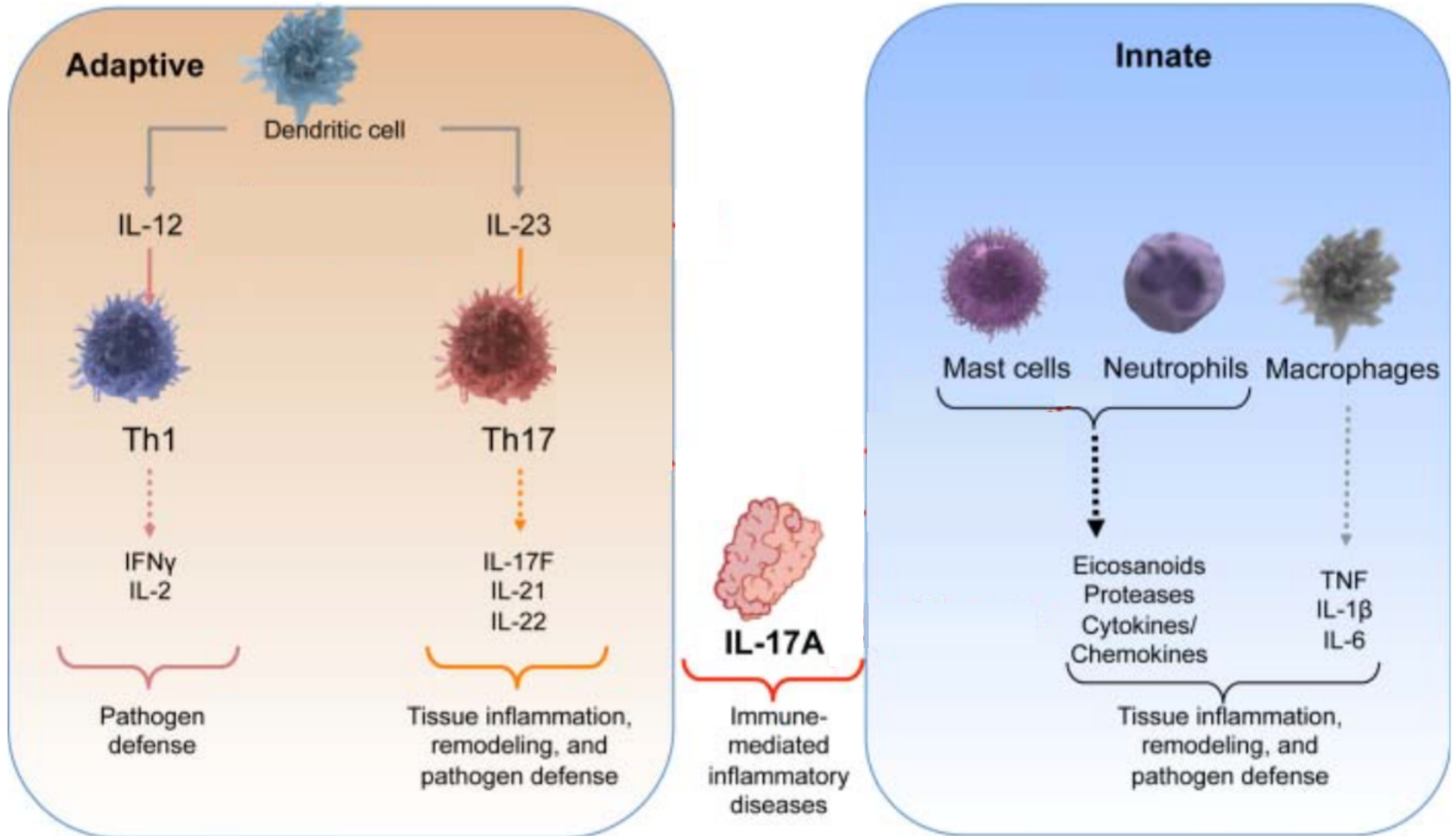
Cellular sources and targets of IL-17A



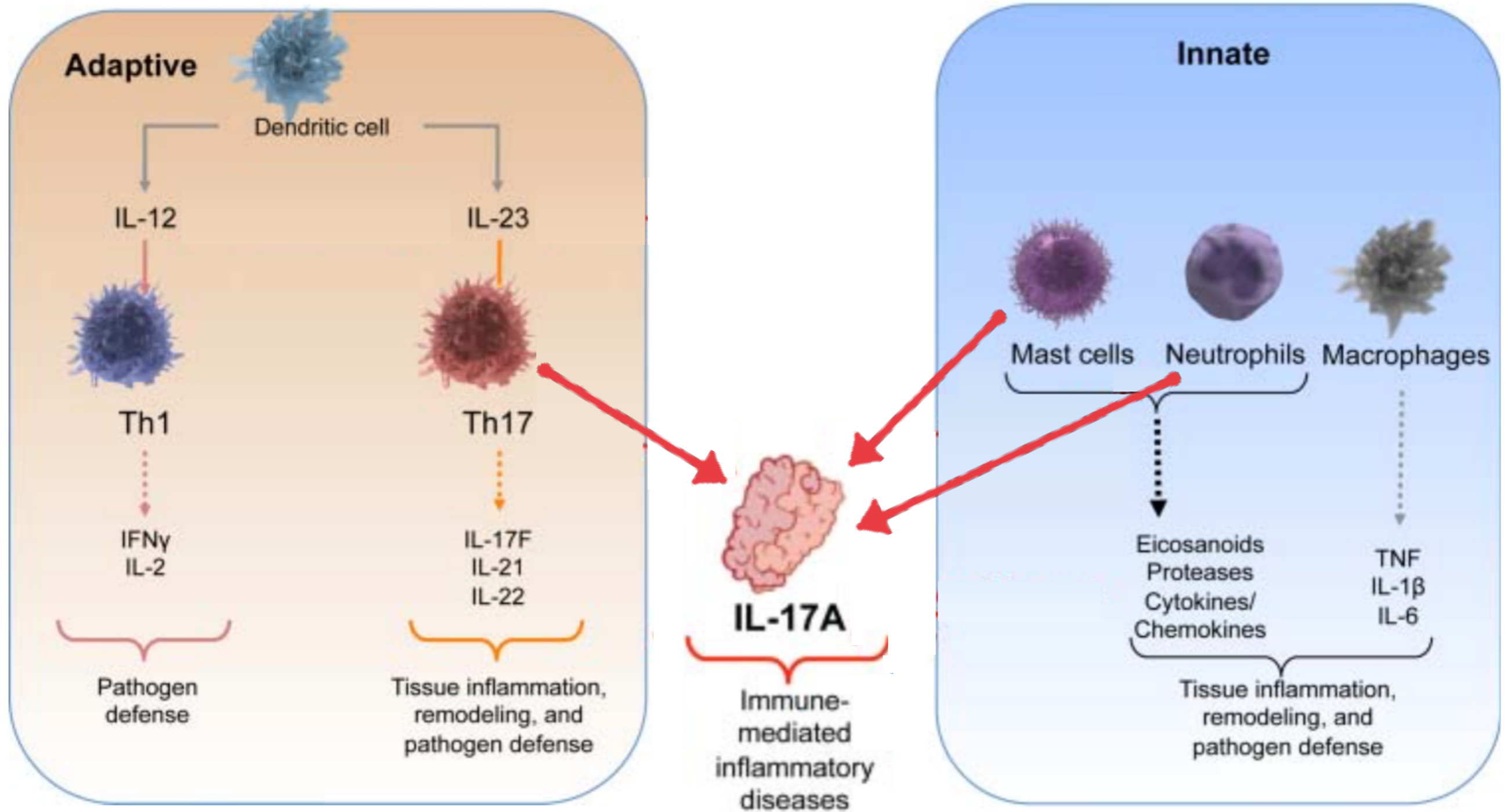
Interleukin-12/23



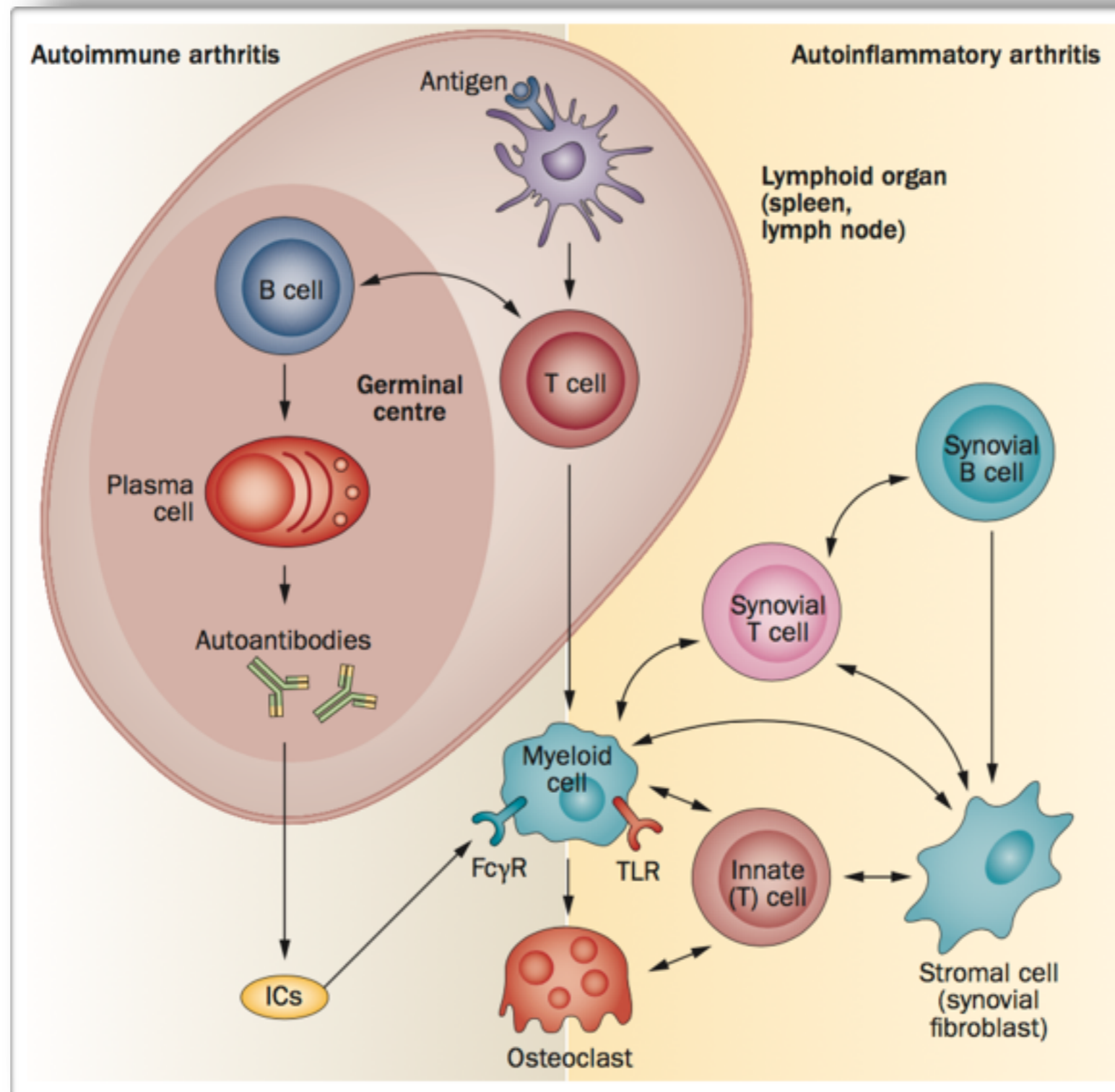
Cellular sources of IL-17A



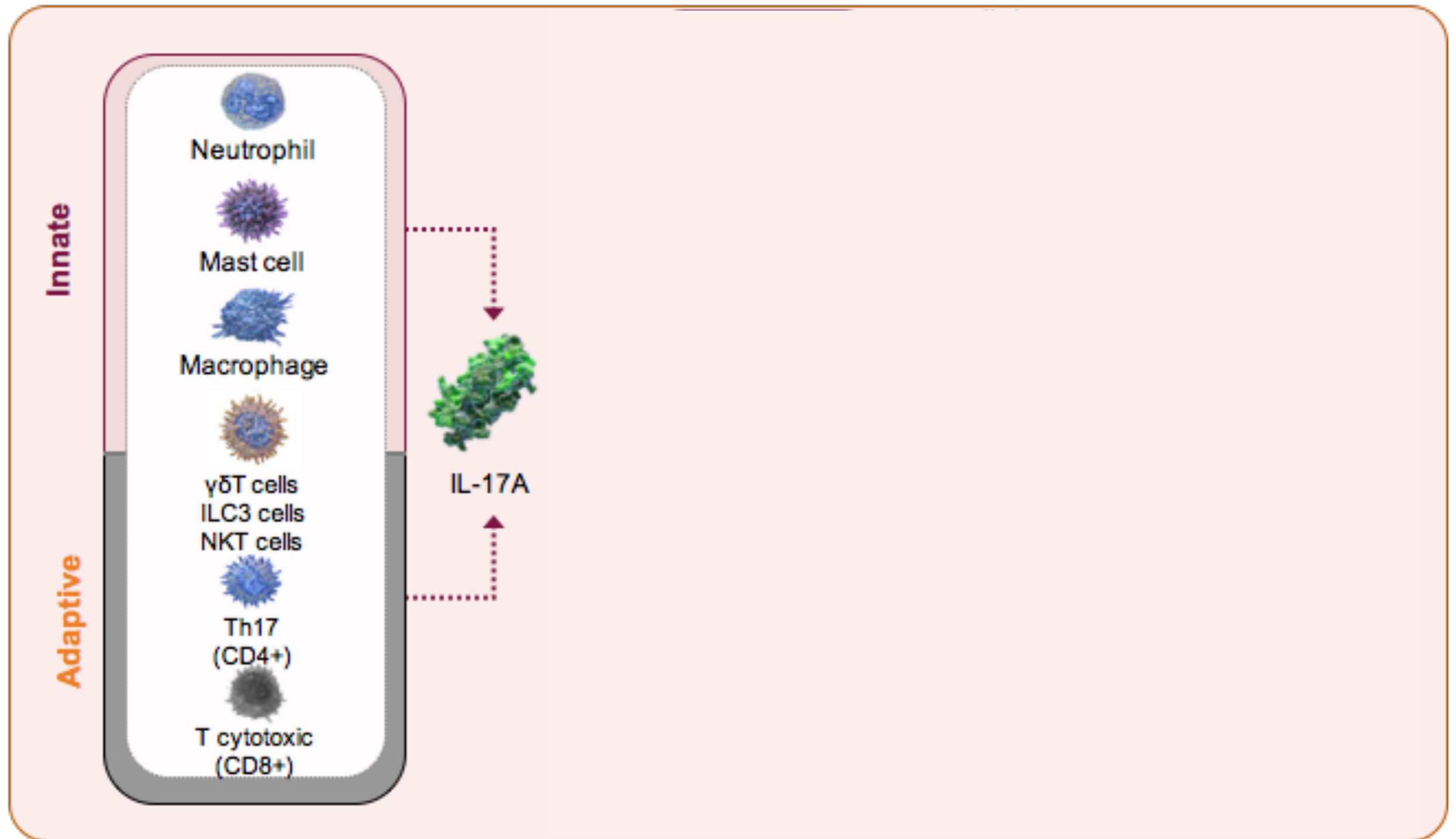
IL-17A as adaptive/innate immune product



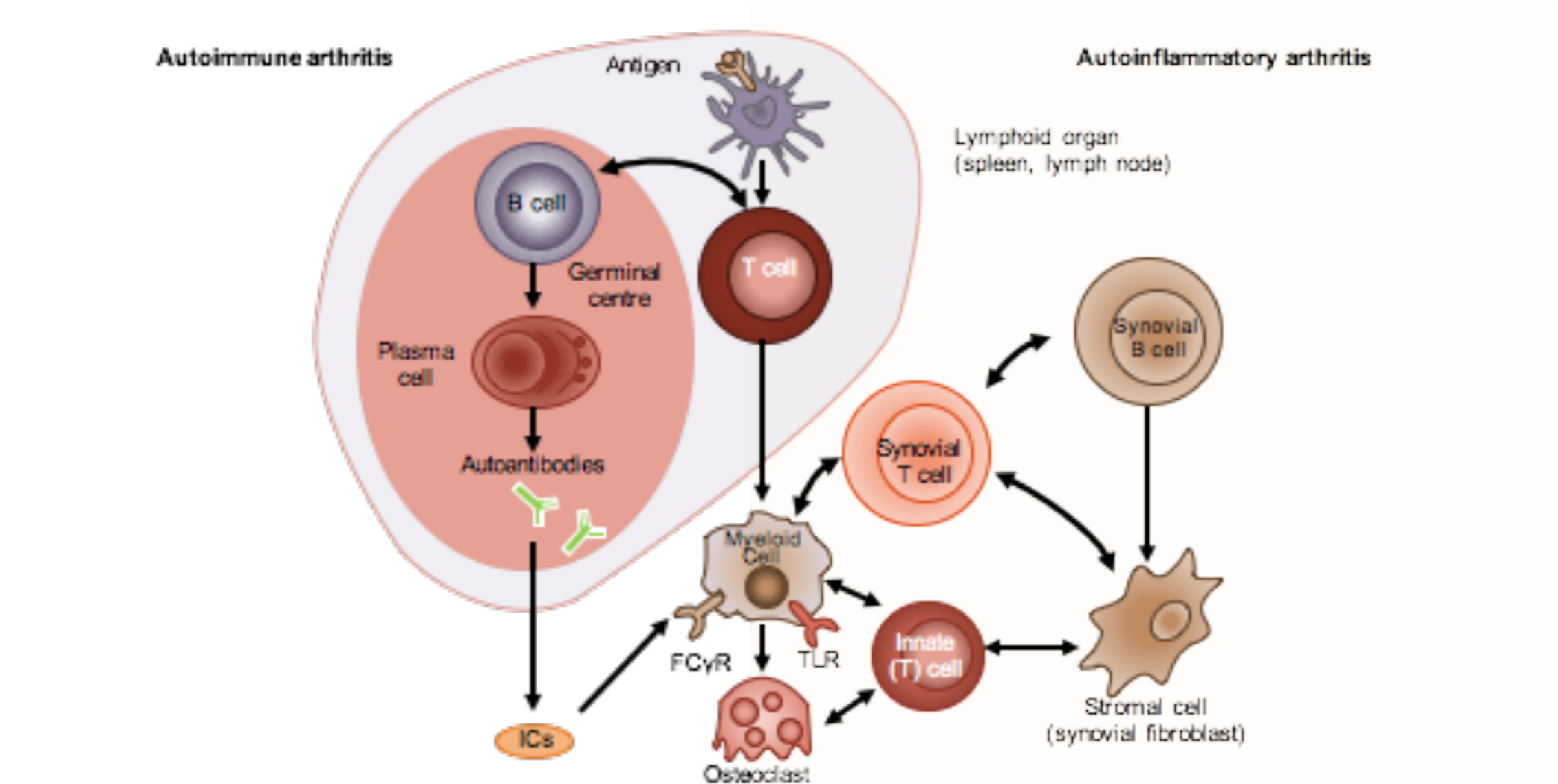
IL-23/IL-17 axis in autoimmune/autoinflammatory arthritis



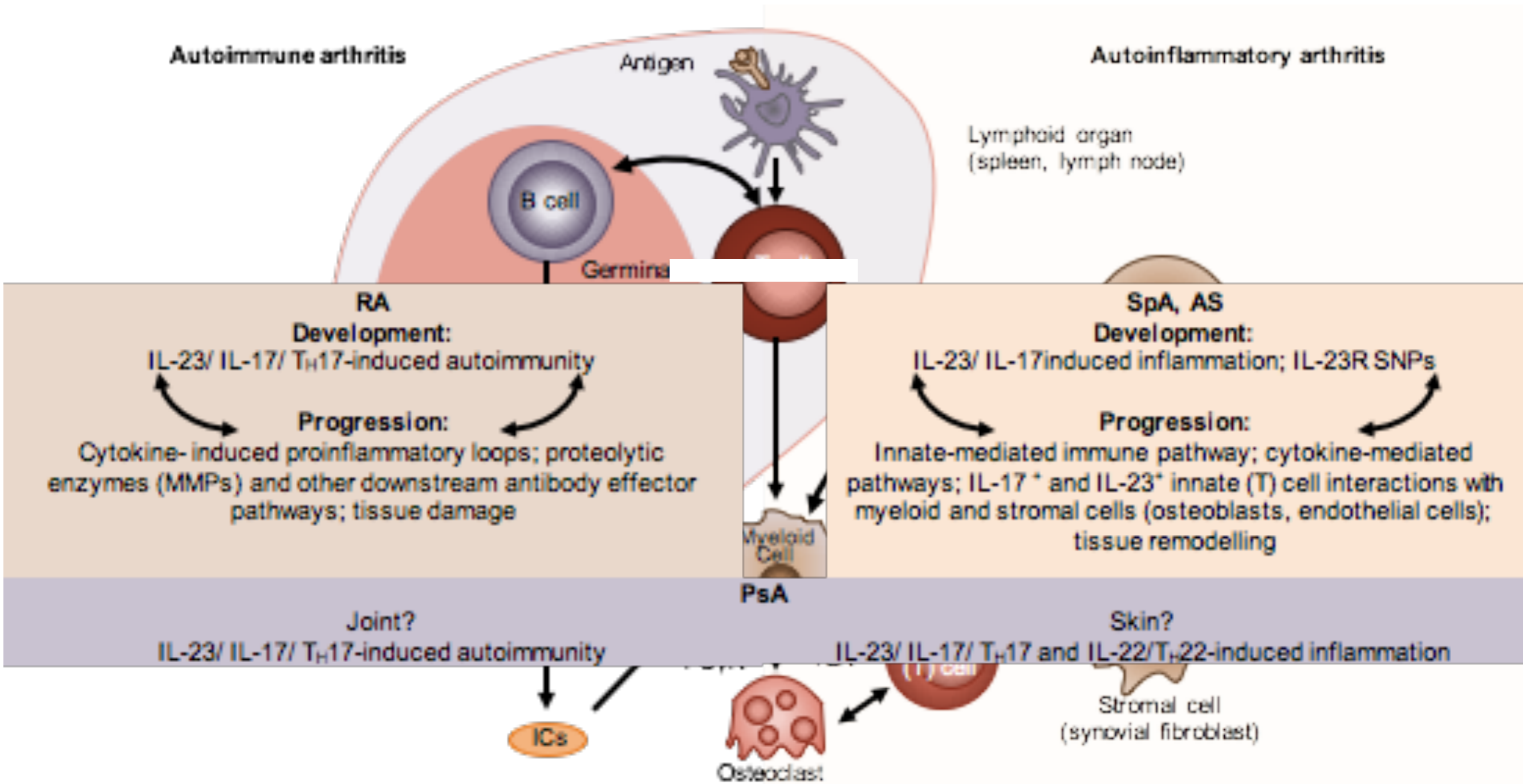
Cellular sources and targets of IL-17A



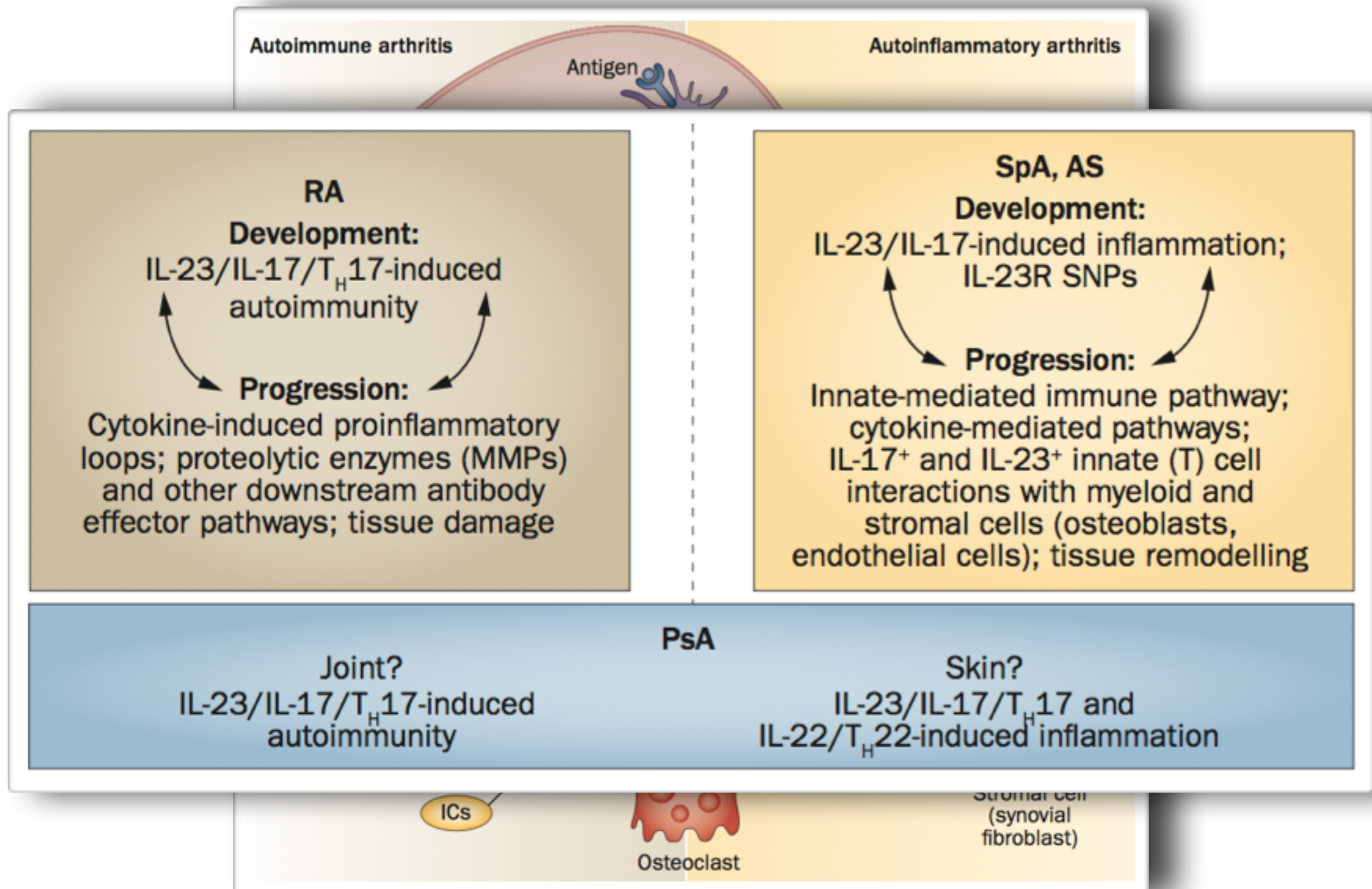
IL-23/IL-17 axis in autoimmune/autoinflammatory arthritis



IL-23/IL-17 axis in autoimmune/autoinflammatory arthritis



IL-23/IL-17 axis in autoimmune/autoinflammatory arthritis



Talk composition

- ☑ IL-17, immunity and inflammation
- ☑ Why IL-17 blockade in SpA?





