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RHEUMATOLOGIE
& IMMUNOLOGIE

EULAR 2022 - Highlights
Axiale Spondyloarthritis

PD Dr. med. Tobias Manigold, 30.06.2022, USZ

axSpA or axPsA oder axSpA mit PsO?

- Schwierigkeit die Entitäten zu unterscheiden
- keine Diagnosekriterien für axPsA

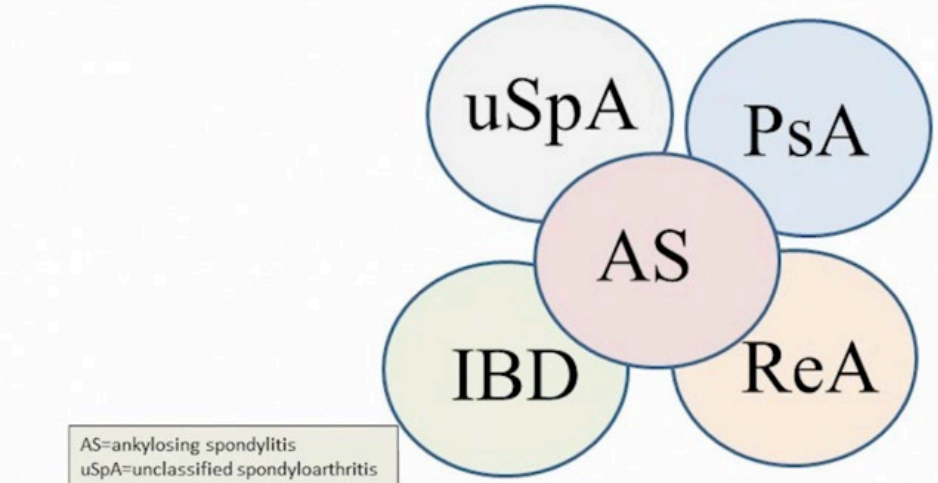
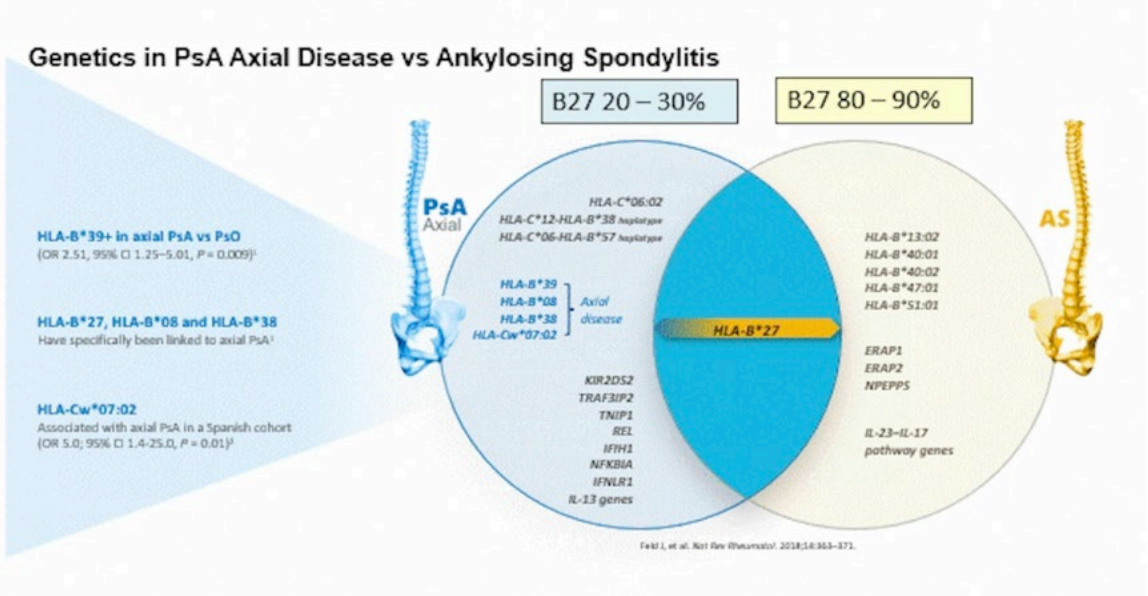