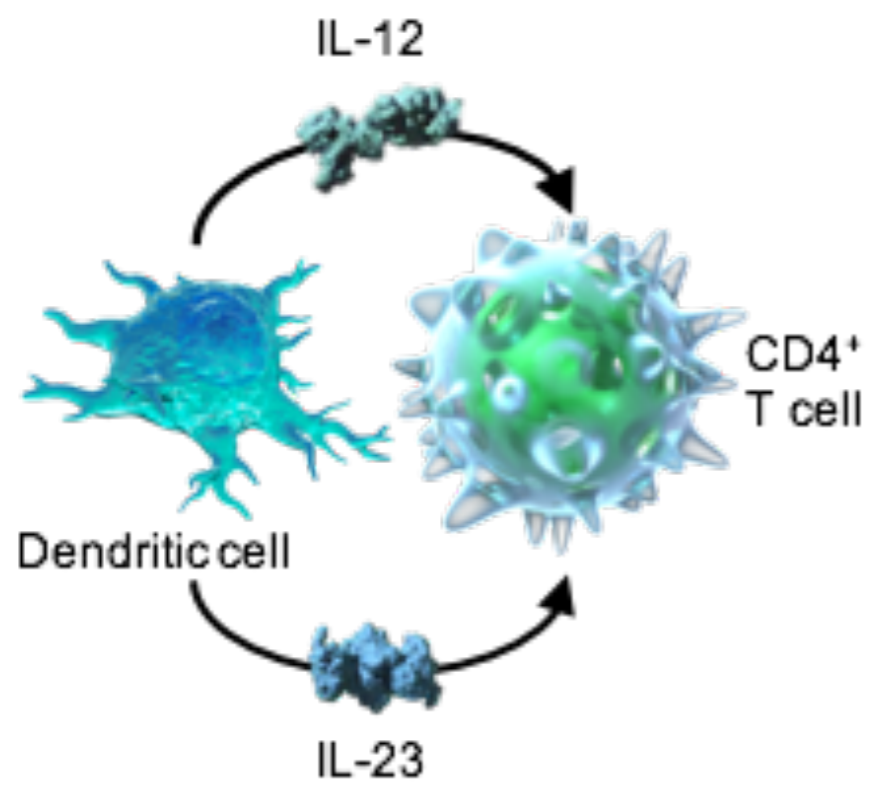
The Bench-to-Bedside Story of IL-17 and the Therapeutic Efficacy of its Targeting in Spondyloarthritis

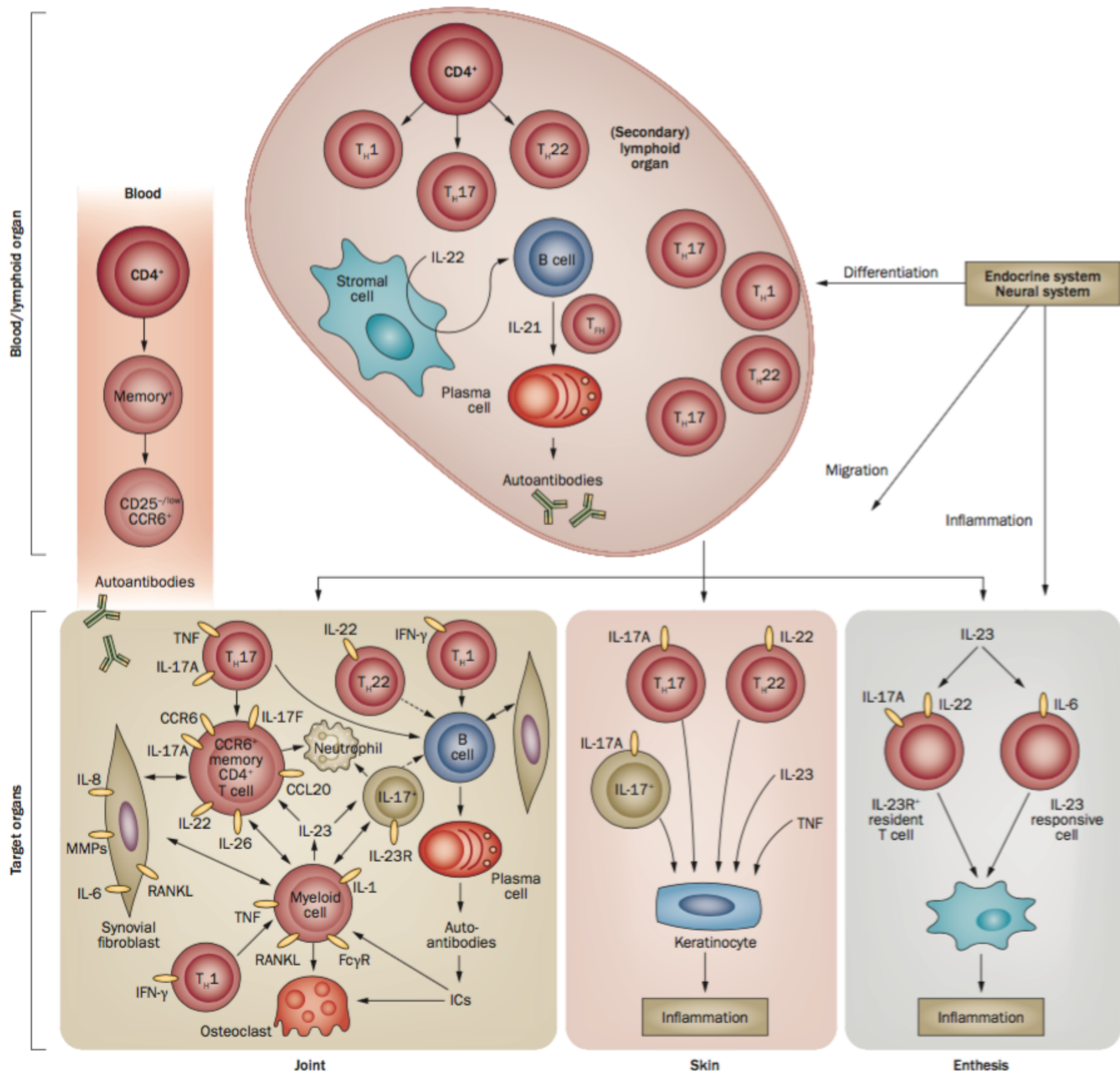
Judith A. Smith¹

Curr Rheumatol Rep 2016

genes associated with ankylosing spondylitis and overlap with psoriatic arthritis (PsA) and

Gene locus	Gene	Odds ratio (AS)	PsA-associated	CD-associated	Function
1p31	<i>IL23R</i>	0.65 ^a	Yes	Yes	IL-23 receptor
1q21	<i>IL6R</i>	0.88	No	No	IL-6 receptor
2q11	<i>IL1R2-R1</i>	0.9, 1.11 ^b	No	Yes	IL-1 receptor
5p13	<i>PTGER4</i>	1.09	No	Yes	Prostaglandin receptor
5q33	<i>IL12B</i>	1.11	Yes	Yes	Shared subunit for IL-12 and IL-23
9q34	<i>CARD9</i>	1.11	No	Yes	Signaling molecule receptor downstream of dectin-1
16p11	<i>IL27</i>	1.1, 1.24 ^b	No	Yes	Pro-Th1, suppresses Th17
17q21	<i>TBX21</i>	1.13	No	No ^c	Master Th1-directing transcription factor T-bet
17q21	<i>STAT3</i>	0.84, 0.86 ^b	Yes	Yes	Th17 differentiation
19p13	<i>TYK2</i>	0.88, 1.1 ^b	Yes	Yes	IL-23R signaling







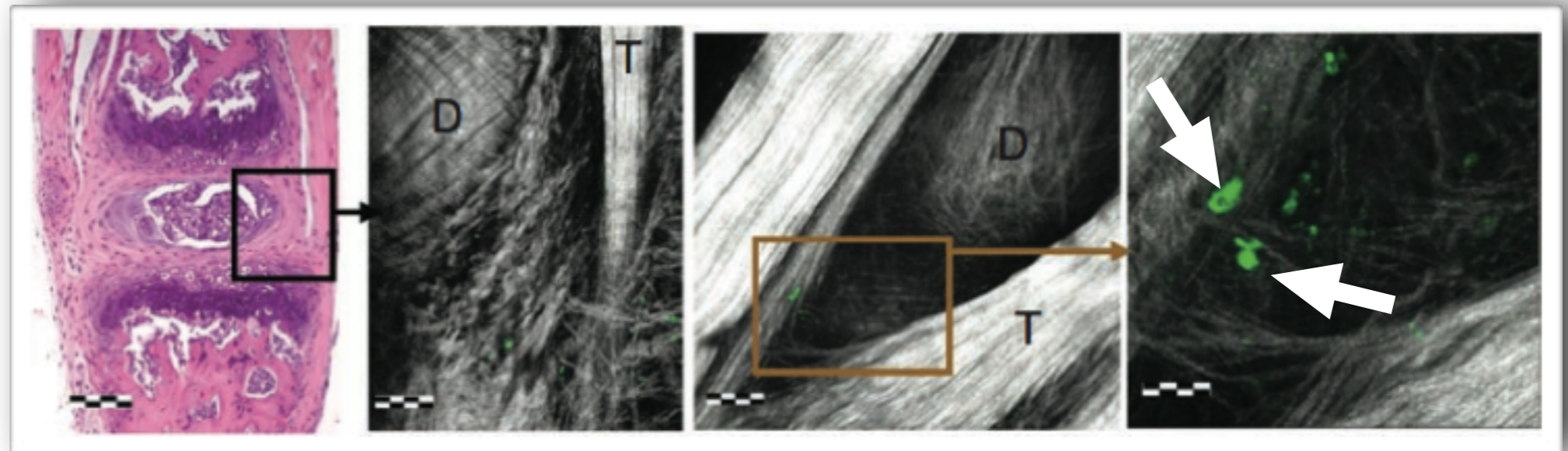
IL-23 induces spondyloarthritis by acting on ROR- γ ⁺ CD3⁺CD4⁻CD8⁻ enthesal resident T cells

Jonathan P Sherlock^{1-3,5}, Barbara Joyce-Shaikh^{1,5}, Scott P Turner¹, Cheng-Chi Chao¹, Manjiri Sathe¹, Jeff Grein¹, Daniel M Gorman¹, Edward P Bowman¹, Terrill K McClanahan¹, Jennifer H Yearley¹, Gérard Eberl⁴, Christopher D Buckley³, Robert A Kastelein¹, Robert H Pierce¹, Drake M LaFace^{1,5} & Daniel J Cua^{1,5}

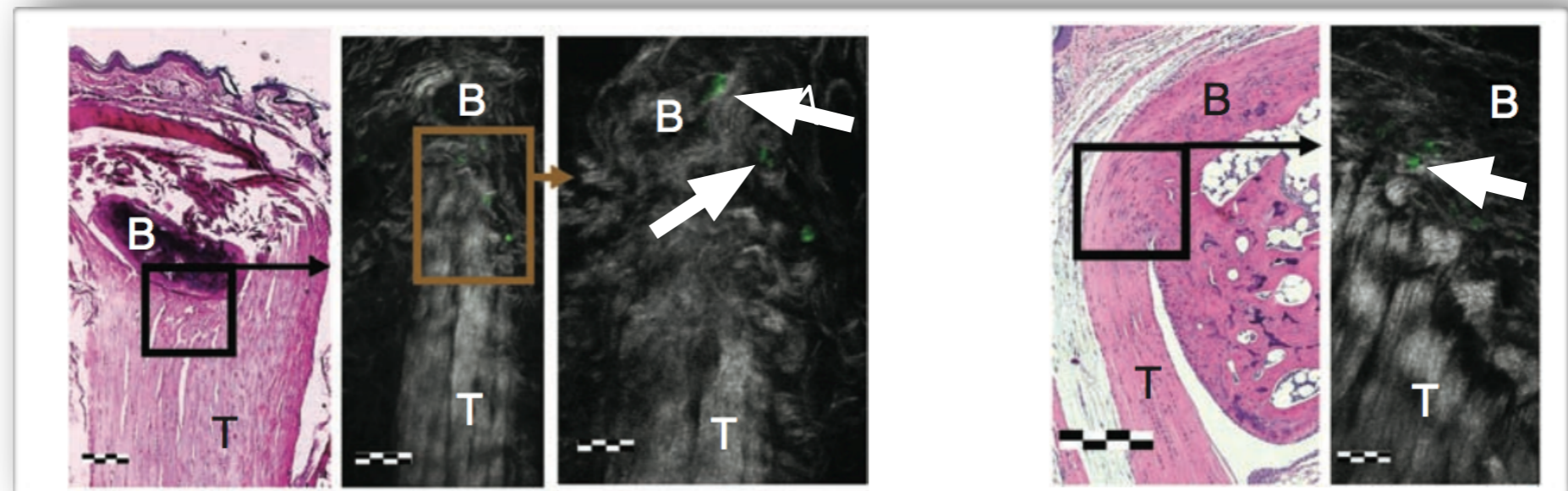
Nat Med 2012

IL-23R⁺ cells detection (by multiphoton microscopy)

Axial tissue



Achilles' tendon



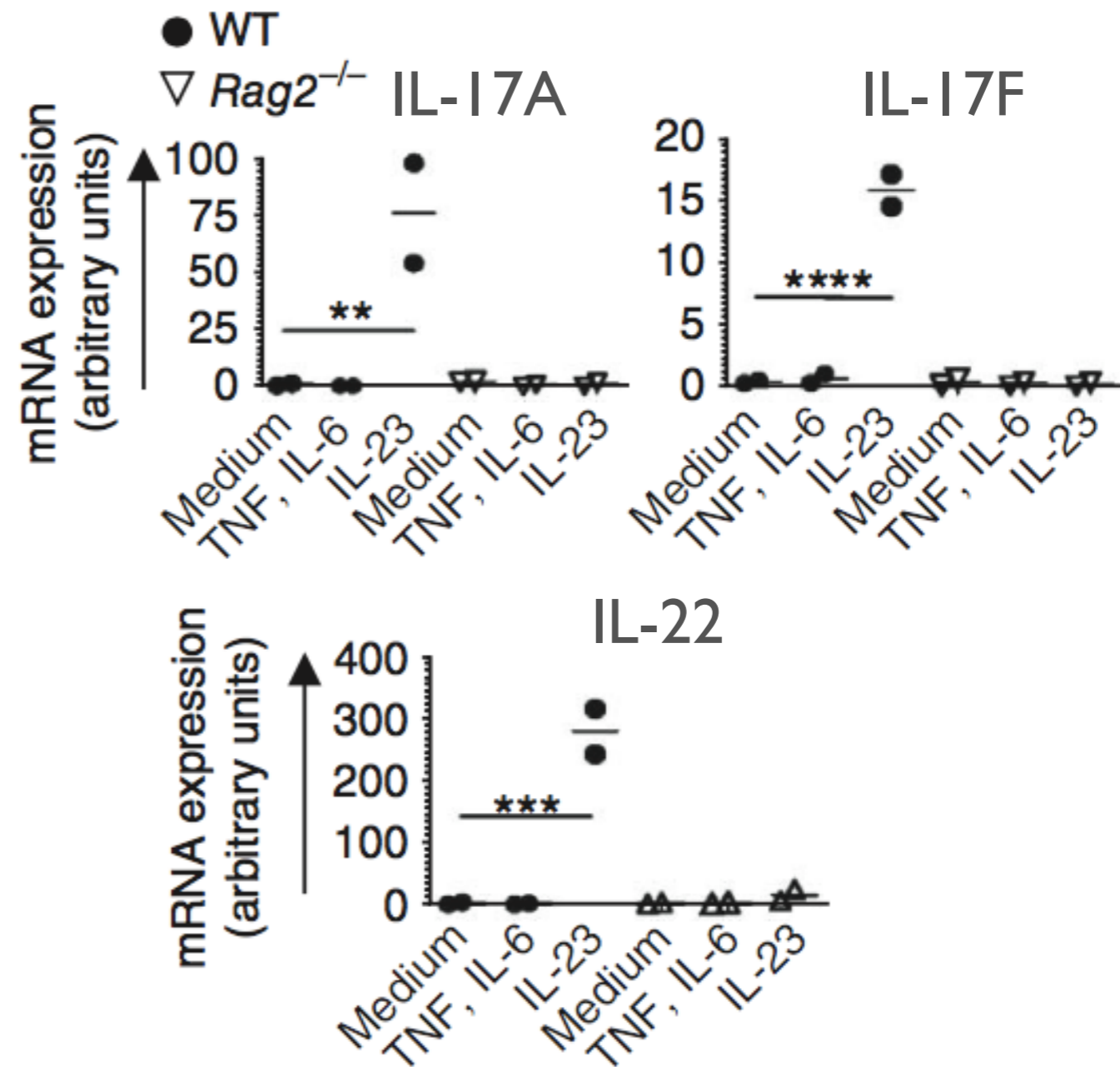


IL-23 induces spondyloarthritis by acting on ROR- γ ⁺ CD3⁺CD4⁻CD8⁻ enthesal resident T cells

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Nat Med 2012

IL-23 promotes
IL-17 and IL-22 expression
by enthesal T-cells

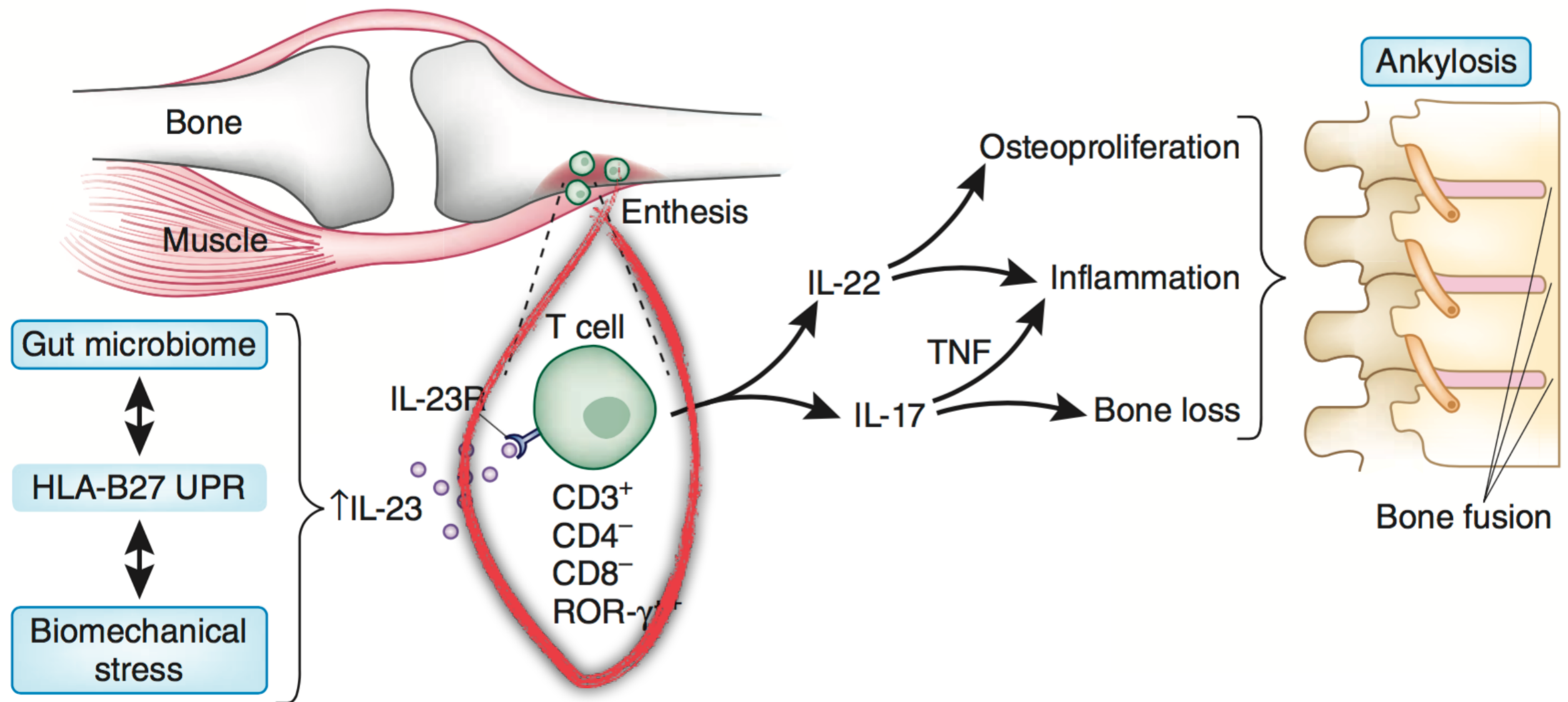




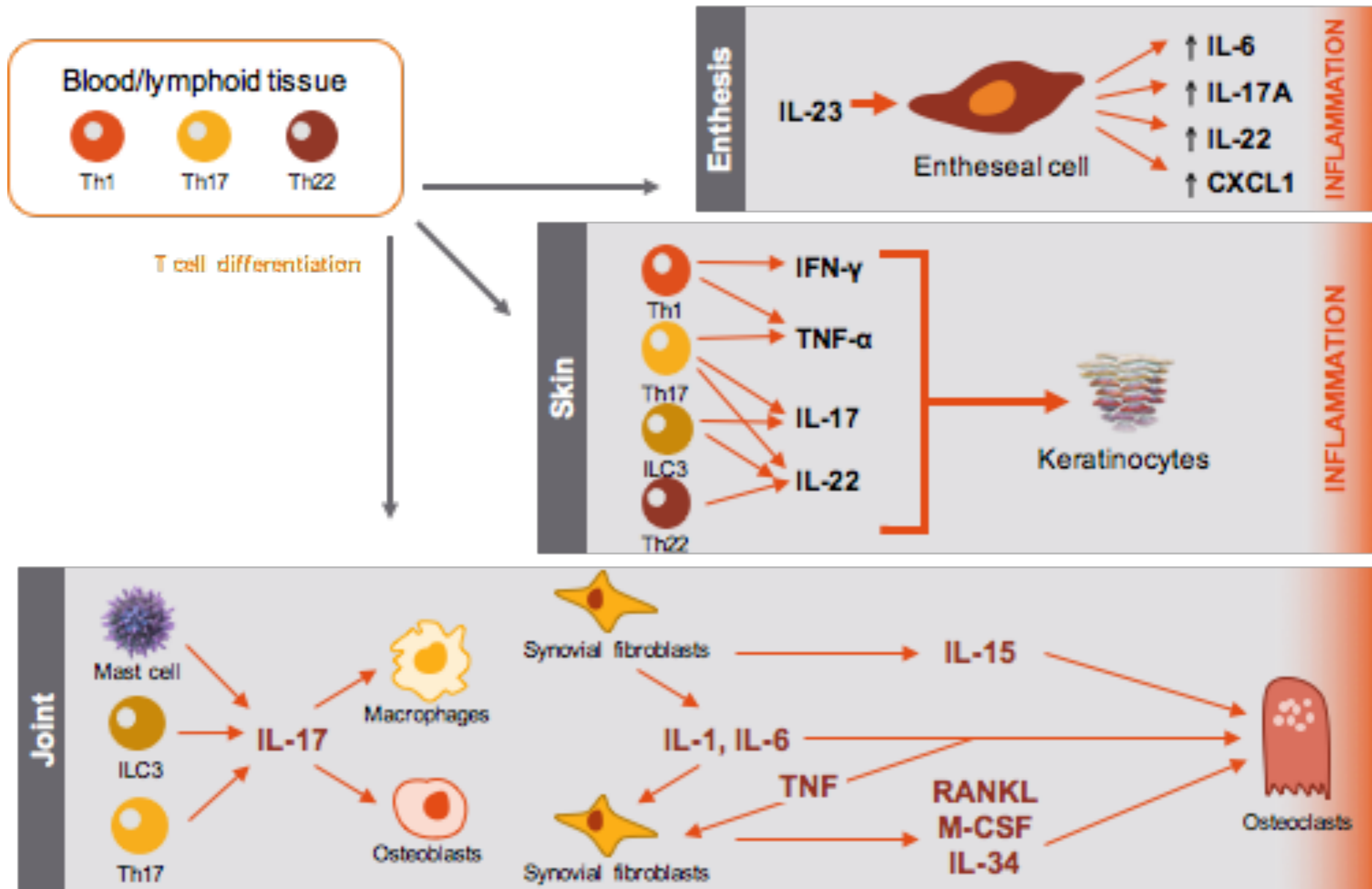
Primed for inflammation: enthesis-resident T cells

Rik J Lories & Iain B McInnes

Nature Med 2012



Role of IL-17 in the pathogenesis of SpA



Talk composition

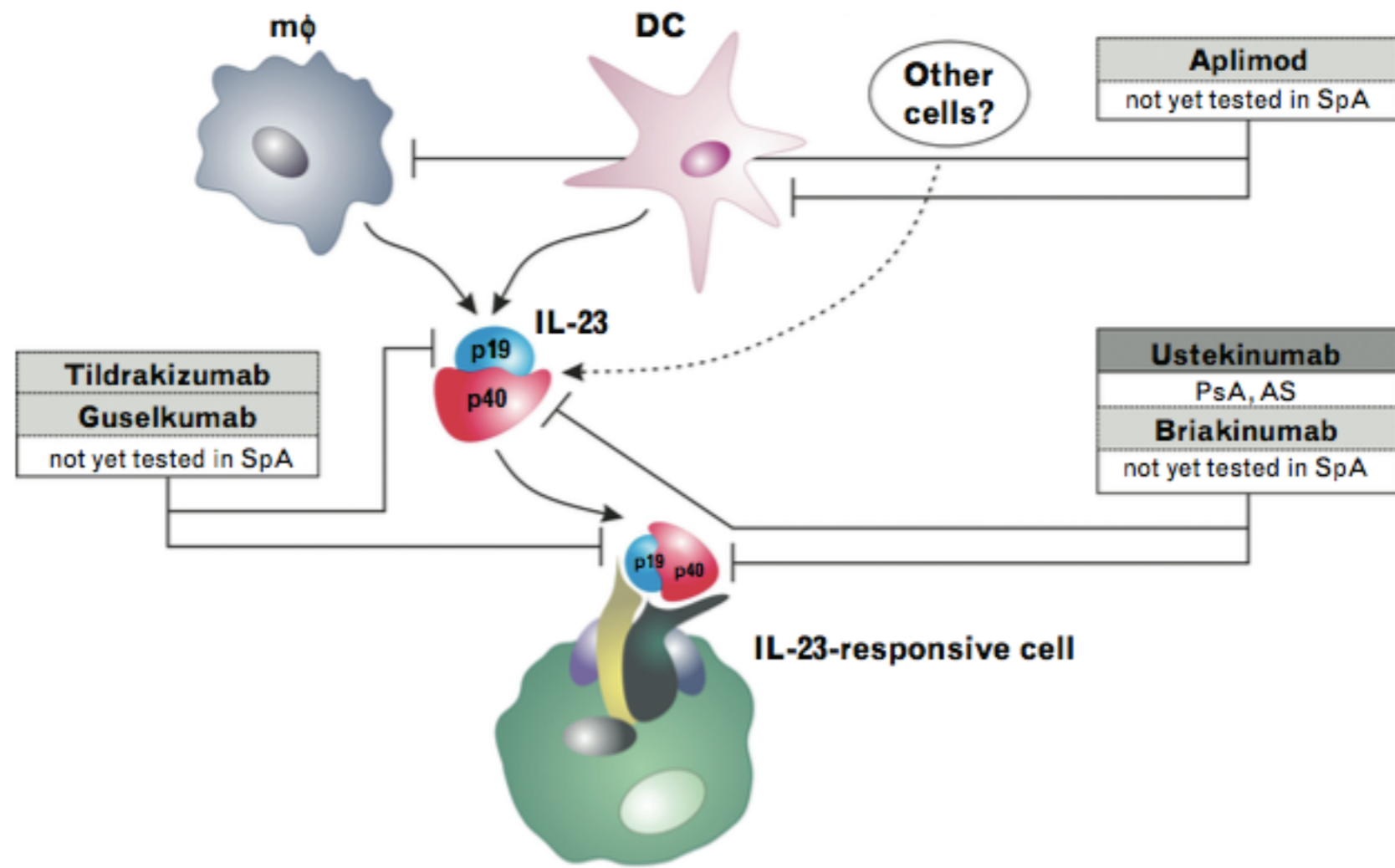
☑ IL-17, immunity and inflammation

☑ Why IL-17 blockade in SpA?

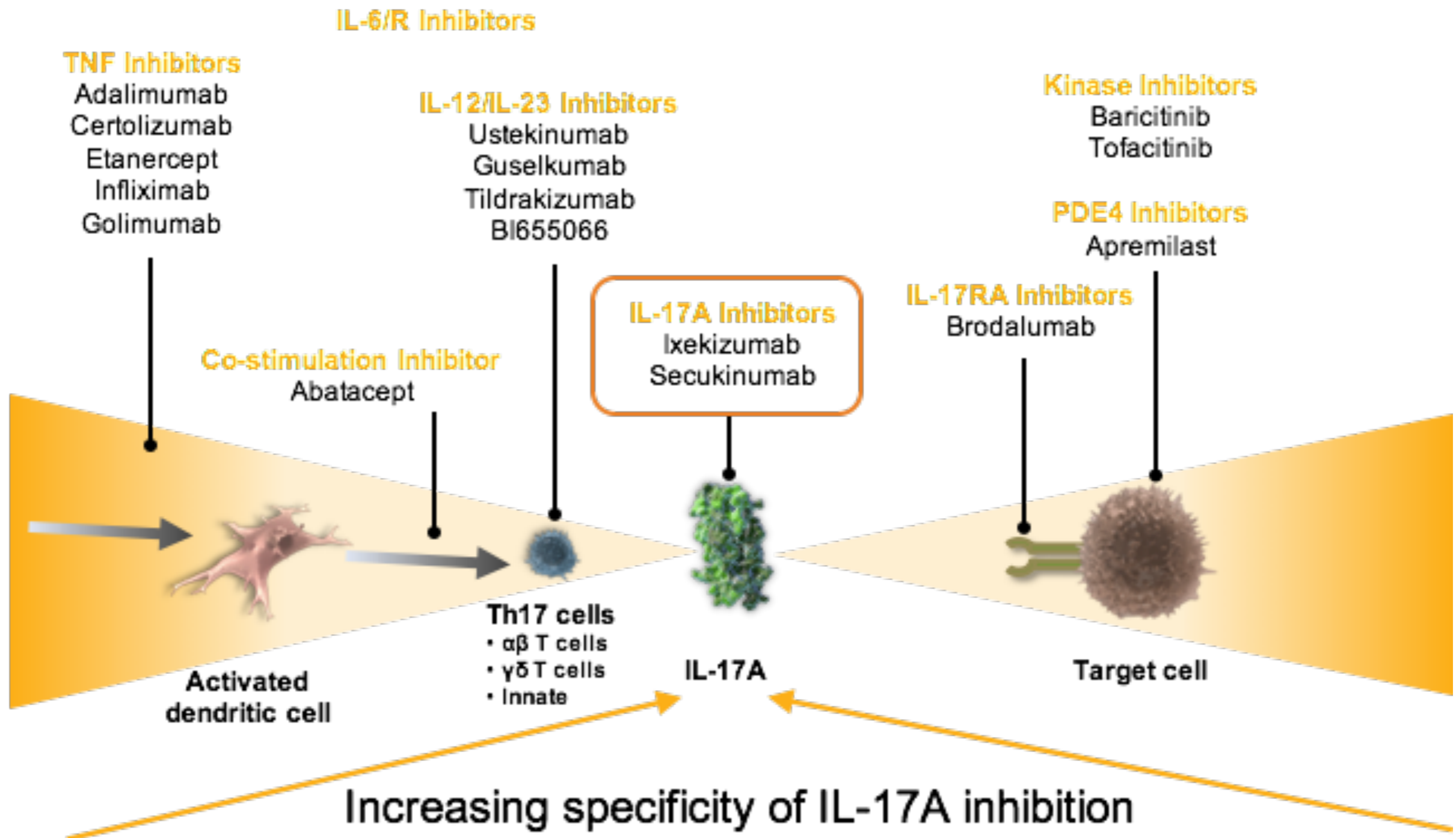
☑ Options for targeting IL-23/IL-17 pathway in SpA



Targeting IL-23/IL-17 pathway in SpA



Pathogenesis Driven Psoriatic Arthritis Treatment



Talk composition

☑ IL-17, immunity and inflammation

☑ Why IL-17 blockade in SpA?

☑ Options for targeting IL-23/IL-17 pathway in SpA

☑ IL-17 blockade in PsA and AS: clinical data



Secukinumab: data from RCTs

PsA



Secukinumab development in PsA: the FUTURE program

2013				2014				2015				2016				2017			
Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4

FUTURE 1 (F2306) – N = 606

i.v. loading (10 mg/kg) → s.c. maintenance dosing (75 and 150 mg)

Extension study

FUTURE 2 (F2312) – N = 397

s.c. loading (75, 150 and 300 mg) → s.c. maintenance dosing (75, 150 and 300 mg)
Pre-filled syringe

FUTURE 3 (F2318) – N = 405

s.c. loading (150 and 300 mg) → s.c. maintenance dosing (150 and 300 mg)
Autoinjector

FUTURE 4 (F2336) – N = 318

s.c 150 mg with or without s.c. loading
Pre-filled syringe

FUTURE 5 (F2342) – N = 990

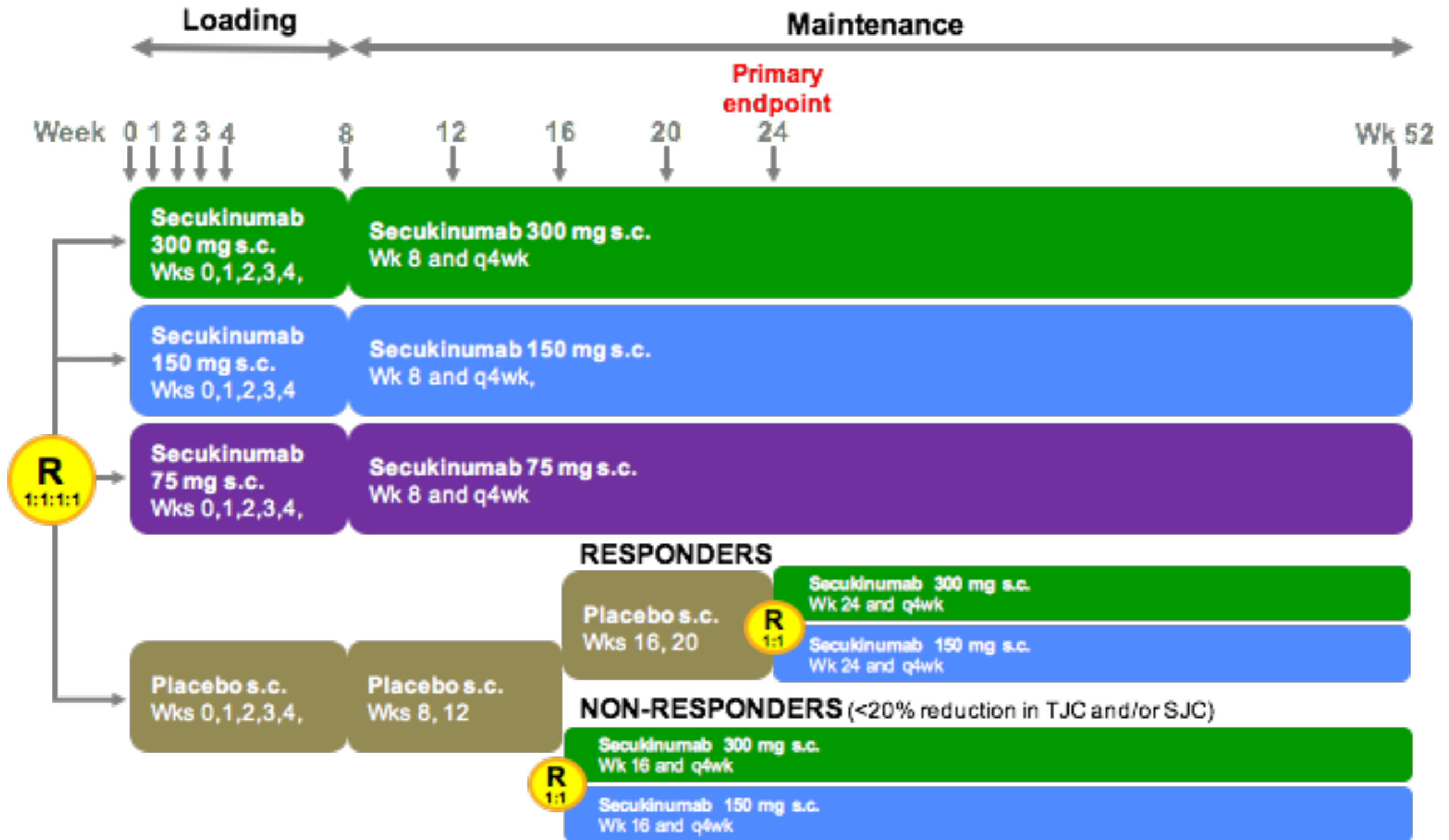
s.c 150 mg and 300 mg with or without s.c. loading (Pre-filled syringe)

EXCEED 1 (F2366) –

H2H with adalimumab



The FUTURE 2 study design



Secukinumab: data from RCTs



PsA

- Efficacy on signs and symptoms

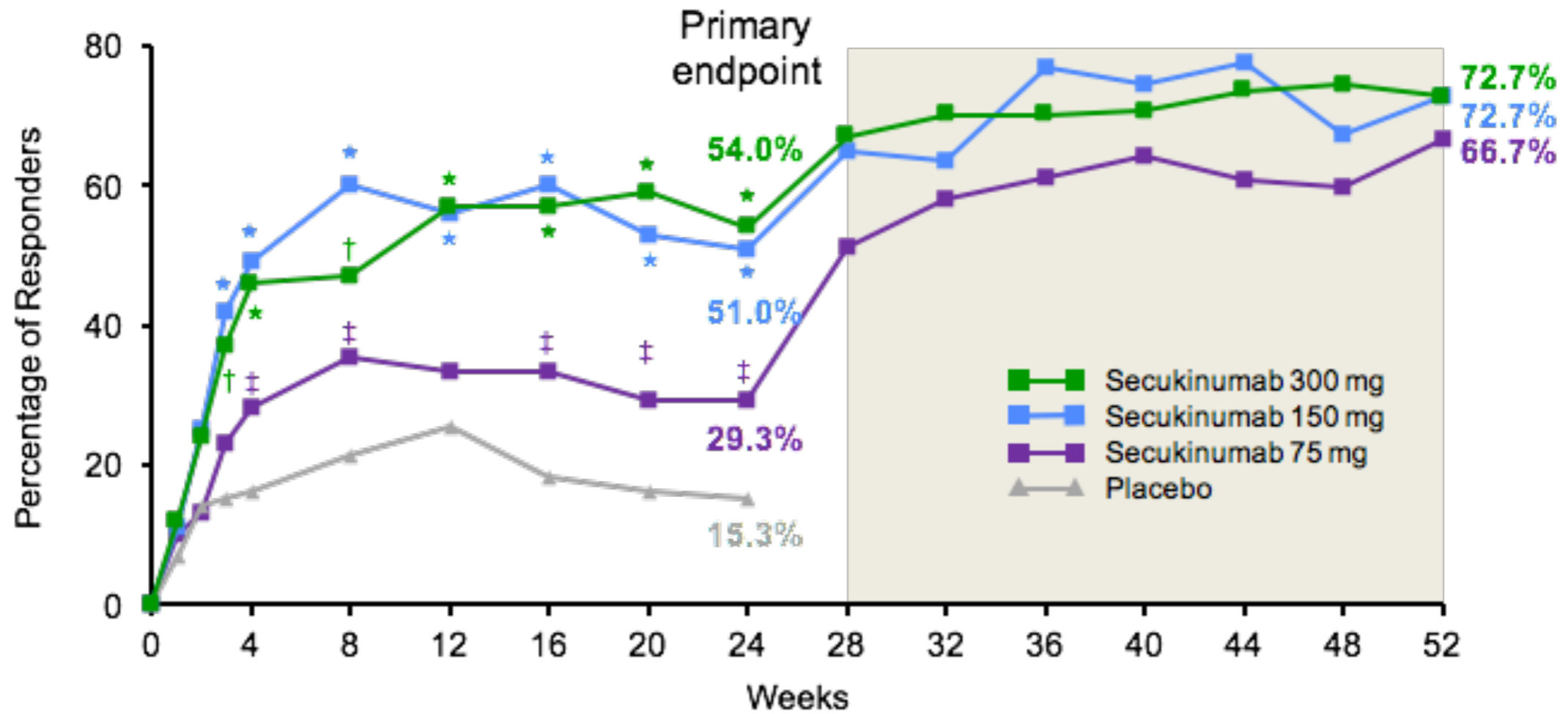


Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial

Iain B McInnes, Philip J Mease, Bruce Kirkham, Arthur Kavanaugh, Christopher T Ritchlin, Proton Rahman, Désirée van der Heijde, Robert Landewé, Philip G Conaghan, Alice B Gottlieb, Hanno Richards, Luminita Pricop, Gregory Ligozio, Manmath Patekar, Shephard Mpofo, on behalf of the FUTURE 2 Study Group

Lancet 2015

ACR 20 response



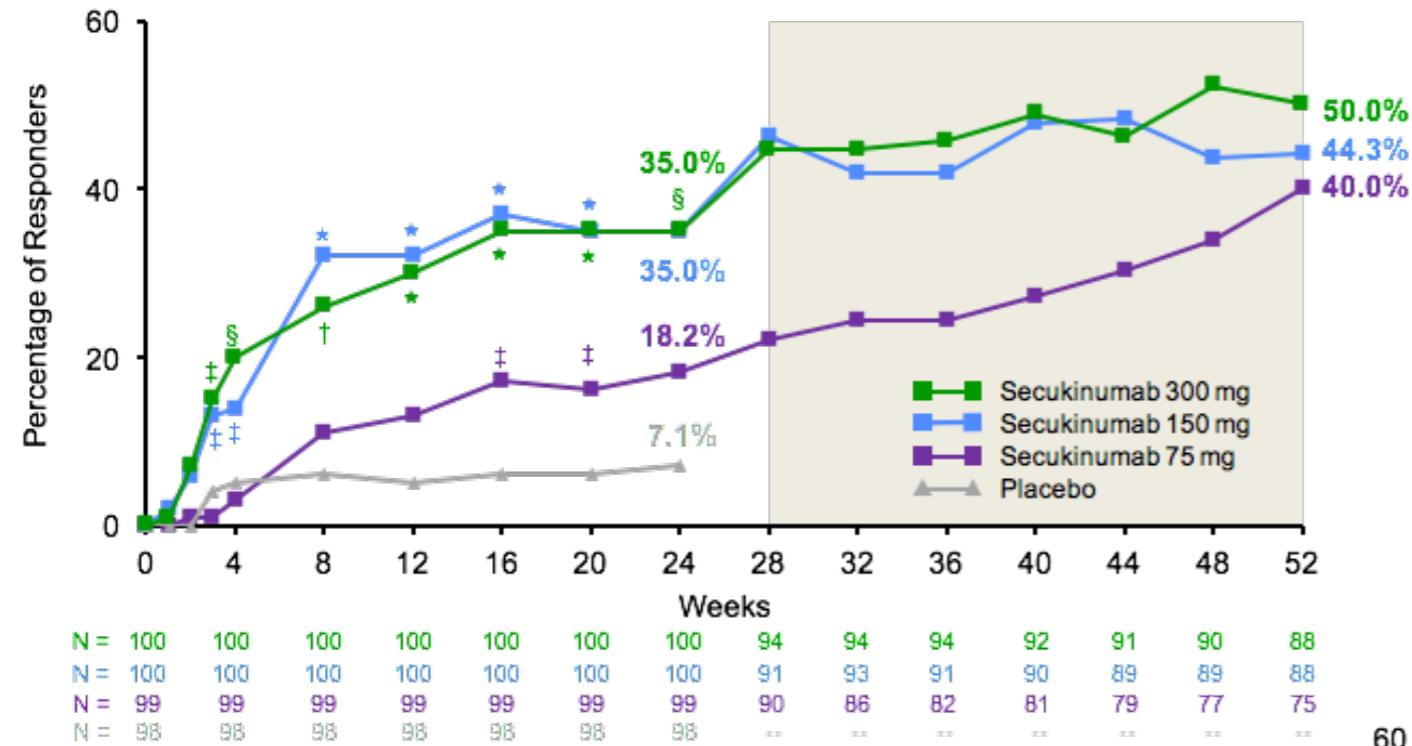
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N = 100	100	100	100	100	100	100	91	93	91	90	89	89	88
N = 99	99	99	99	99	99	99	90	86	82	81	79	77	75
N = 98	98	98	98	98	98	98	--	--	--	--	--	--	--



Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial

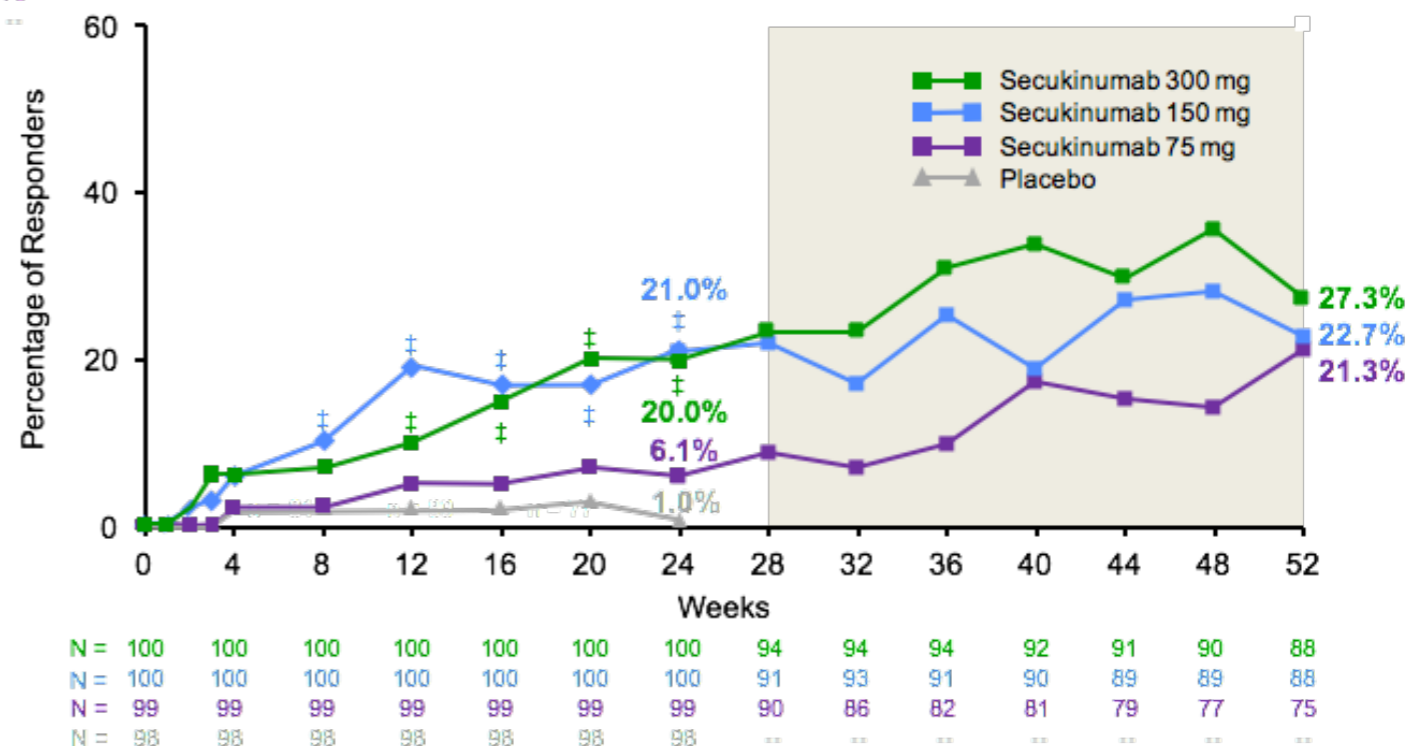
Iain B McInnes, Philip J Mease, Bruce Kirkham, Arthur Kavanaugh, Christopher T Ritchlin, Proton Rahman, Désirée van der Heijde, Robert Landewé, Philip G Conaghan, Alice B Gottlieb, Hanno Richards, Luminita Pricop, Gregory Ligozio, Manmath Patekar, Shephard Mpofo, on behalf of the FUTURE 2 Study Group

Lancet 2015



ACR 50 response

ACR 70 response

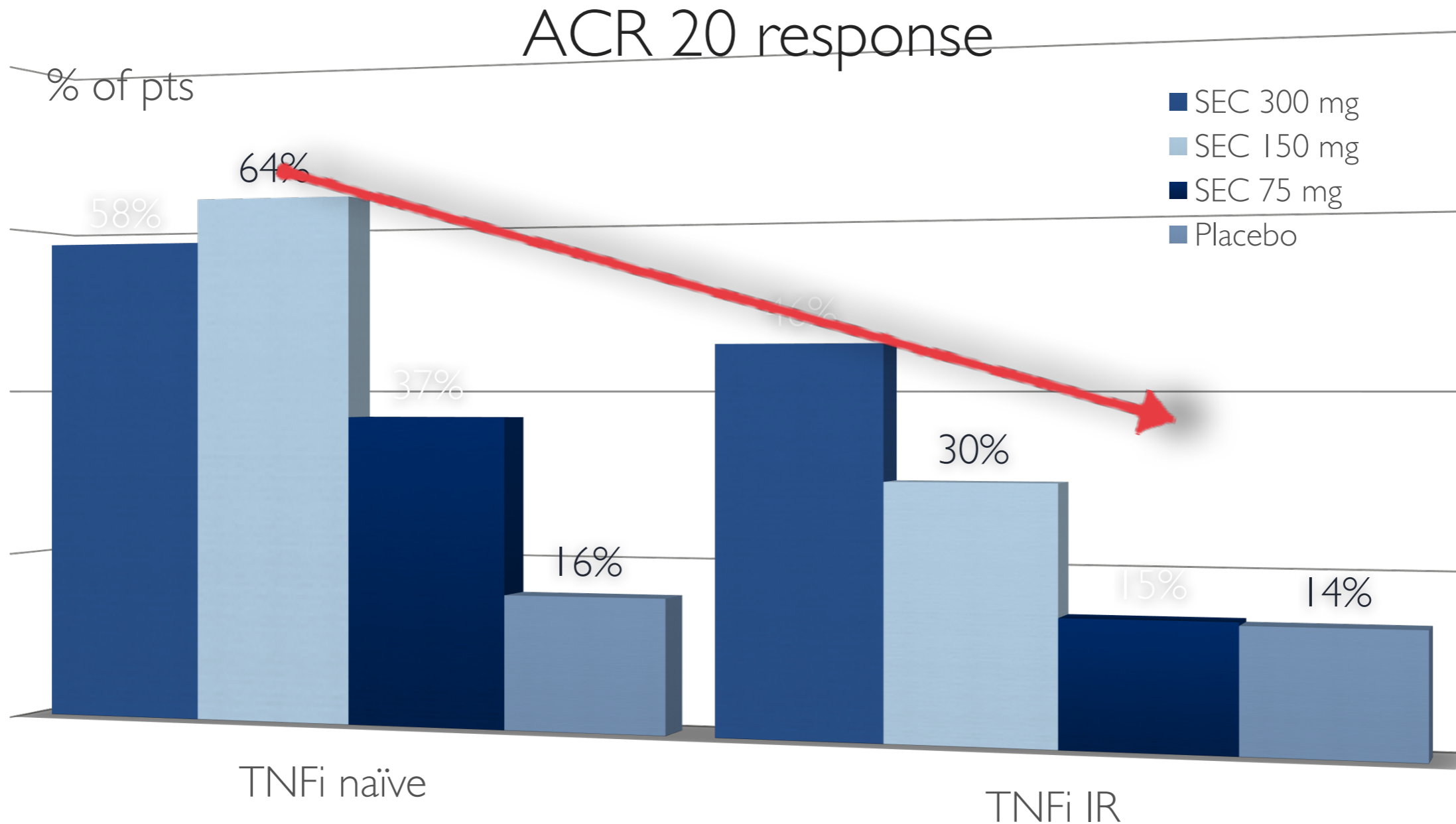




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Lancet 2015

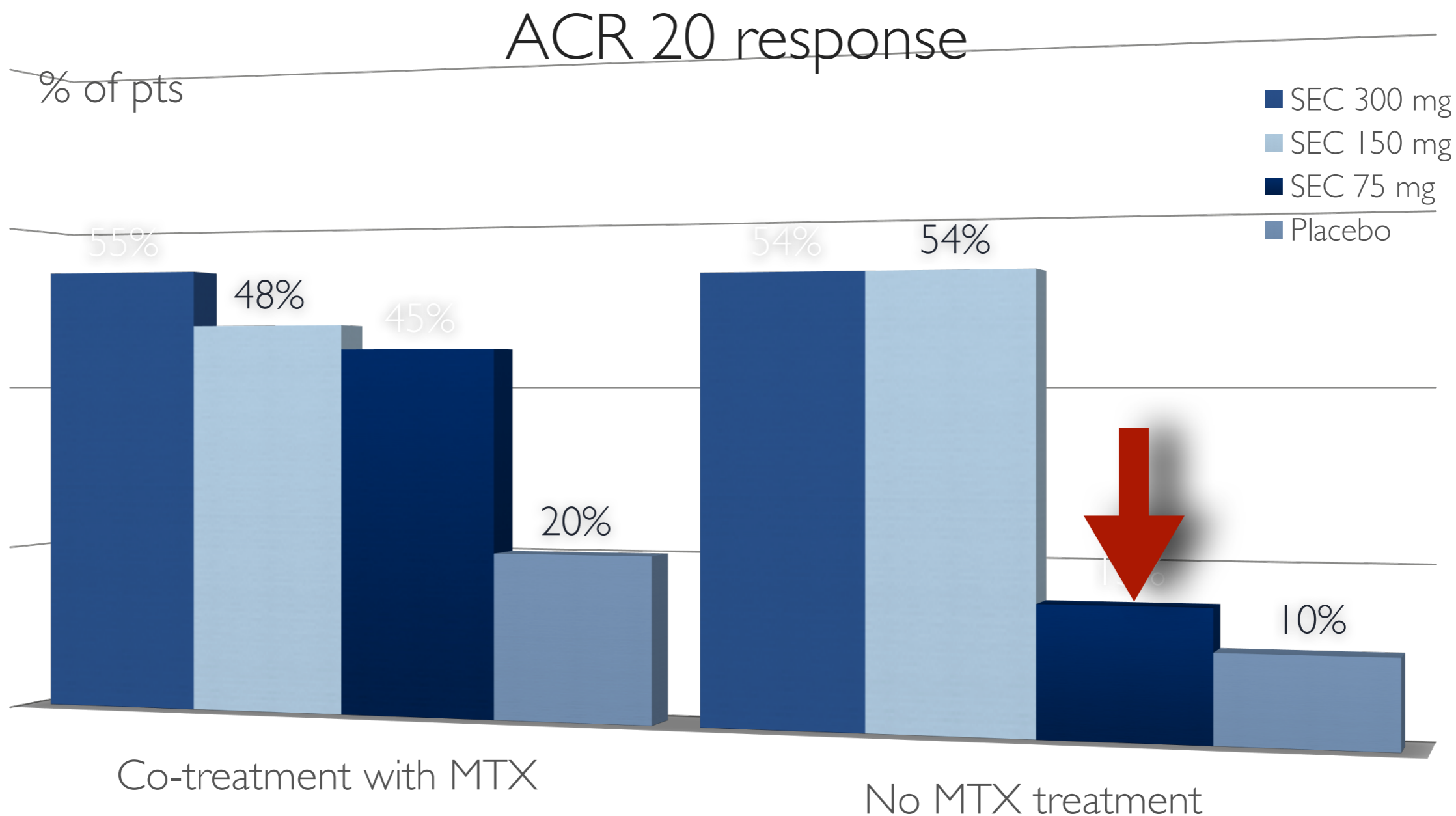




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Lancet 2015

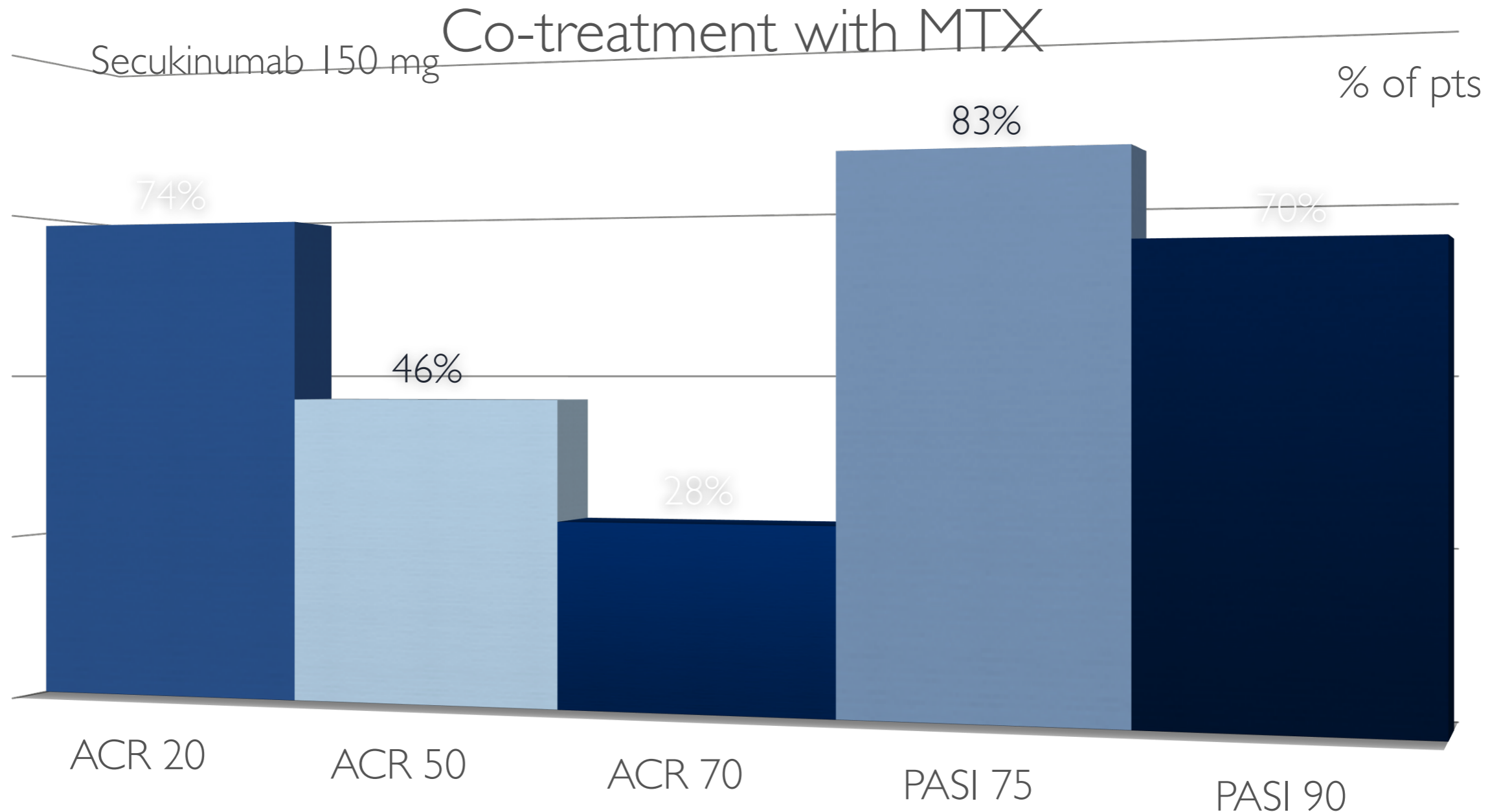




Secukinumab Provides Sustained Improvements in Psoriatic Arthritis: 2-Year Efficacy and Safety Results from a Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial

Philip J. Mease¹, Iain B. McInnes², Bruce Kirkham³, Arthur Kavanaugh⁴, Proton Rahman⁵, Désirée van der Heijde⁶, Robert B.M. Landewé⁷, P Nash⁸, Luminita Pricop⁹, Zailong Wang¹⁰ and Shephard Mpofo¹¹

ACR Congress 2015, n. 2148



Secukinumab: data from RCTs



PsA

- Efficacy on signs and symptoms
- Efficacy on dactylitis and enthesitis



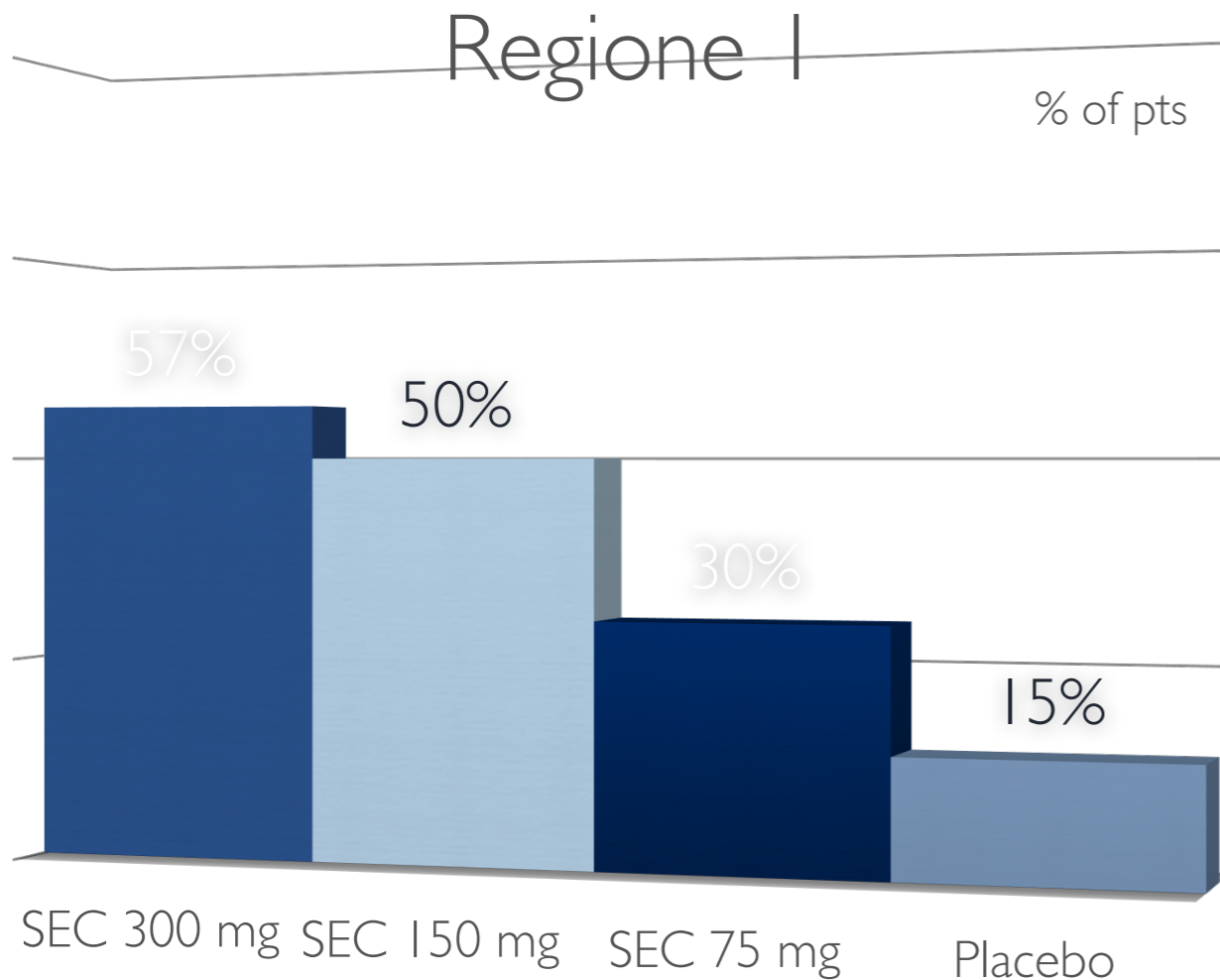
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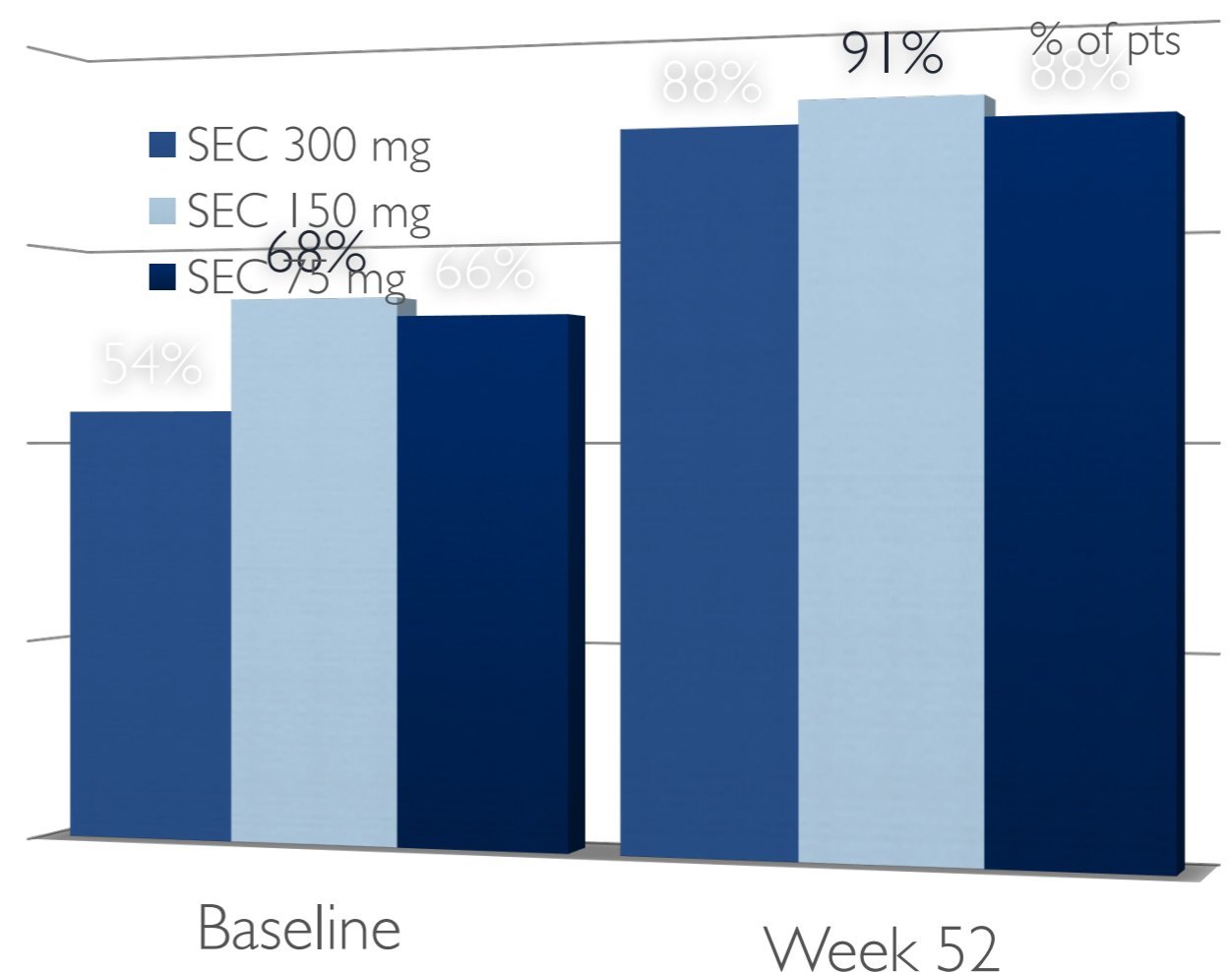
Lancet 2015

Resolution of dactylitis

Regione I



Pts free from dactylitis





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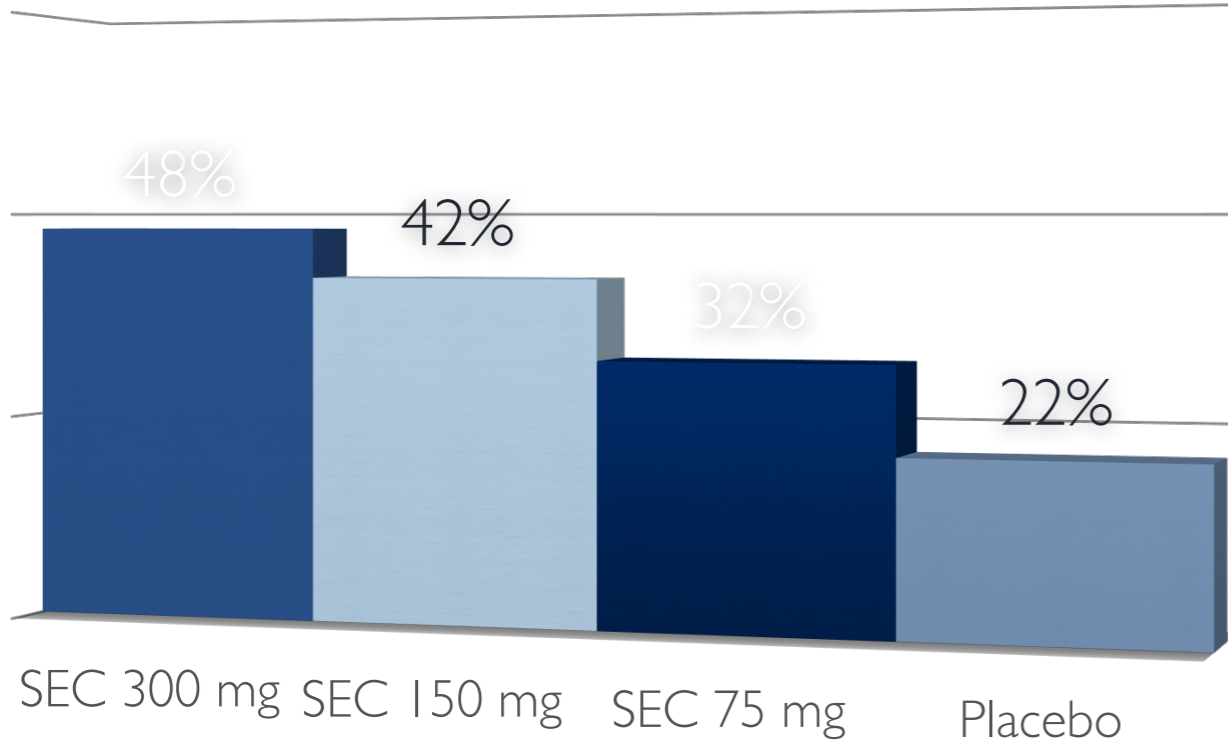
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Lancet 2015