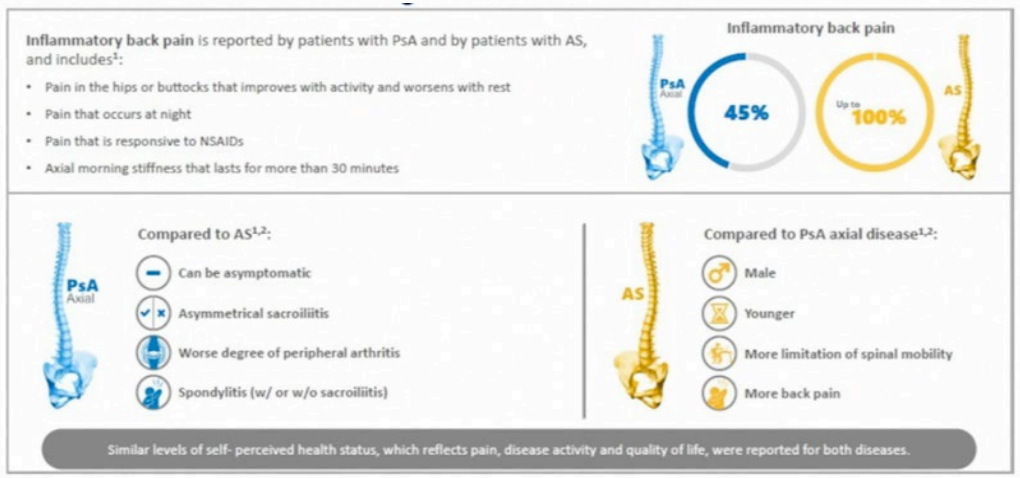
Table 1 Summary of radiological differences reported by McEwen et al[6]

Feature	*Ankylosing spondylitis and spondylitis of ulcerative colitis and regional enteritis*	*Spondylitis associated with psoriasis and reactiv arthritis*
Sacroiliitis	Severe and symmetrical	Sacroiliitis sometimes unilateral or bilaterally asymmetrical
Symphisitis	More frequent	Less frequent
Osteoporosis	More frequent	Less frequent
Lumbar straightening	More frequent	Less frequent
Apophyseal joint involvement	More frequent	Less frequent
Squaring	More frequent	Less frequent
Syndesmophytes	More frequent, usually symmetrical	Less frequent, usually asymmetrical
Shape and size of syndesmophytes	Marginal (see text)	Usually "other than marginal" (see text)
Ligamentous ossification	More frequent	Less frequent
Progression of syndesmophytes	Lumbar to dorsal to cervical	Random progression

Helliwell PS, Hickling P, Wright V. Annals of the Rheumatic Diseases. 1998;57(3):135-40

Rolle von HLA-B27 – entscheidend für axialen Phänotyp?





Feld J, Ye JY, Chandran V, Inman RD, Haroon N, Cook R, et al. Is axial psoriatic arthritis distinct from ankylosing spondylitis with and without concomitant psoriasis? Rheumatology. 2019;59(6):1340-6.

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]