Resolution of enthesitis

Regione I

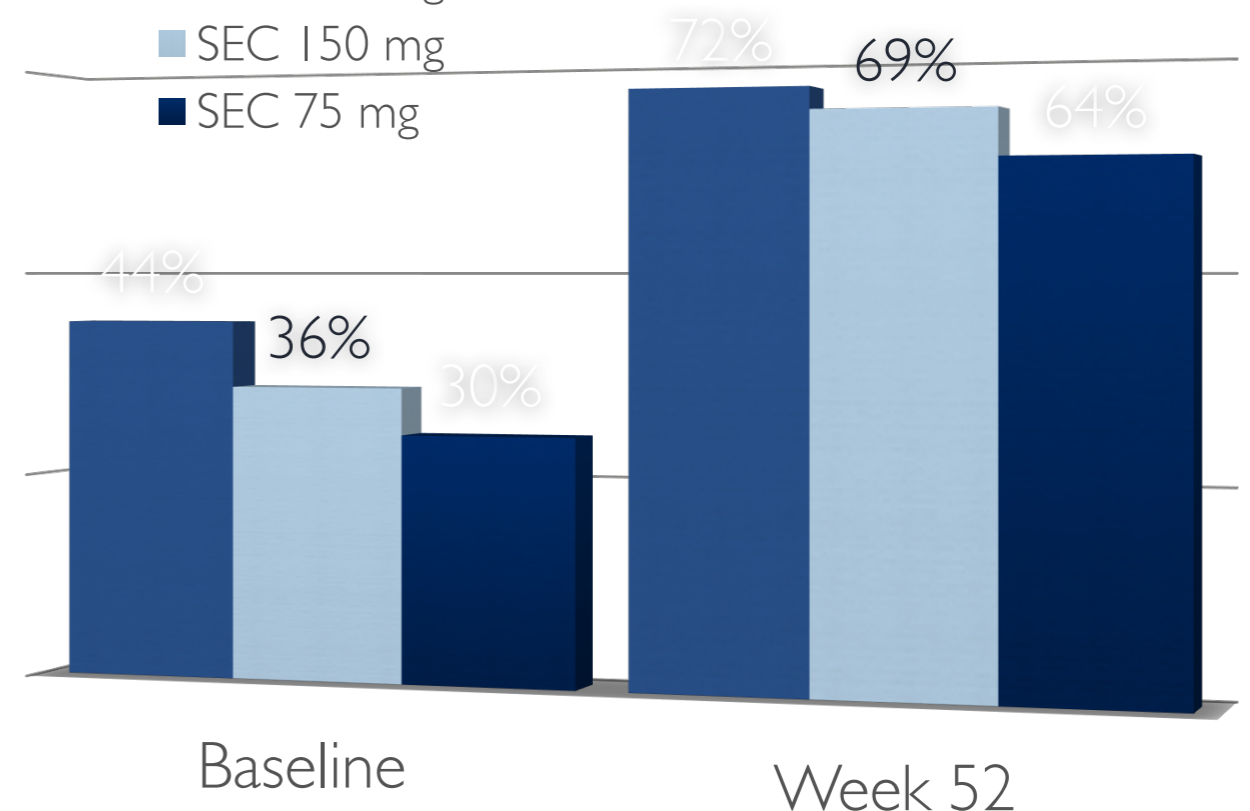
% os pts



Pts free from enthesitis

% os pts

- SEC 300 mg
- SEC 150 mg
- SEC 75 mg



Secukinumab: data from RCTs



PsA

- Efficacy on signs and symptoms
- Efficacy on dactylitis and enthesitis
- Efficacy on skin involvement

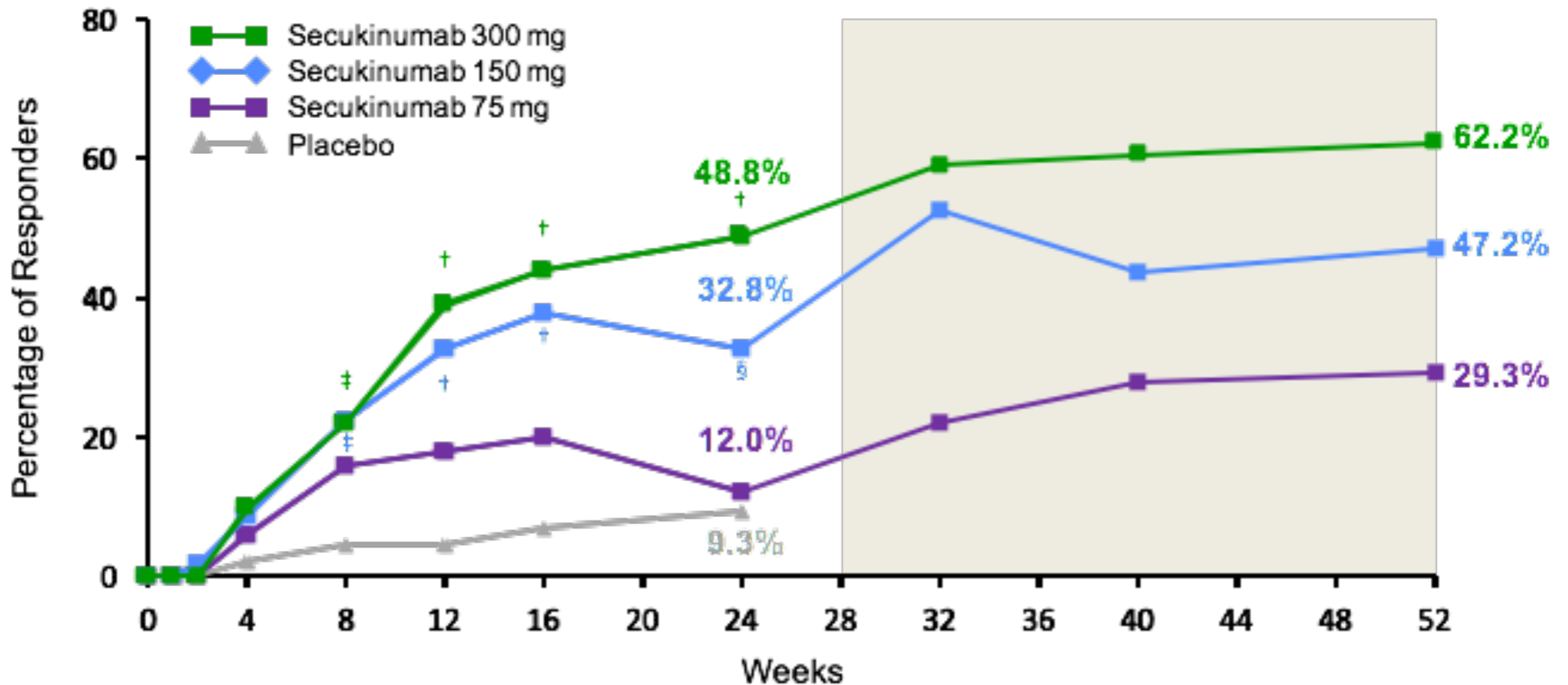


Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial

Iain B McInnes, Philip J Mease, Bruce Kirkham, Arthur Kavanaugh, Christopher T Ritchlin, Proton Rahman, Désirée van der Heijde, Robert Landewé, Philip G Conaghan, Alice B Gottlieb, Hanno Richards, Luminita Pricop, Gregory Ligozio, Manmath Patekar, Shephard Mpofo, on behalf of the FUTURE 2 Study Group

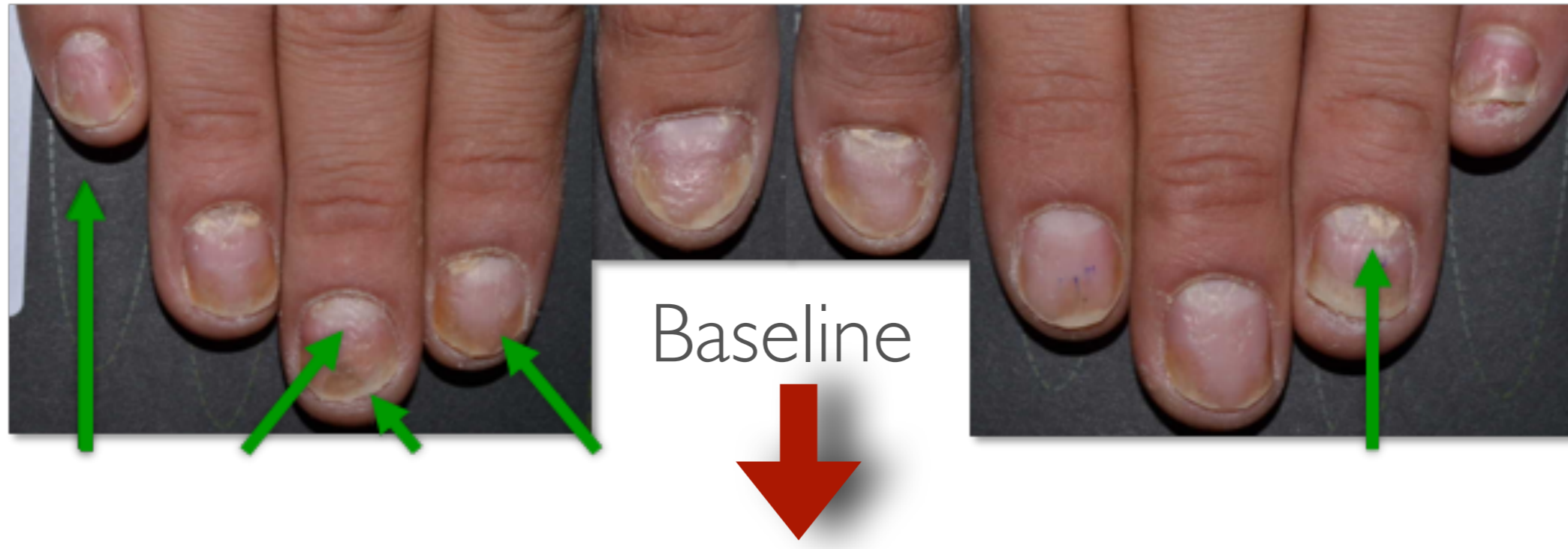
Lancet 2015

PASI 90 response



[3086561] SECUKINUMAB IS EFFECTIVE IN SUBJECTS WITH NAIL PSORIASIS: 16 WEEK RESULTS FROM THE TRANSFIGURE STUDY

Kristian Reich [Hamburg, Germany]¹, John Sullivan [Sydney, Australia]², Petr Arenberger [Prague, Czech Republic]³, Ulrich Mrowietz [Kiel, Germany]⁴, Sasha Jazayeri [Phoenix, United States]⁵, Pascaline Regnault [Basel, Switzerland]⁶, Pengcheng Chen [Basel, Switzerland]⁶, Marina Milutinovic [Basel, Switzerland]⁶

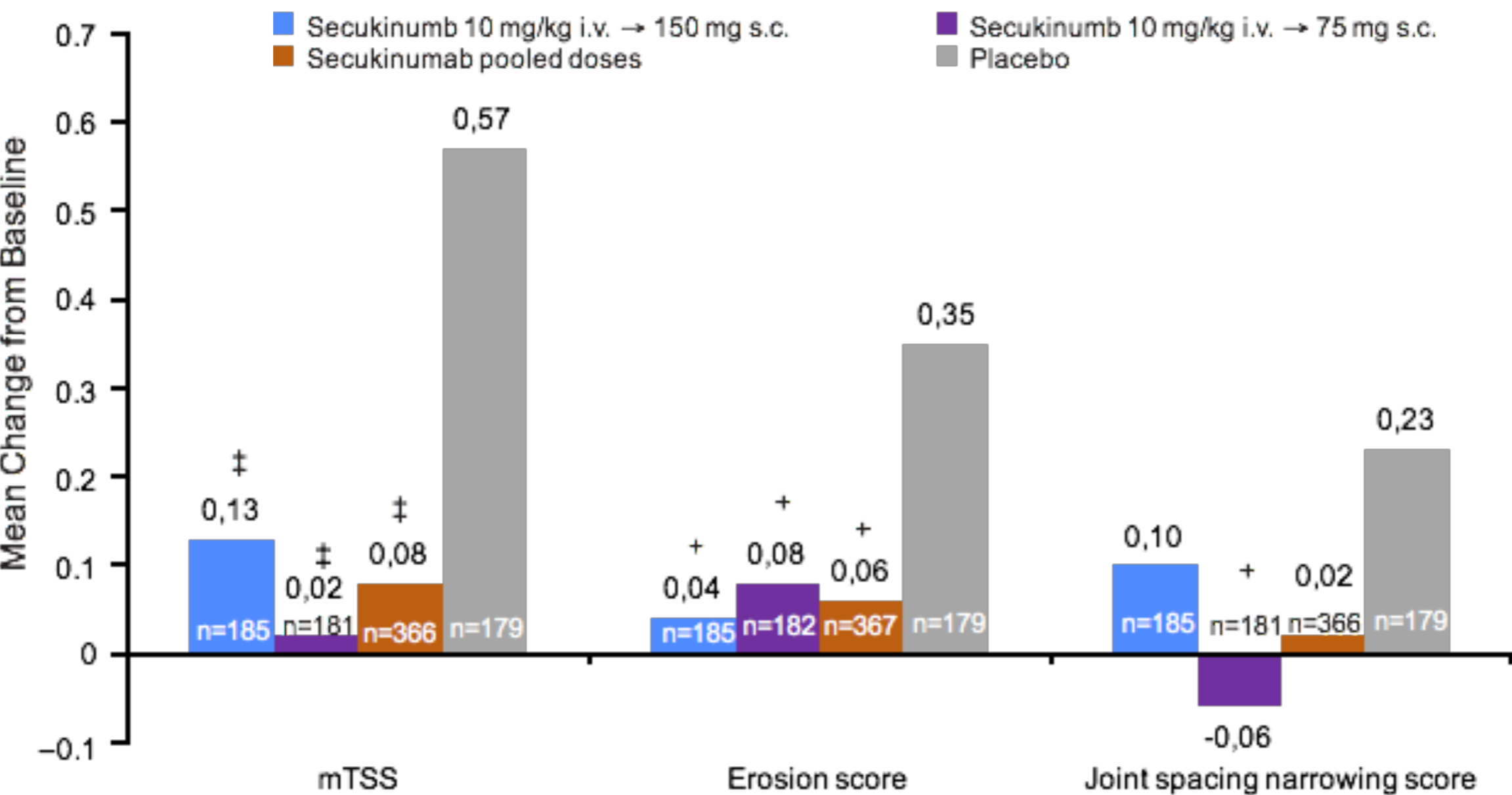


Secukinumab: data from RCTs



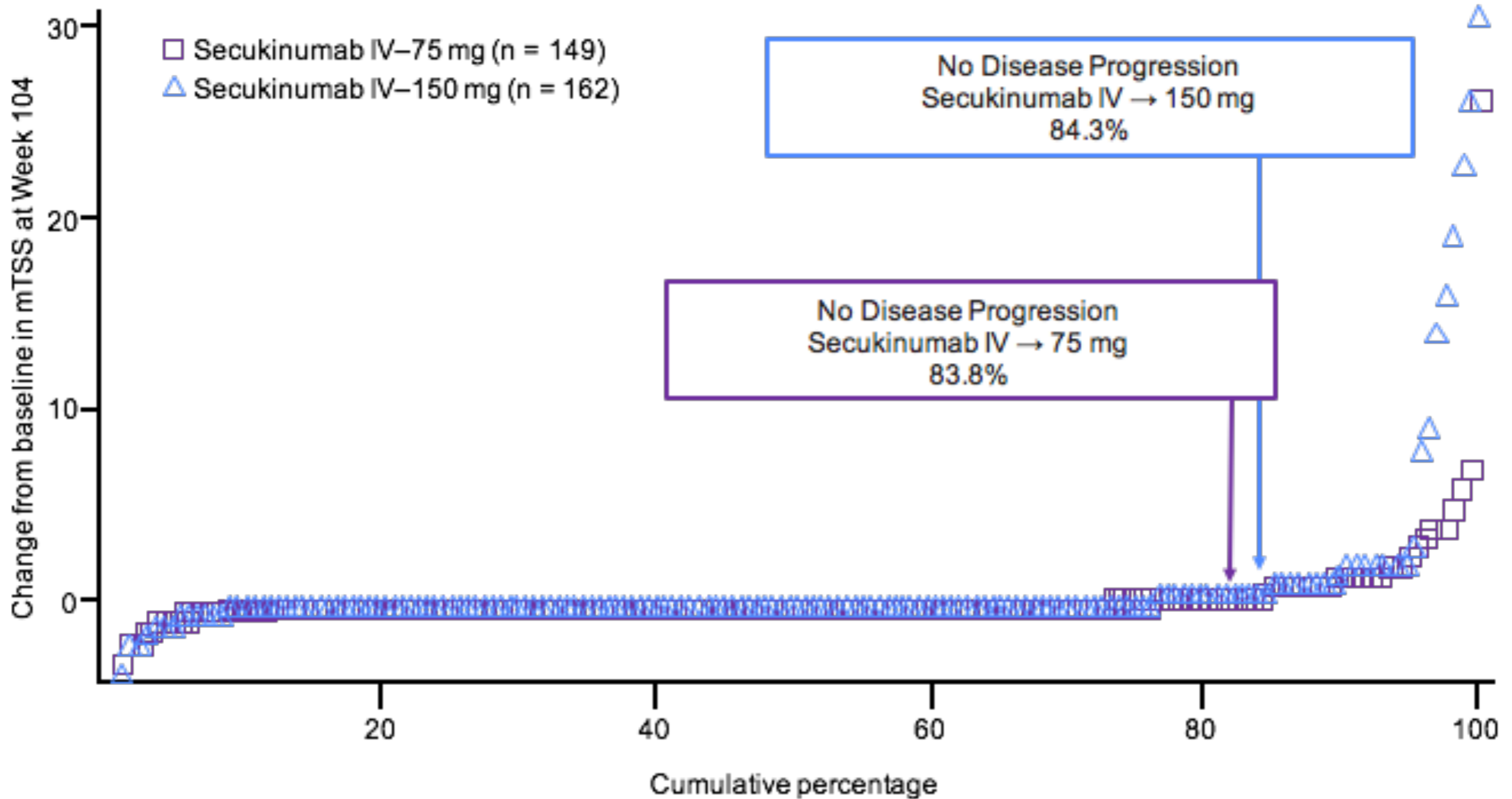
PsA

- Efficacy on signs and symptoms
- Efficacy on dactylitis and enthesitis
- Efficacy on skin involvement
- Efficacy on radiographic progression



Future I study: Radiographic progression

Mease P. ACR Congress 2015



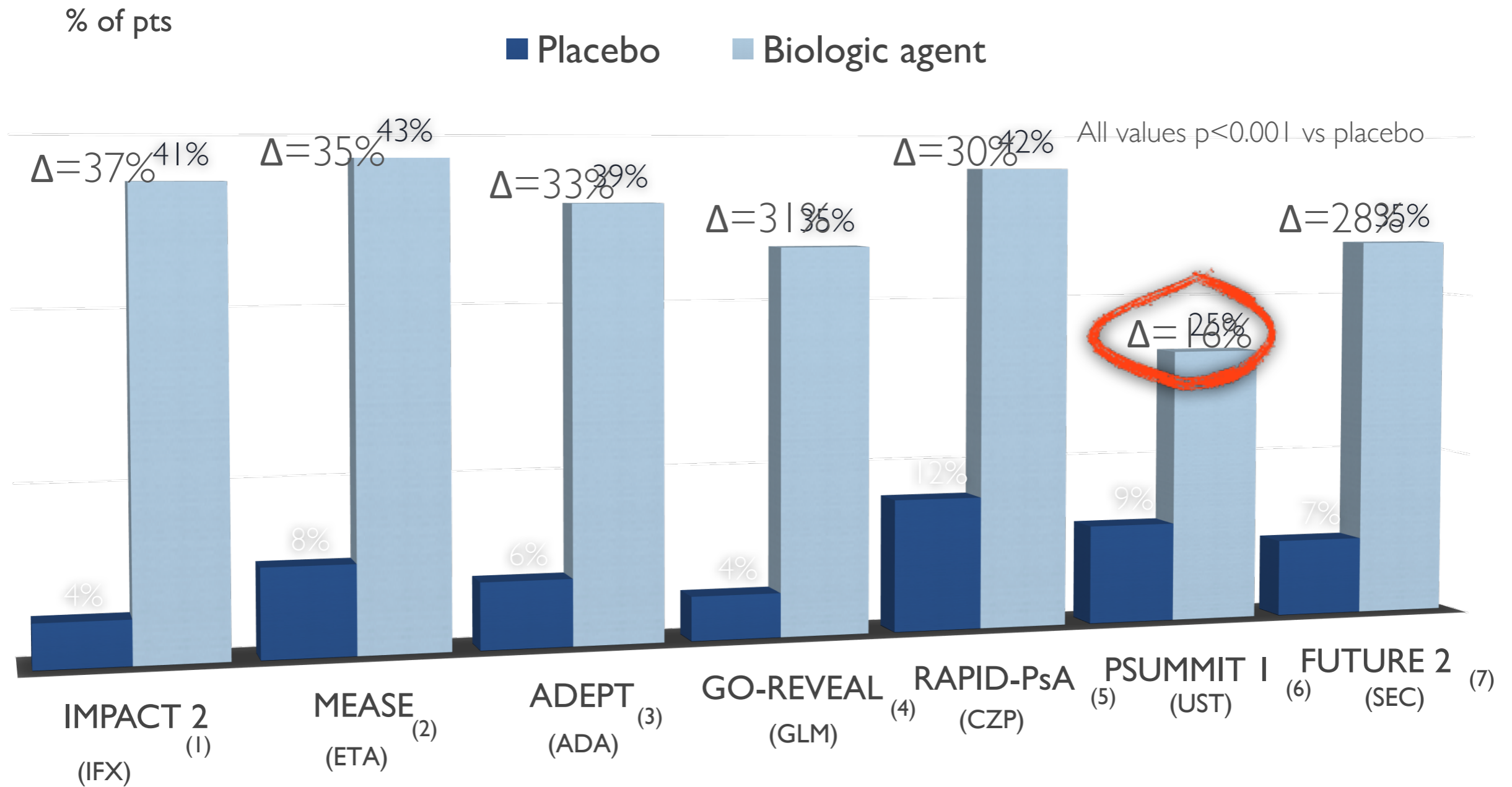
Secukinumab: data from RCTs



PsA

- Efficacy on signs and symptoms
- Efficacy on dactylitis and enthesitis
- Efficacy on skin involvement
- Efficacy on radiographic progression
- Comparison with other bDMARDs

ACR₅₀ response at 24 weeks in PsA



(1) Antoni C, et al., Ann Rheum Dis 2005

(2) Mease PJ, et al. Arthritis Rheum 2004

(3) Mease PJ, et al. Arthritis Rheum 2005

(4) Kavanaugh A, et al., Arthritis Rheum 2009

(5) Mease PJ, et al., Ann Rheum Dis 2014

(6) McInnes IB, et al., Lancet 2013

(7) McInnes IB, et al., Lancet 2015

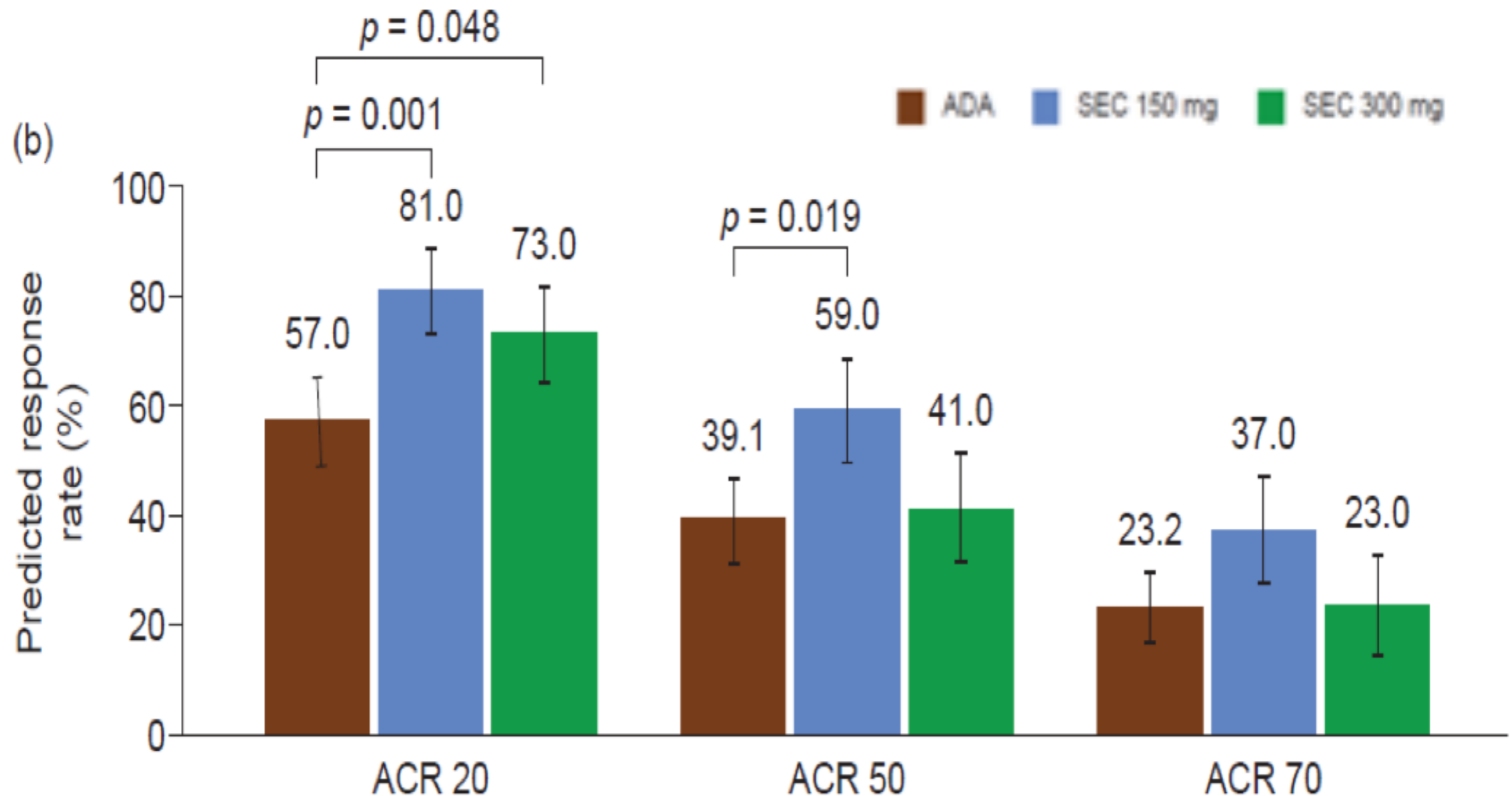


THU0448

SECUKINUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS: COMPARATIVE EFFECTIVENESS RESULTS VERSUS ADALIMUMAB UP TO 48 WEEKS USING A MATCHING-ADJUSTED INDIRECT COMPARISON

P. Nash¹, I.B. McInnes², P. Mease³, H. Thom⁴, S. Cure⁵, E. Palaka⁶, K. Gandhi⁷, S. Mpofu⁸, S. Jugl⁸.

EULAR 2016, poster presentation

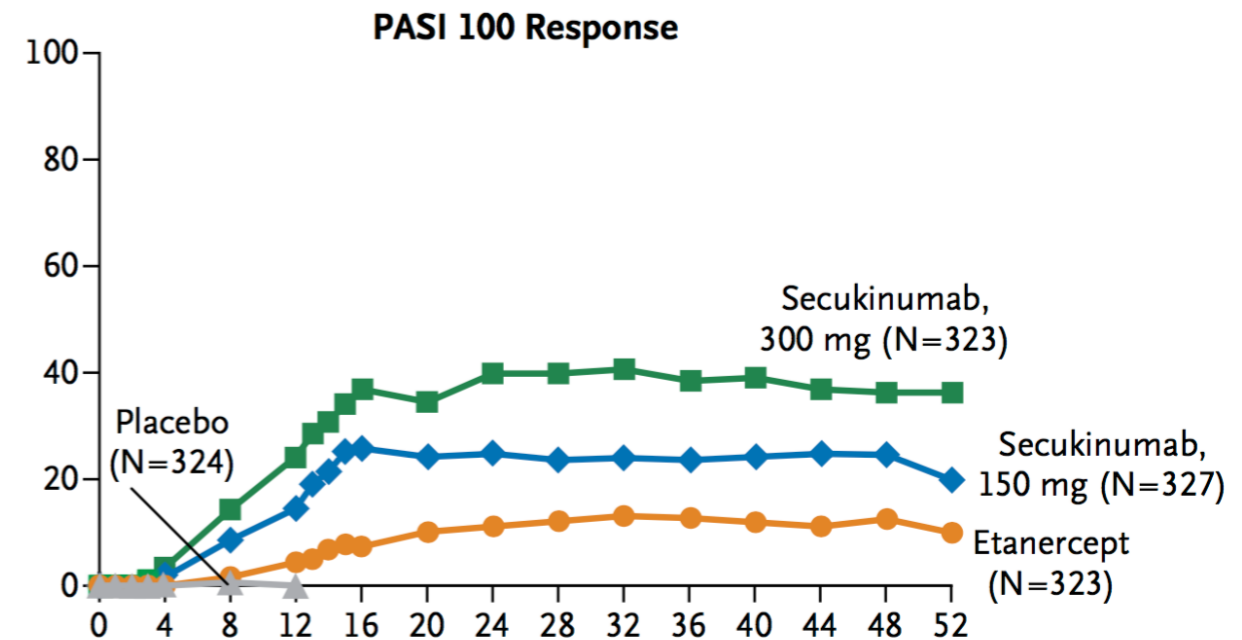
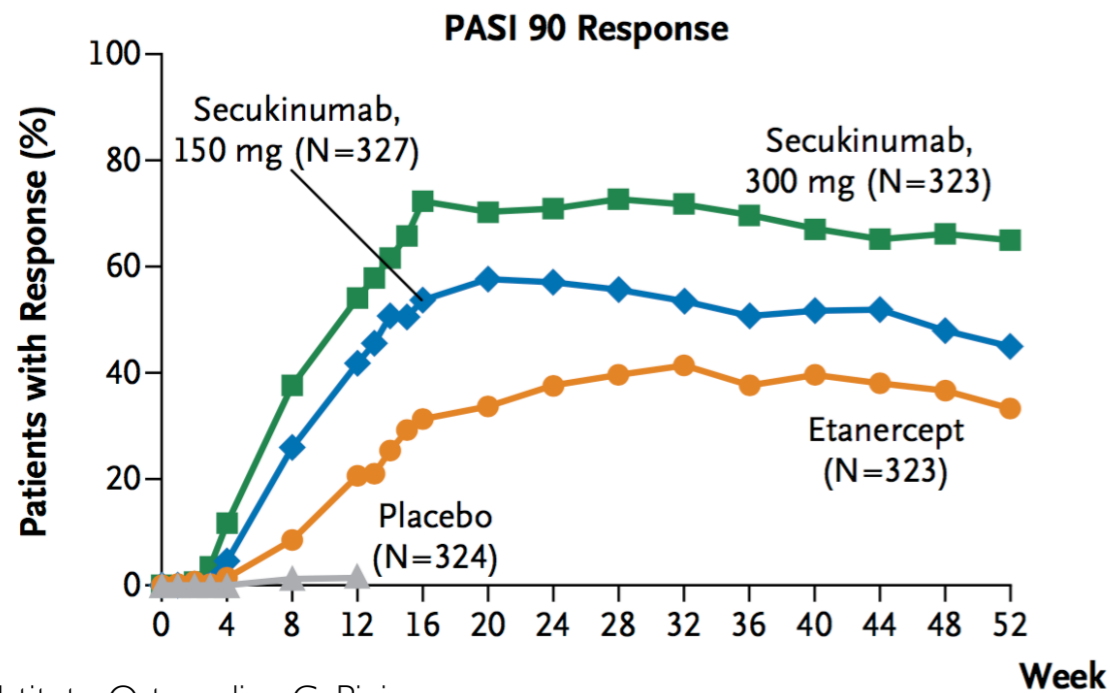
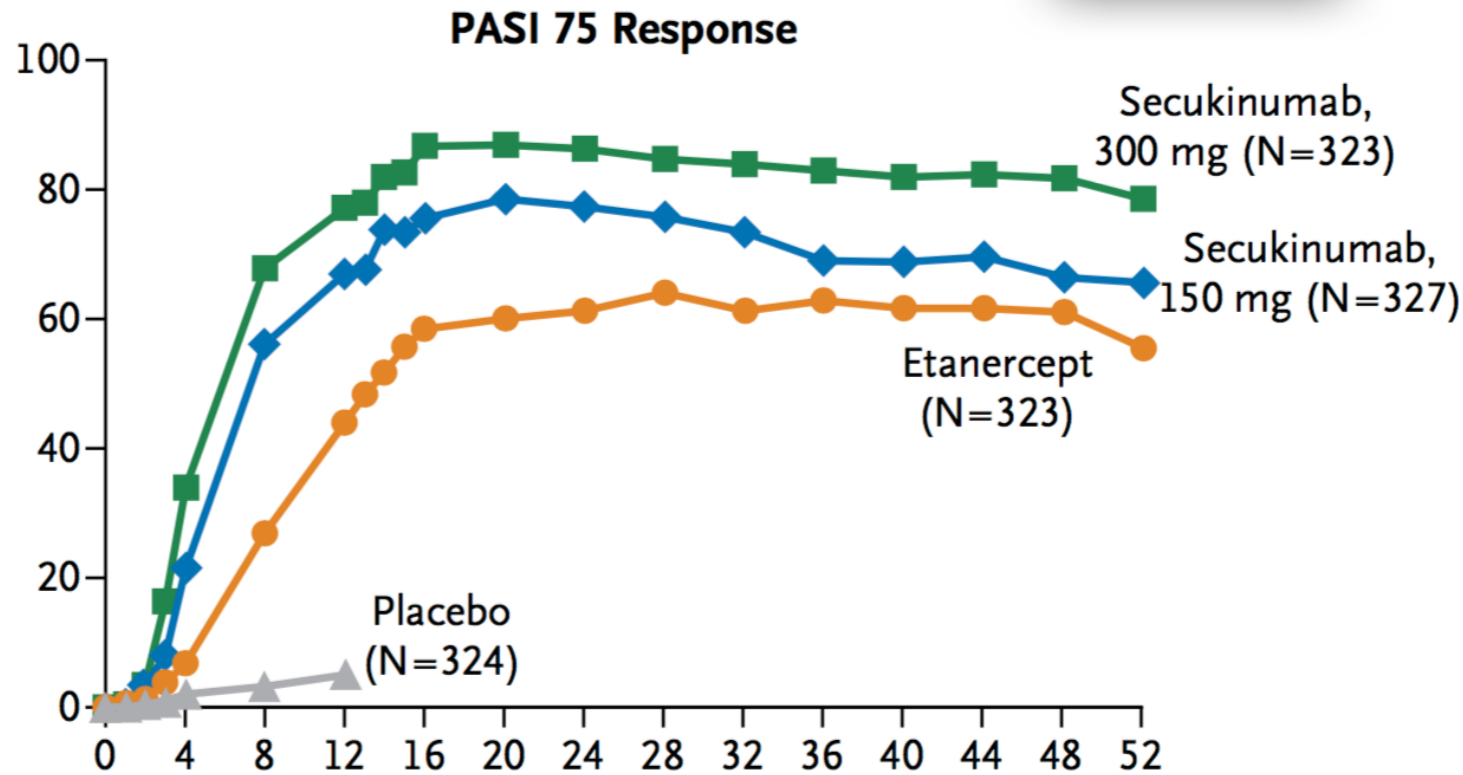


Secukinumab in Plaque Psoriasis — Results of Two Phase 3 Trials

Richard G. Langley, M.D., Boni E. Elewski, M.D., Mark Lebwohl, M.D.,
Kristian Reich, M.D., Ph.D., Christopher E.M. Griffiths, M.D., Kim Papp, M.D., Ph.D.,
Lluís Puig, M.D., Ph.D., Hidemi Nakagawa, M.D., Ph.D., Lynda Spelman, M.B., B.S.,
Bárður Sigurgeirsson, M.D., Ph.D., Enrique Rivas, M.D., Tsen-Fang Tsai, M.D.,
Norman Wasel, M.D., Stephen Tyring, M.D., Ph.D., Thomas Salko, B.A.,
Isabelle Hampele, Ph.D., Marianne Notter, M.S., Alexander Karpov, Ph.D.,
Silvia Helou, M.D., Ph.D., and Charis Papavassilis, M.D., Ph.D.,
for the ERASURE and FIXTURE Study Groups*



NEJM 2014

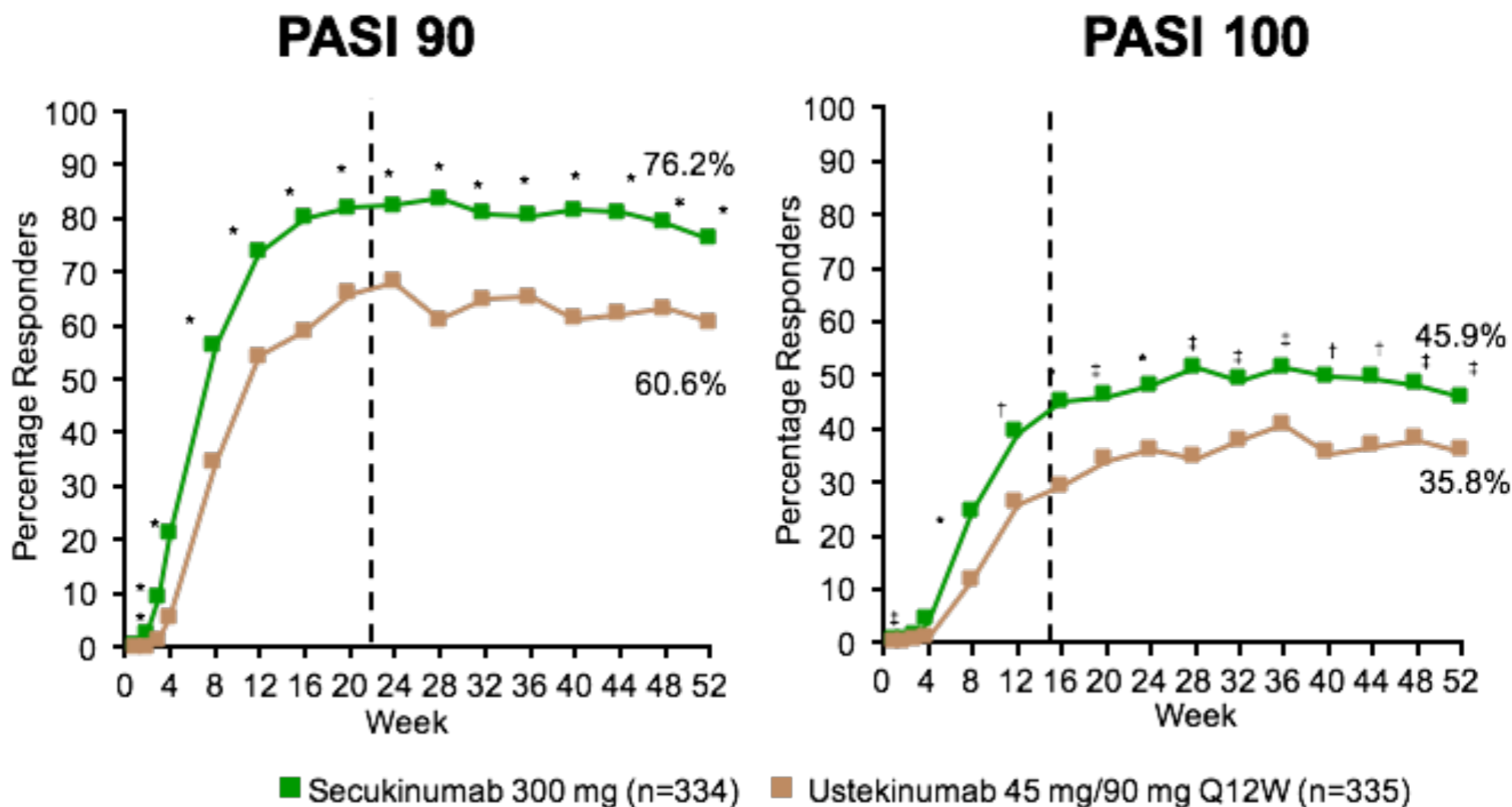




Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate-to-severe plaque psoriasis up to 1 year: Results from the CLEAR study

Andrew Blauvelt, MD, MBA,^a Kristian Reich, MD,^b Tsen-Fang Tsai, MD,^c Stephen Tying, MD, PhD,^d Francisco Vanaclocha, MD,^e Külli Kingo, MD, PhD,^f Michael Ziv, MD, BSc,^g Andreas Pinter, MD,^h Ronald Vender, MD, FRCPC,ⁱ Sophie Hugot, MSc,^j Ruquan You, MSc,^k Marina Milutinovic, MD,^j and Diamant Thaçi, MD^l

J Am Acad Dermatol 2014



*P < 0.0001, **P = 0.0001 vs. ustekinumab

Secukinumab: data from RCTs



PsA

AS

Secukinumab development in AS: the MEASURE program

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

MEASURE 1 – N = 371

i.v. loading (10 mg/kg) →
s.c. maintenance dosing (75 or 150 mg)

Extension Study

MEASURE 2 – N = 219

s.c. loading (75 or 150 mg) → s.c. maintenance dosing (75 or 150 mg)
Pre-filled syringe

MEASURE 3 – N = 222*

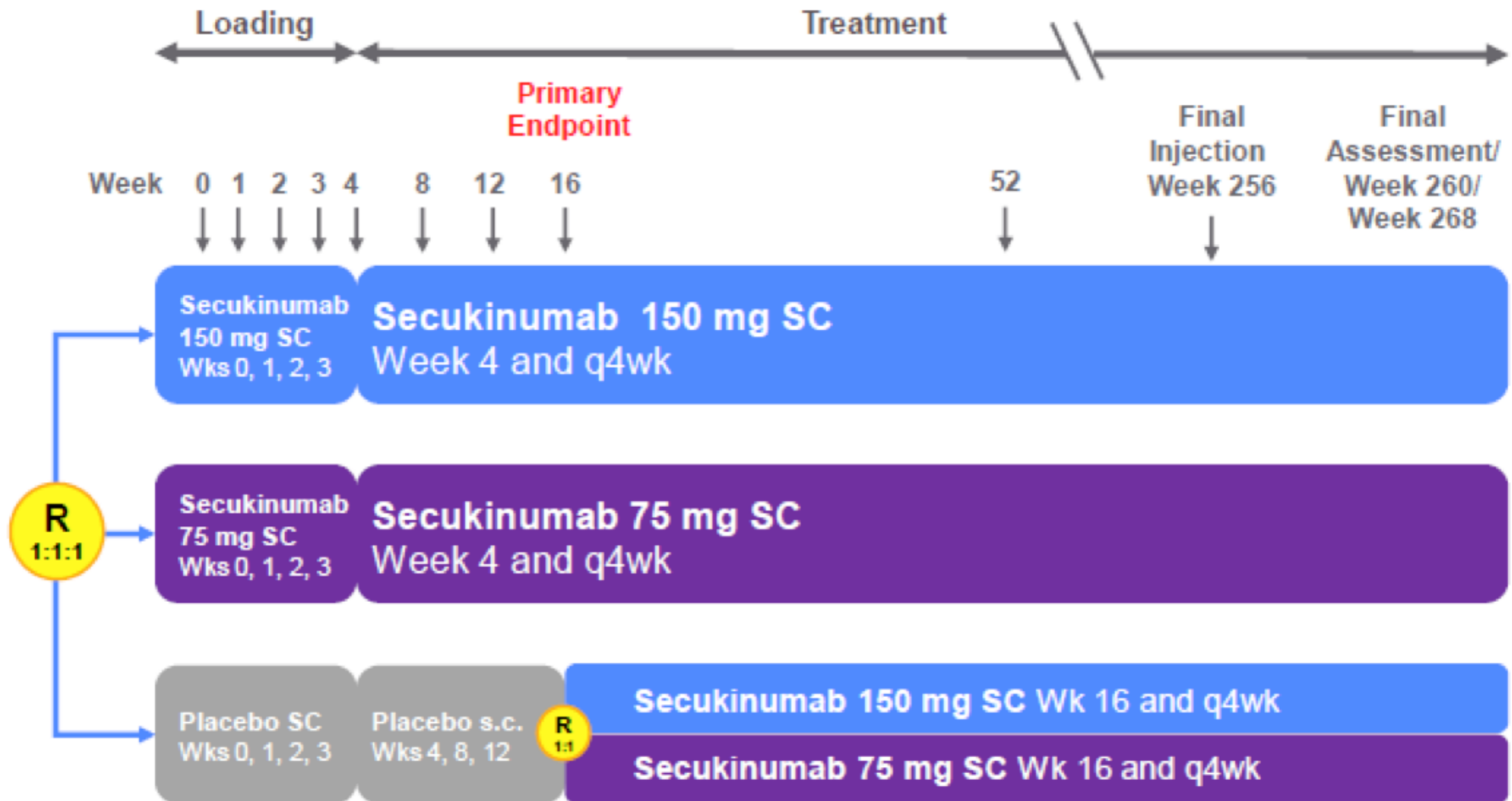
i.v. loading (10 mg/kg) → s.c. maintenance dosing (150 or 300 mg)

MEASURE 4 – N = 324*†

s.c. 150 mg with or without
s.c. loading (Pre-filled syringe)

*Estimated enrolment; †Not yet recruiting

The MEASURE 2 study design



Secukinumab: data from RCTs



- PsA
- AS
 - Efficacy on signs and symptoms

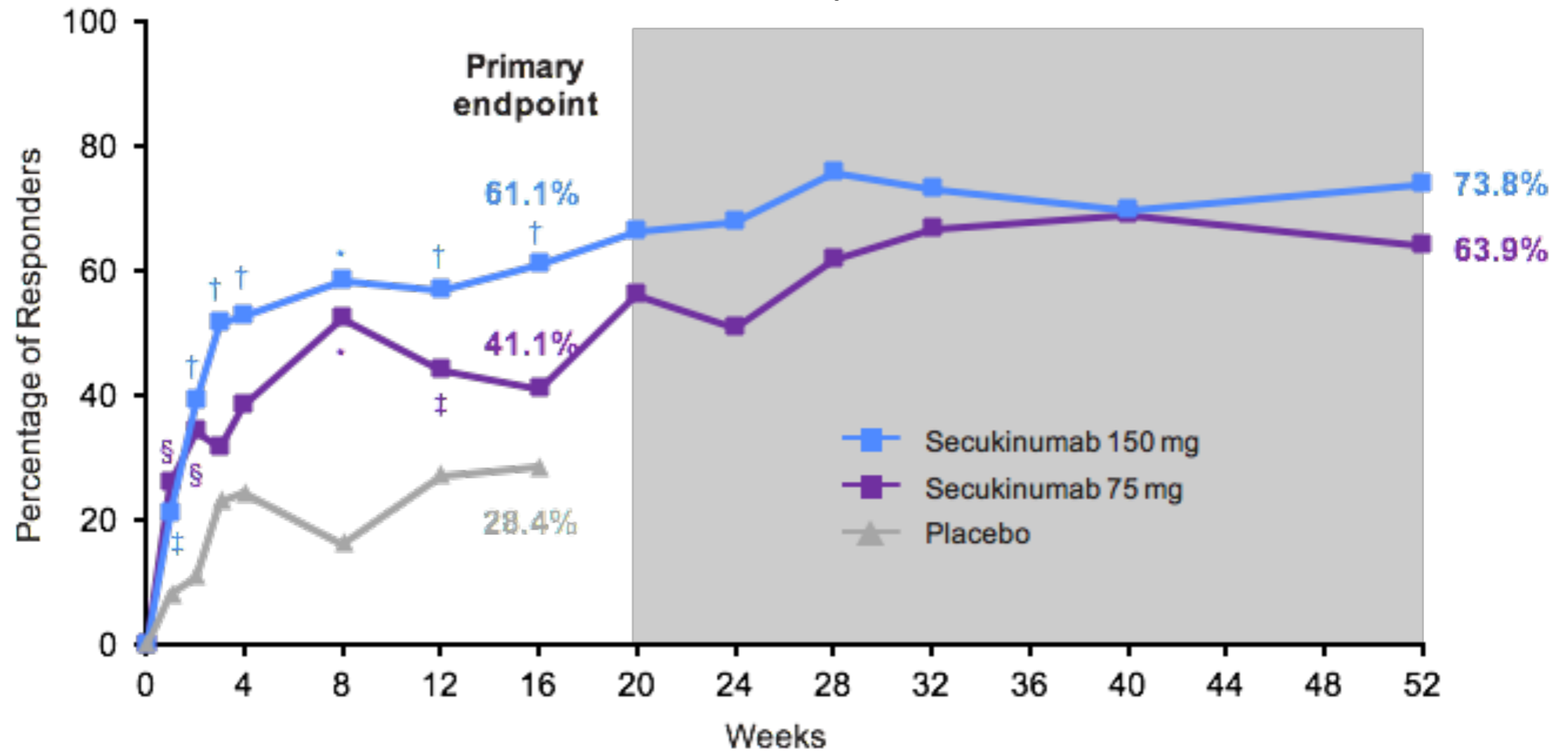


Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis

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*

NEJM 2015

ASAS 20 response



SEC 150 mg:	72	72	72	72	72	65	65	62	63	63	61
SEC 75 mg:	73	73	73	73	73	68	67	68	66	64	61
Placebo:	74	74	74	74	74	-	-	-	-	-	-

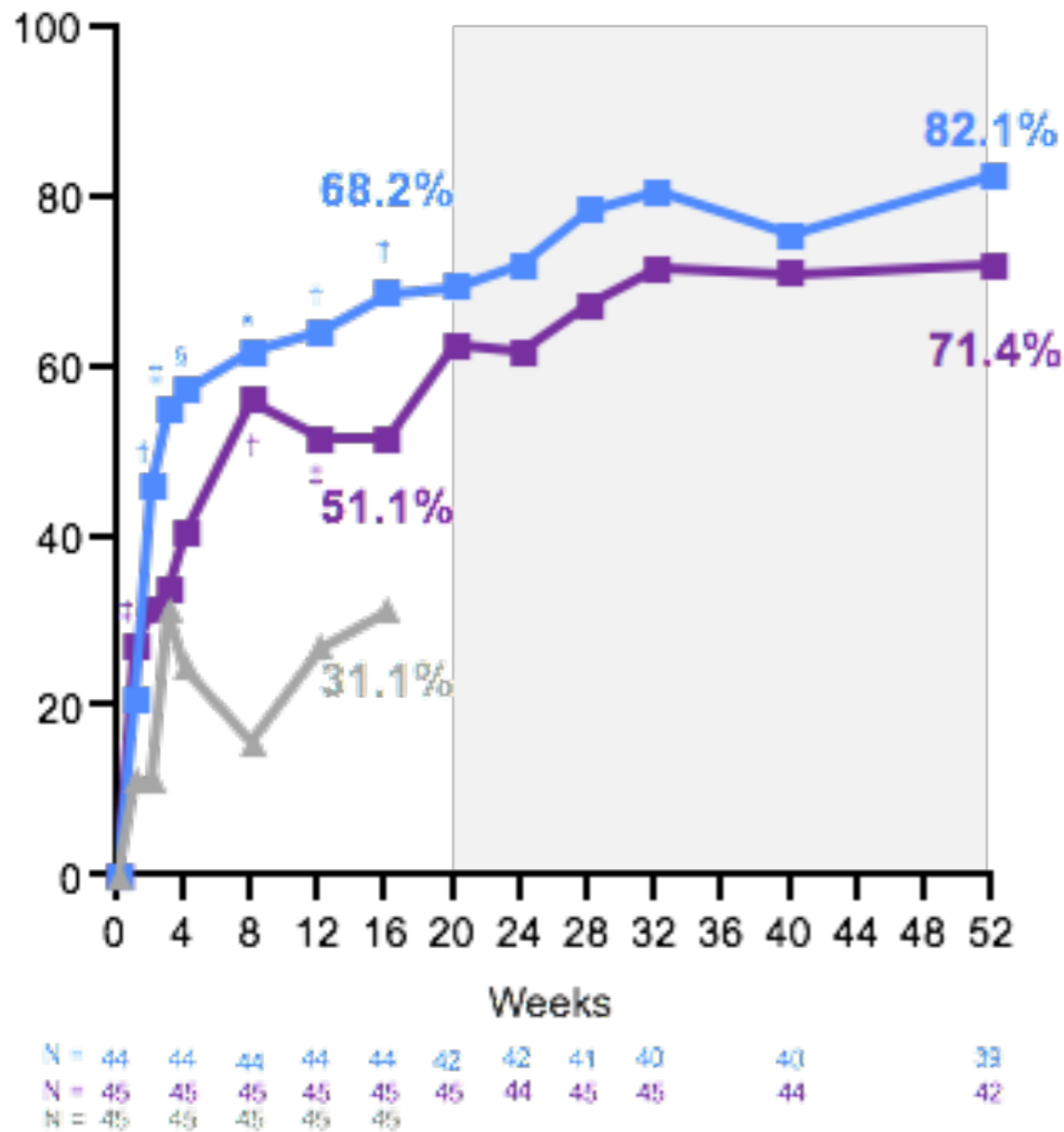


Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis

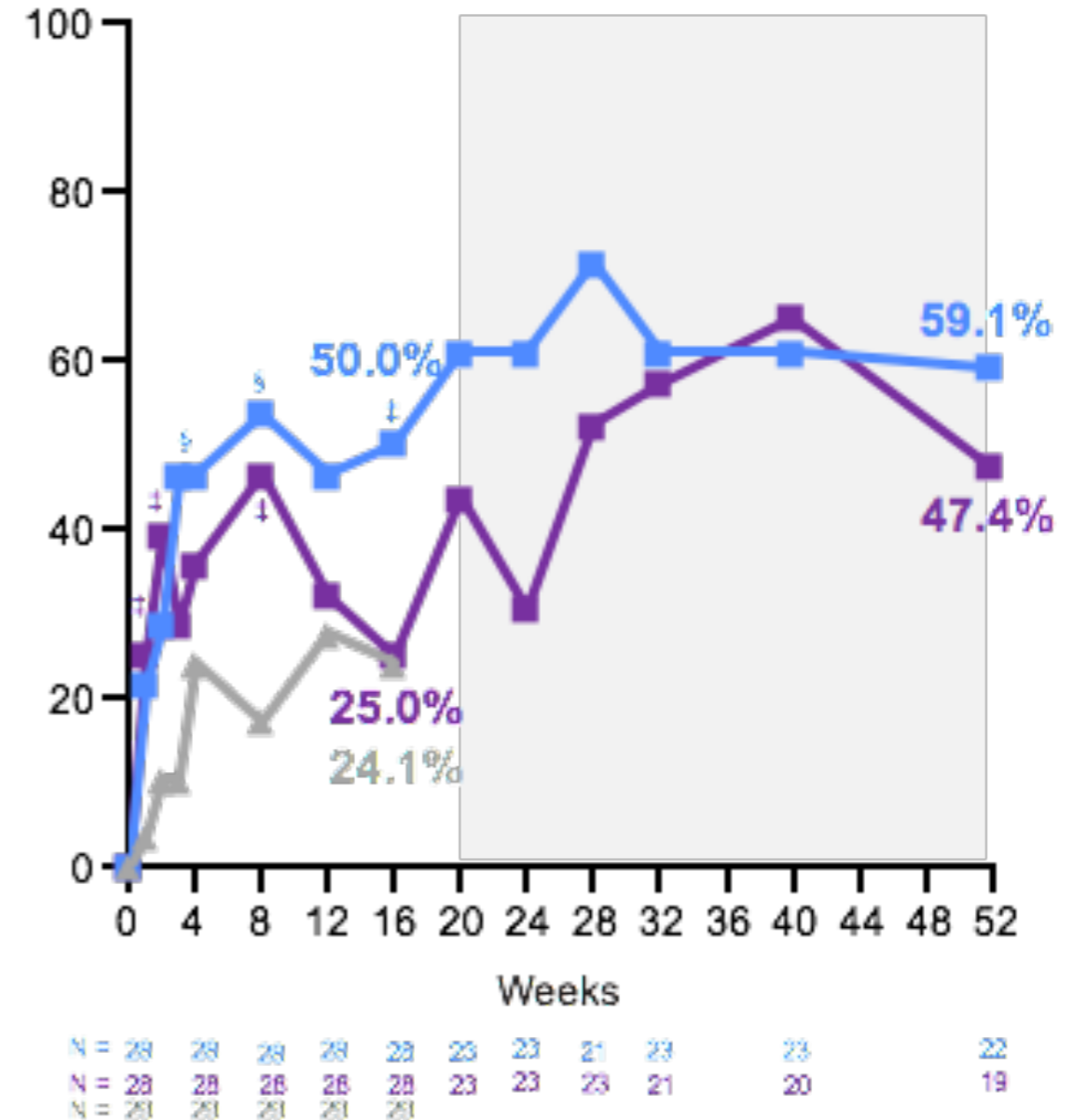
Dominique Baeten, M.D., Joachim Sieper, M.D., Jürgen Braun, M.D., Xenofon Baraliakos, M.D., Maxime Dougados, M.D., Paul Emery, F.R.C.P., Atul Deodhar, M.D., Brian Porter, M.D., Ph.D., M.P.H., Ruvie Martin, Ph.D., Mats Andersson, M.Sc., Shephard Mpofu, M.D., and Hanno B. Richards, M.D., for the MEASURE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

NEJM 2015

bDMARD naïve



TNFi IR



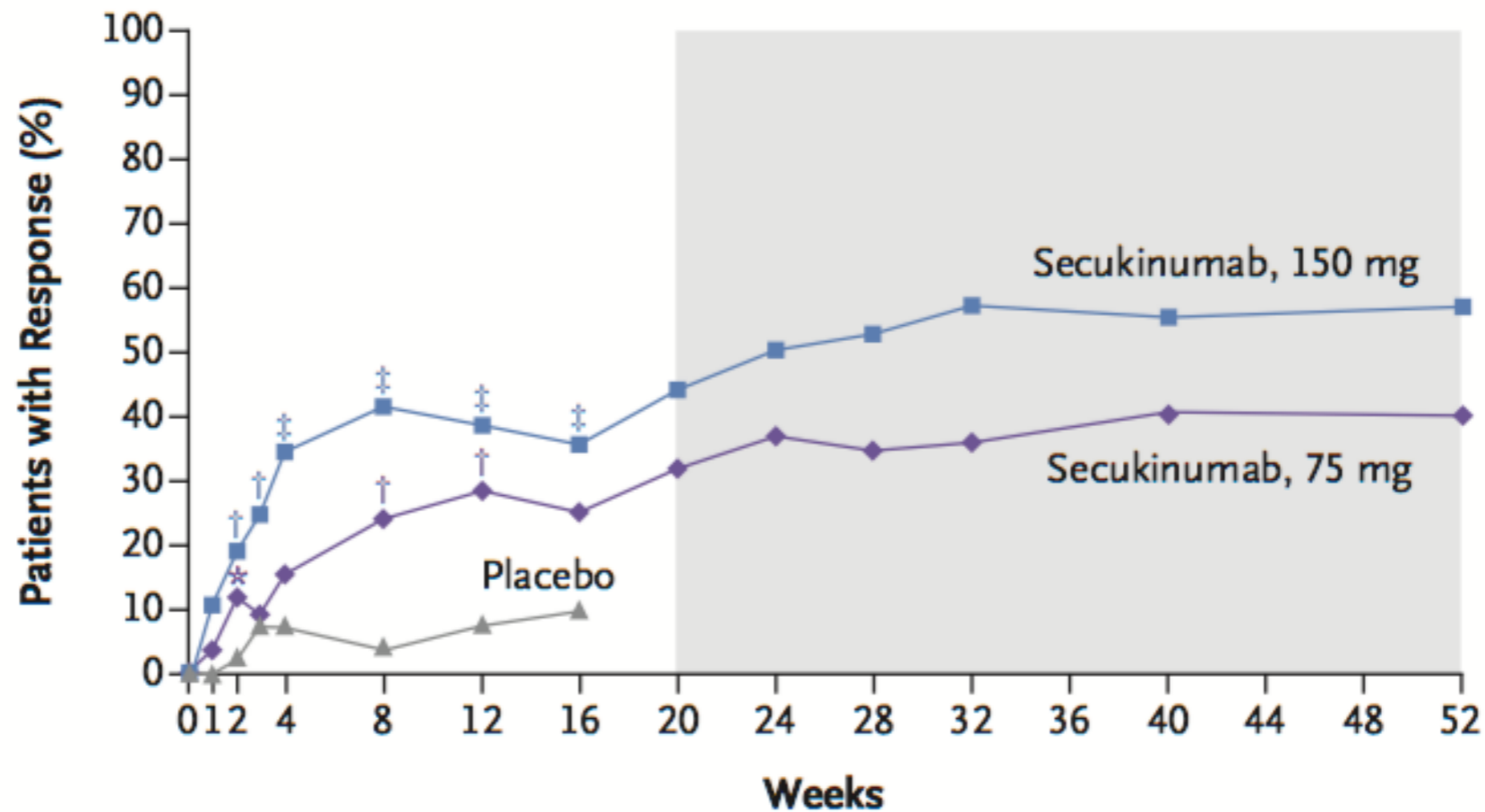


Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis

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*

NEJM 2015

ASAS 40 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						

Secukinumab: data from RCTs



PsA

AS

- Efficacy on signs and symptoms
- Efficacy on damage progression



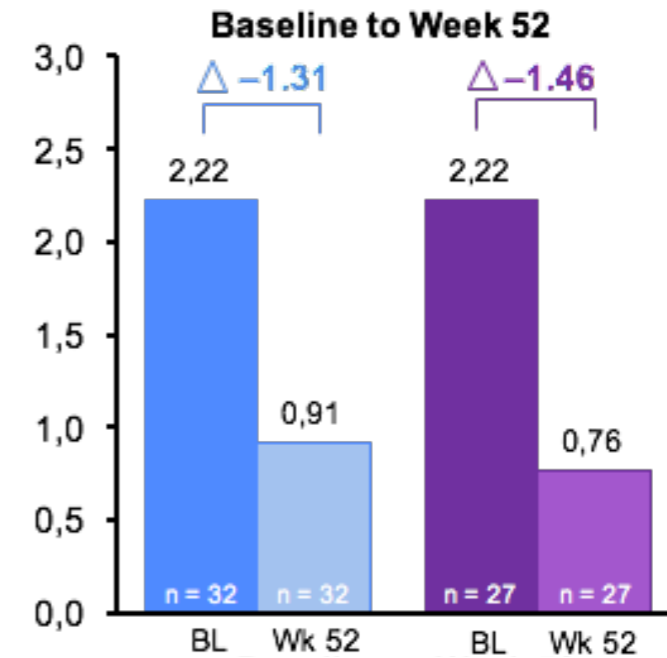
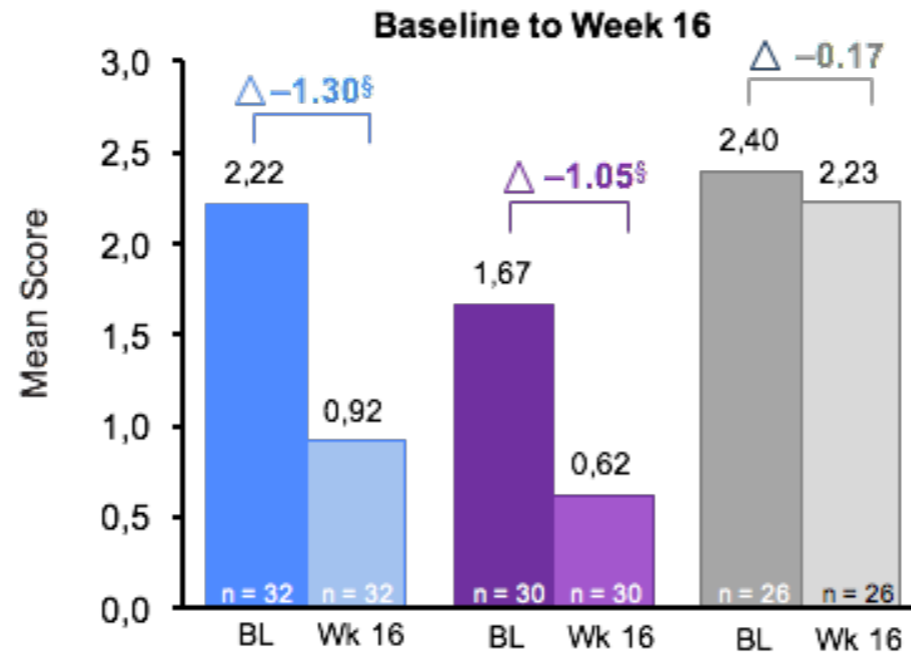
THU0233

SECUKINUMAB REDUCES SACROILIAC JOINT AND SPINAL INFLAMMATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS: MRI DATA FROM A PHASE 3 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY (MEASURE 1)

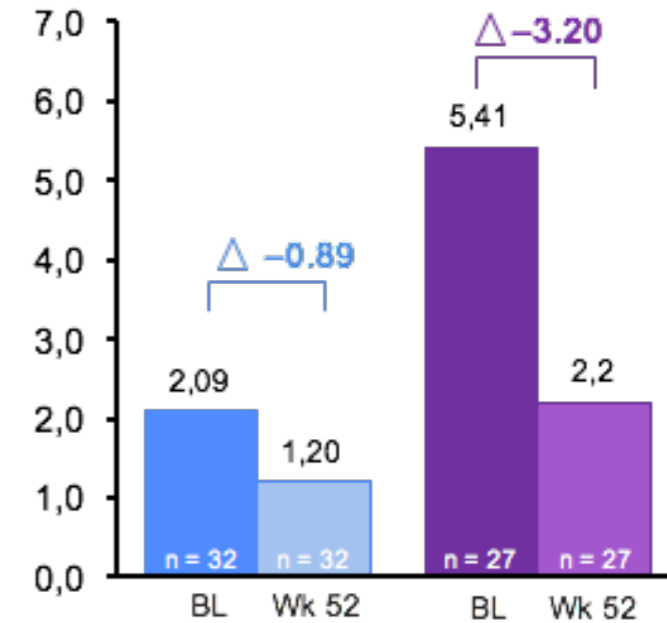
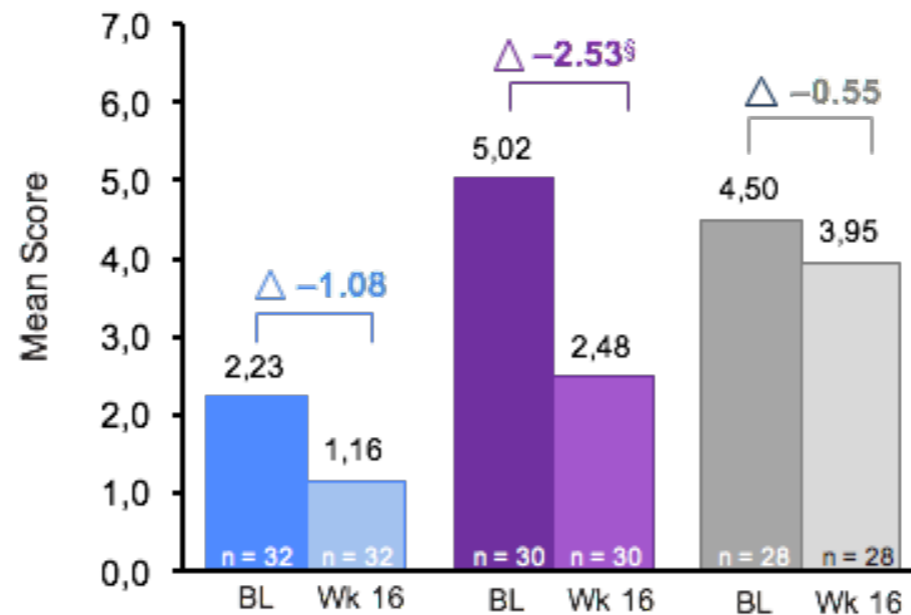
X. Baraliakos¹, J. Braun¹, J. Sieper², D.L. Baeten³, A. Readie⁴, G. Ligozio⁴, H. Richards⁵.

EULAR 2015, Poster presentation

Sacroiliac joints



Spine



Secukinumab 10 mg/kg i.v. → 150 mg s.c.

Secukinumab 10 mg/kg i.v. → 75 mg s.c.

Secukinumab 10 mg/kg i.v. → 150 mg s.c.

Secukinumab 10 mg/kg i.v. → 75 mg s.c.

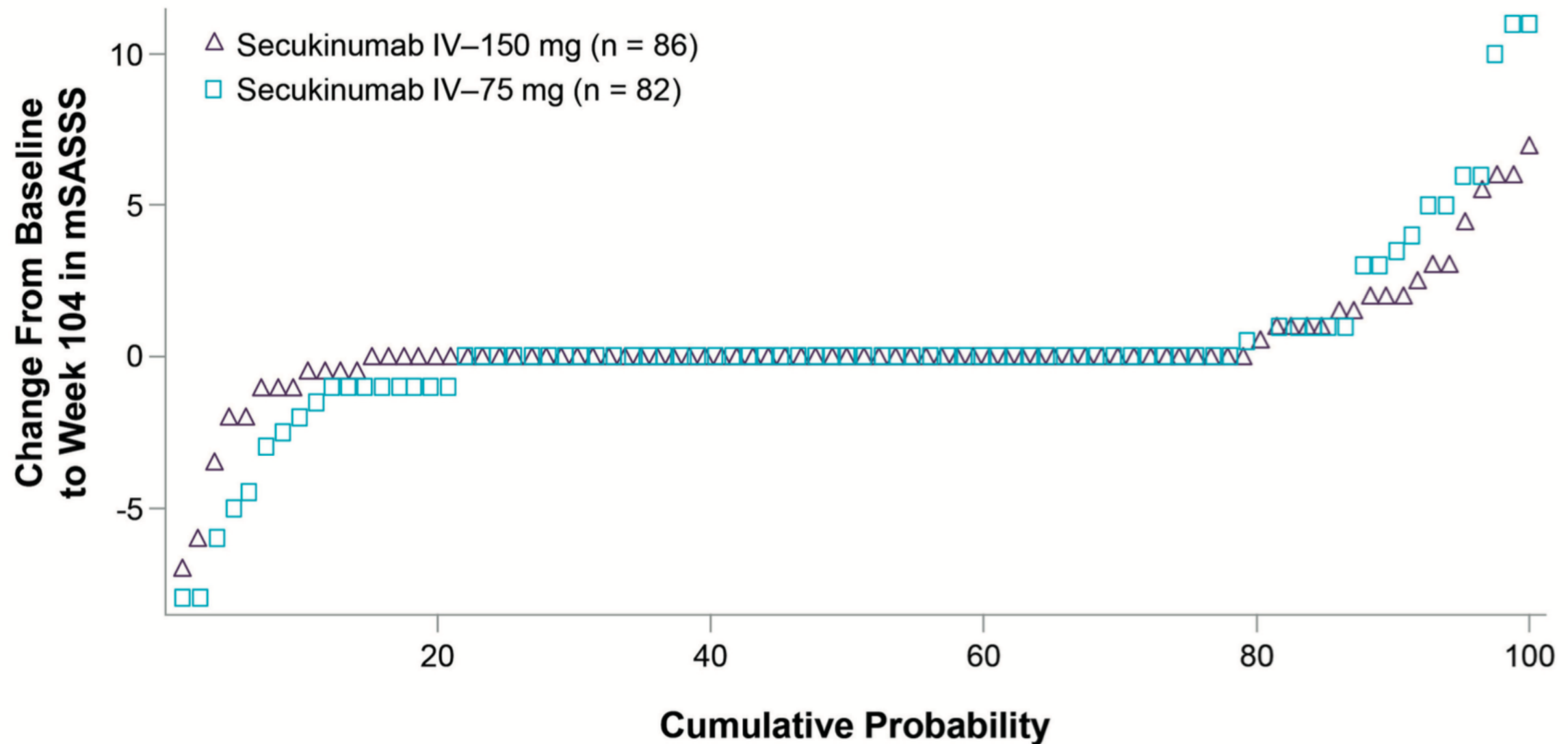


OP0001

EFFECT OF SECUKINUMAB, AN INTERLEUKIN-17A INHIBITOR, ON SPINAL RADIOGRAPHIC CHANGES THROUGH 2 YEARS IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS OF THE PHASE 3 STUDY, MEASURE 1

J. Braun¹, X. Baraliakos¹, A. Deodhar², D. Baeten³, J. Sieper⁴, P. Emery⁵, Z. Talloczy⁶, R. Martin⁶, H.B. Richards⁷.

EULAR 2016. Oral presentation



Only **5%** of pts without syndesmophytes at BL showed **new syndesmophytes** at 104 weeks

Secukinumab: data from RCTs



PsA

AS

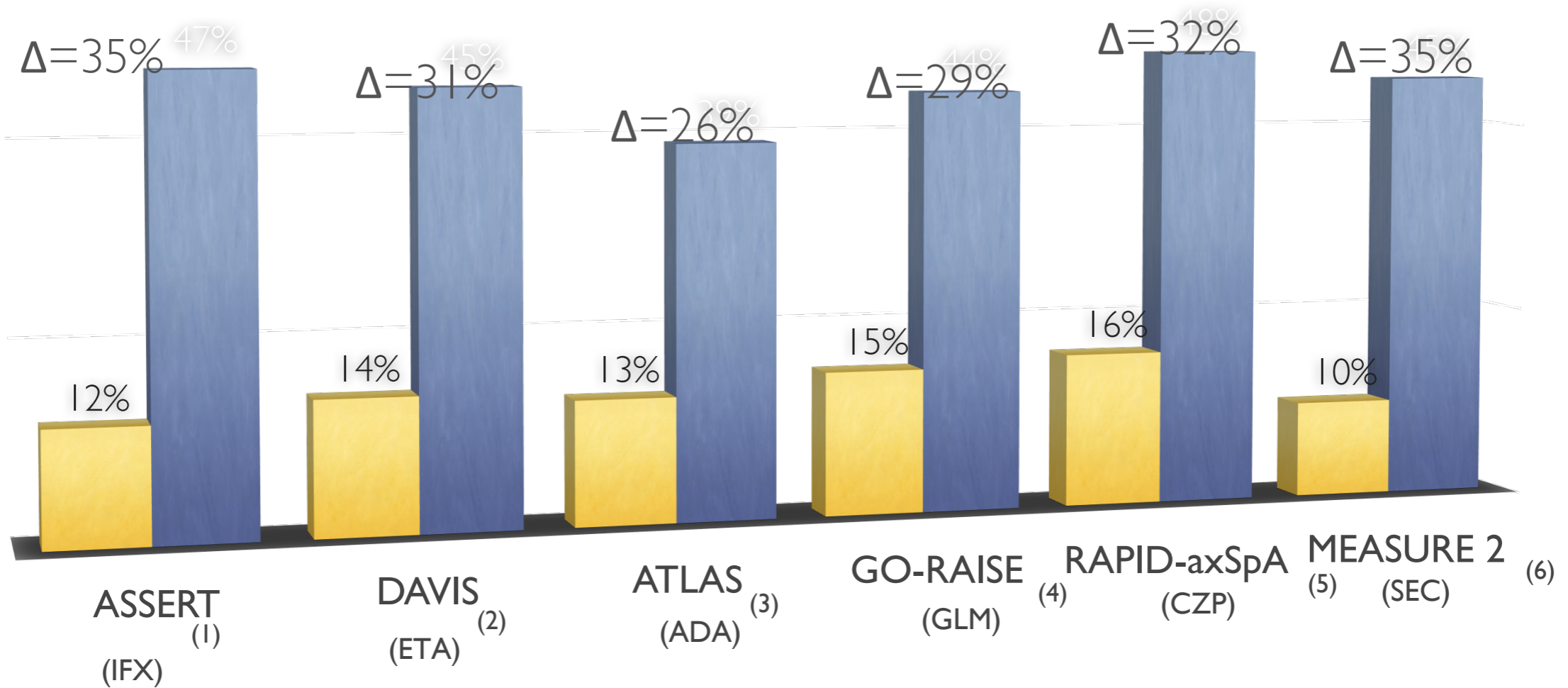
- Efficacy on signs and symptoms
- Efficacy on radiographic progression
- Comparison with other bDMARDs

ASAS₄₀ response at 24 weeks in AS/axSpA

% of pts

■ Placebo ■ Biologic agent

All values p<0.001 vs placebo



(1) van der Heijde D, et al., Arthritis Rheum 2005

(2) Davis JC, et al. Arthritis Rheum 2003

(3) van der Heijde D, et al., Arthritis Rheum 2006

(4) Inman RD, et al., Arthritis Rheum 2008

(5) Landewè, R et al., Ann Rheum Dis 2014

(6) Baeten D, et al. NEJM 2015

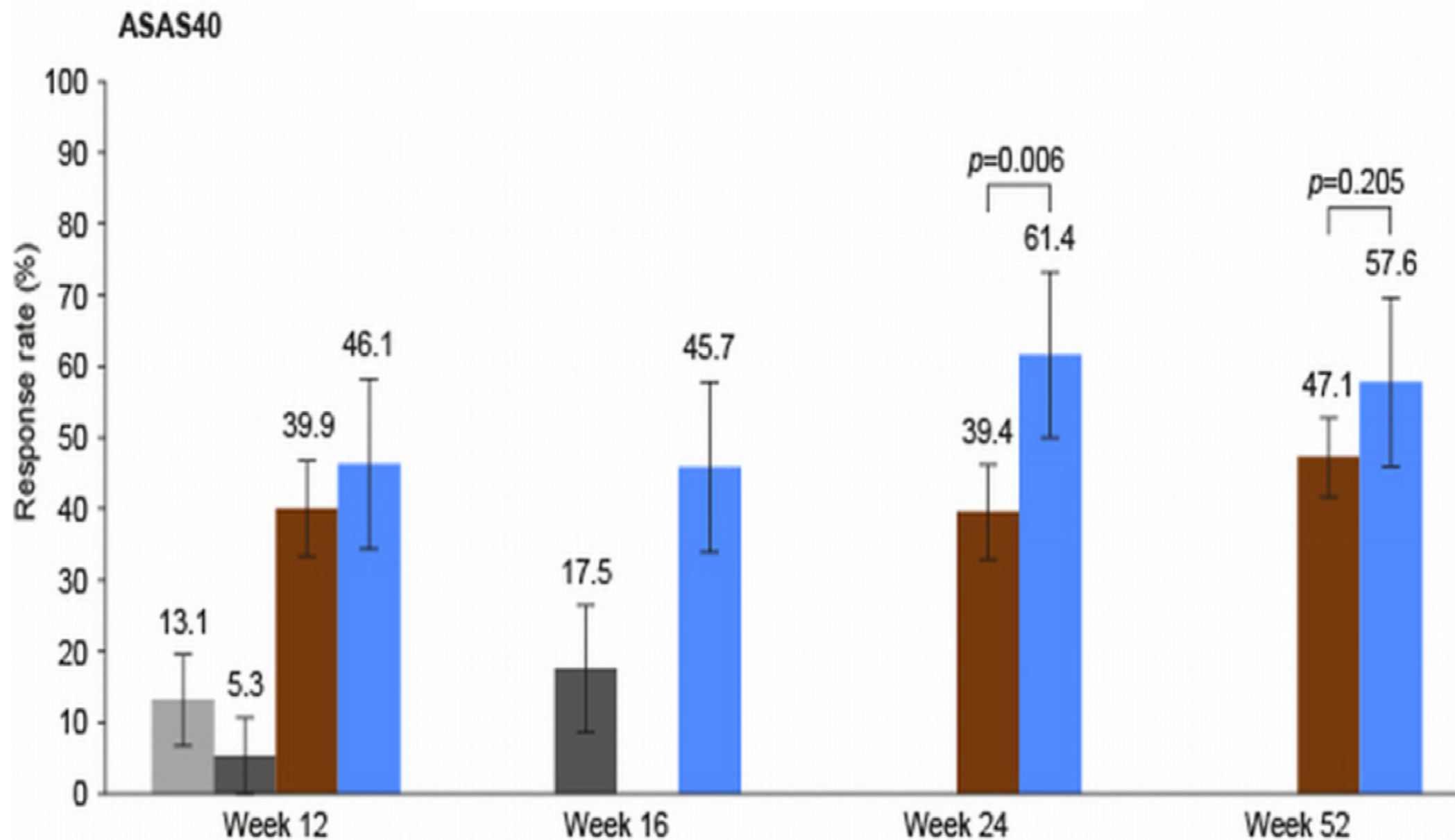


OP0114

SECUKINUMAB FOR THE TREATMENT OF ANKYLOSING SPONDYLITIS: COMPARATIVE EFFECTIVENESS RESULTS VERSUS ADALIMUMAB USING A MATCHING-ADJUSTED INDIRECT COMPARISON

W. Maksymowych¹, V. Strand², D. Baeten³, P. Nash⁴, H. Thom⁵, S. Cure⁶, E. Palaka⁷, K. Gandhi⁸, H. Richards⁹, S. Jugl⁹.

EULAR 2016, Oral presentation



Secukinumab: data from RCTs



- PsA
- AS
- Safety profile

Secukinumab pooled safety data

(FUTURE 1 and 2, MEASURE 1 and 2)

	Double-blind period (16 wks)		Entire safety period	
	Secukinumab (n=1097)	Placebo (n=496)	Secukinumab (n=1545)	Placebo (n=496)
Discontinuation due to AEs	22 (2%)	16 (3.2%)	51 (3.3%)	25 (5%)
Deaths	1	1	2	1
	N. of events (%)		N. of events per 100 pt/yr	
Any AE	673 (61.3%)	290 (58.4%)	416	678
Any serious AE	37 (3.3%)	20 (4%)	16.9	26.4
MACE	2 (0.1%)	0	1.1	0
IBD	5 (0.4%)	1 (0.2%)	1.5	0.9
Infections	326 (29.7%)	112 (22.5%)	151.2	159.2
Candida	7 (0.6%)	0	2.5	0
Neutropenia	19 (1.7%)	8 (1.6%)	5.8	8.3
Malignancies and skin cancers	3 (0.2%)	2 (0.4%)	1.1	2.5

Baeten D, et al. NEJM 2015

Mease PJ, et al. NEJM 2015

McInnes IB, et al. Lancet 2015

Secukinumab Safety and Tolerability in Patients with Active Psoriatic Arthritis and Psoriasis: Results from a Pooled Safety Analysis

Philip J. Mease¹, Iain B. McInnes², Alice B. Gottlieb³, Albert Widmer⁴, Luminita Pricop⁵ and Shephard Mpofo⁴,

ACR Congress 2015

Table. Summary of pooled safety across PsO and PsA studies

	Any secukinumab	Placebo
	N=3928	N=994
Exposure, mean days (SD)	299.8 (131.1)	105.7 (56.8)
Min-max exposure, days	1-721	8-377
	Events per 100-pt years (95% confidence interval)	
Any AE	240.5 (231.9-249.4)	329.6 (302.3-358.7)
Any SAE	7.9 (6.9-8.9)	9.9 (6.6-14.3)
AEs of special interest		
Infections and infestations	92.8 (88.7-97.0)	93.9 (82.1-107.0)
IBD	0.3 (0.1-0.6)	0.3 (0.0-1.9)
Crohn's	0.1 (0.0-0.3)	0.3 (0.0-1.9)
Neutropenia	1.5 (1.1-2.0)	2.4 (1.0-5.0)
MACE (unadjudicated)	0.6 (0.4-1.0)	0.0 (0.0-1.3)
Malignant or unspecified tumors	0.8 (0.6-1.2)	1.4 (0.4-3.6)



OP0113

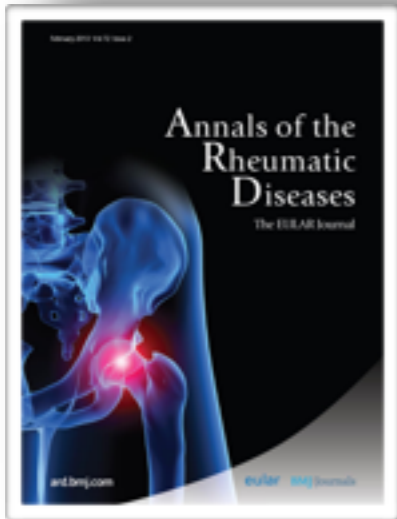
NO INCREASED INCIDENCE OF INFLAMMATORY BOWEL DISEASE AMONG SECUKINUMAB-TREATED PATIENTS WITH MODERATE TO SEVERE PSORIASIS, PSORIATIC ARTHRITIS, OR ANKYLOSING SPONDYLITIS: DATA FROM 14 PHASE 2 AND PHASE 3 CLINICAL STUDIES

S. Schreiber¹, B.E. Sands², A. Deodhar³, D. Baeten⁴, J. Huang⁵, K. Gandhi⁵, C. Karyekar⁵, T. Fox⁶, C. Gaillez⁶.

EULAR 2016, Oral presentation

Table: Incidence of CD and UC Across the PsO, PsA and AS Secukinumab Clinical Trial Programs							
Short-term period, n (%)							
	PsO Studies ^{4,5}			PsA Studies		AS Studies	
	Any SEC (N=2877)	PBO (N=793)	ETN (N=323)	Any SEC (N=703)	PBO (N=300)	Any SEC (N=394)	PBO (N=196)
Mean exposure, days	83.2	81.2	82.6	112.0	110.1	112.1	108.6
Crohn's disease	1 (0.03)	0	0	0	1 (0.3)	2 (0.5)	0
Exacerbations ^b	1	0	0	0	0	2	0
Ulcerative colitis	1 (0.03)	0	1 (0.3)	0	0	1 (0.3)	0
Exacerbations ^b	0	0	0	0	0	0	0
Entire treatment period, n (EAIR per 100 pt-years) [95% CI]							
	PsO Studies ^{4,5}		PsA Studies		AS Studies		
	Any SEC* (N=3430)	ETN (N=323)	Any SEC* (N=974)	Any SEC* (N=591)			
Mean exposure, days	290.1	331.9	542.4	670.0			
Crohn's disease	3 (0.11) [0.02–0.32]	0 [0–1.26]	1 (0.07) [0.00–0.39]	8* (0.77) [0.33–1.51]			
Exacerbations ^b	3	0	0	3			
Ulcerative colitis	4 (0.15) [0.04–0.38]	1 (0.34) [0.01–1.90]	2 (0.14) [0.02–0.50]	3 (0.29) [0.06–0.84]			
Exacerbations ^b	2	0	1	1			

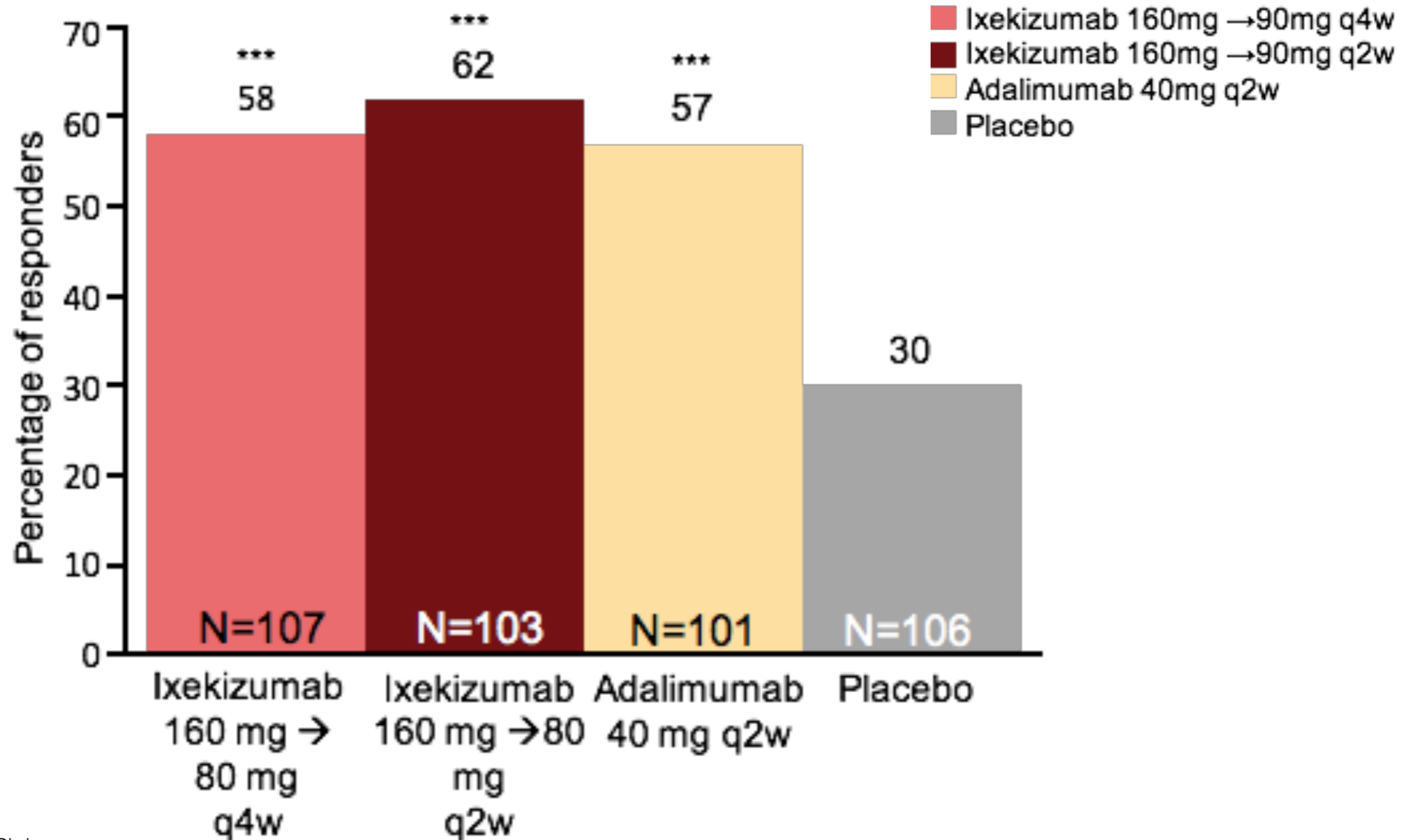
*Final diagnosis was not confirmed in 2 cases; *includes pts switched from placebo (PBO);
^bExacerbations count to the overall incidence rate

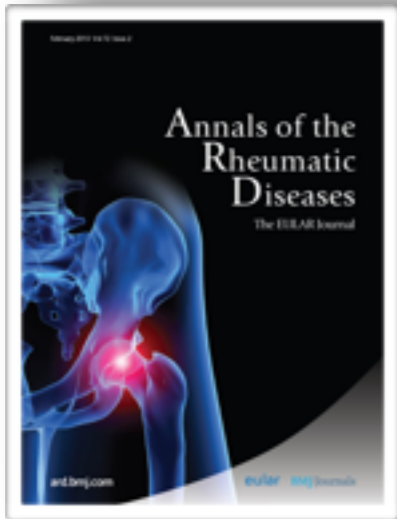


Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1

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

Ann Rheum Dis 2016

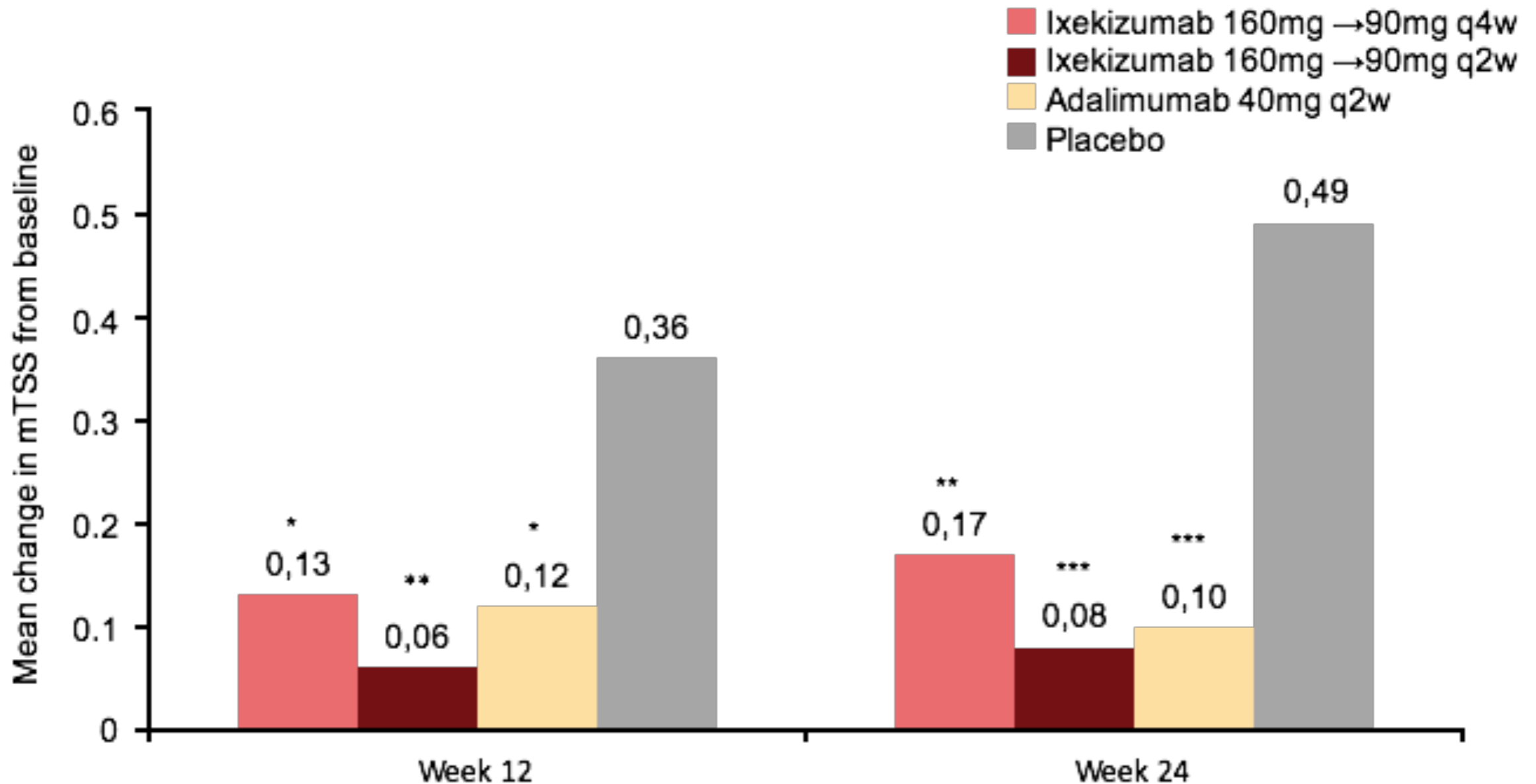




Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1

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

Ann Rheum Dis 2016



Take home messages





Toward a cytokine-based disease taxonomy

Georg Schett, Dirk Elewaut, Iain B McInnes, Jean-Michel Dayer & Markus F Neurath

Nature Med 2013

CID	TNF	IL-6R	IL-1	IL-12/23	IL-17A
Rheumatoid arthritis	Green	Green	Grey	Grey	Grey
Giant cell arthritis	Green	Green	Grey	Grey	Grey
JIA/AID	Green	Green	Green	Grey	Grey
Gout	Light Green	Grey	Green	Grey	Grey
Crohn's disease	Green	Grey	Grey	Light Green	Red
Ulcerative colitis	Green	Grey	Grey	Grey	Grey
Psoriasis	Green	Grey	Grey	Green	Green
Psoriatic arthritis	Green	Grey	Grey	Green	Green
Ankylosing spondylitis	Green	Grey	Grey	Light Green	Green
Multiple sclerosis	Red	Grey	Grey	Grey	Light Green
Drugs	Adalimumab Certolizumab Etanercept Golimumab Infliximab	Tocilizumab Sarilumab*	Anakinra Canakinumab Rilonacept	Ustekinumab Briakinumab*	Brodalumab* Ixekizumab* Secucinumab*



Toward a cytokine-based disease taxonomy

Georg Schett, Dirk Elewaut, Iain B McInnes, Jean-Michel Dayer & Markus F Neurath

Nature Med 2013



TNF α



Thank you

Take home messages

- New **ASAS** criteria allowed to better define **axial SpA**

- In **clinical practice** treatment with anti-TNF agents is often prescribed to patients fulfilling **ASAS axial SpA** but not **modified NY criteria**

- **Adalimumab** is the **only** anti-TNF agent tested in **ASAS** criteria defined axial SpA

- To date, **adalimumab** is the only anti-TNF agent **indicated** for the treatment of **axial SpA**