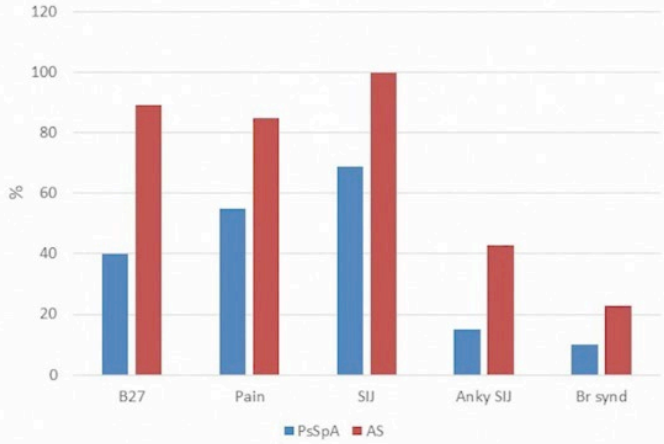


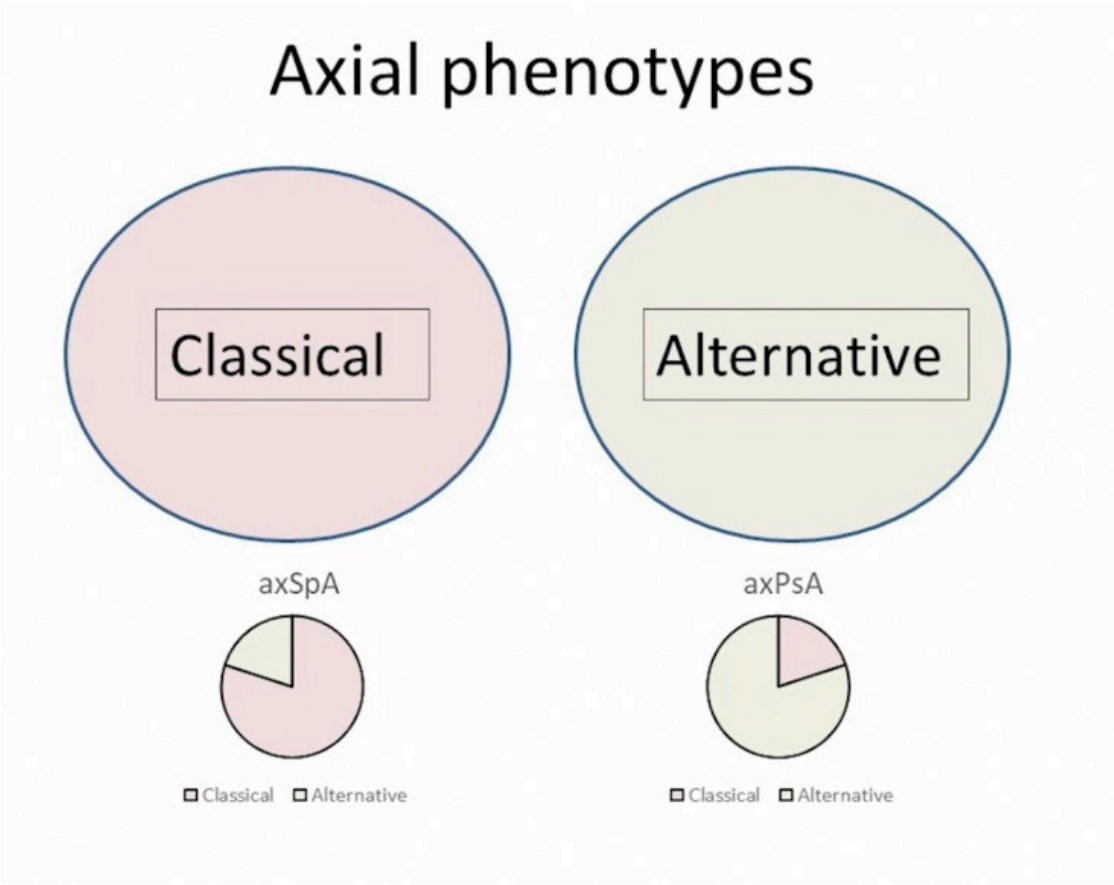
Table 1. Demographic details of the cohort, fulfillment of ASAS criteria, and radiographic damage scores*

	HLA-B27 positive (n = 208)	HLA-B27 negative (n = 234)	Difference between B27+ and B27– (continuous data) and odds ratios (categorical data)	*P*
Age, mean ± SD years	49.1 ± 14.2	53.8 ± 13.8	–4.7 (–7.4, –2.1)†	< 0.0001
Male	152 (73)	138 (59)	1.9 (1.3, 2.8)‡	0.002
Duration of disease, mean ± SD years	13.6 ± 11.9	11.0 ± 10.2	2.6 (0.5, 4.7)†	0.02
Fulfills clinical arm, ASAS criteria	68 (33)	0	NA	< 0.0001
Fulfills radiographic arm, ASAS criteria	177 (85)	149 (64)	3.3 (2.1, 5.2)‡	< 0.0001
mSASSS score, median (range)	6 (0–72)	2 (0–72)	0.5 (0–3)§	0.04
PASRI score, median (range)	12 (0–71)	6 (0–71)	5 (3–7)§	< 0.0001
BASDAI, mean ± SD	4.1 ± 2.0	3.5 ± 2.4	0.6 (0.2, 1.1)†	0.009

Coates LC,, et al. Arthritis Care & Research. 2021;73(6):856-60.

Zwei Phenotypen des axialen Befalls (Helliwell et al.)

80:20



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Das Vorhandensein des klassischen Phenotyps scheint mit der Prävalenz von HLA-B27 zu korrelieren

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RHEUMATOLOGIE & IMMUNOLOGIE

POS1078

Comparison of patients with axial PsA and patients with axSpA with concomitant psoriasis

Anne C Regierer[1], Anja Weiß[1], Xenofon Baraliakos[2], Frank Behrens[3], Denis Poddubnyy[4], Georg Schett[5], Hanns-Martin Lorenz[6], Matthias Worsch[7], Anja Strangfeld[1,4]
[1]German Rheumatism Research Centre Berlin (DRFZ), Epidemiology and Health Services Research, Berlin; [2]Rheumazentrum Ruhrgebiet, Herne; [3]Goethe University, Frankfurt, [4]Charité University Medicine Berlin, Department for Rheumatology and Clinical Immunology, [5]Rheumatology and Immunology, Universitätsklinikum Erlangen, [6]Division of Rheumatology, Dept. Med. V, University Hospital, Heidelberg, [7] Rheumatologist, Muehlhausen; all Germany

RABBIT SpA

RABBIT-SpA Register (ca 2800Pat) → **axPsA Definition in PsA Patienten**

- Clinical: axial manifestation by rheumatologist

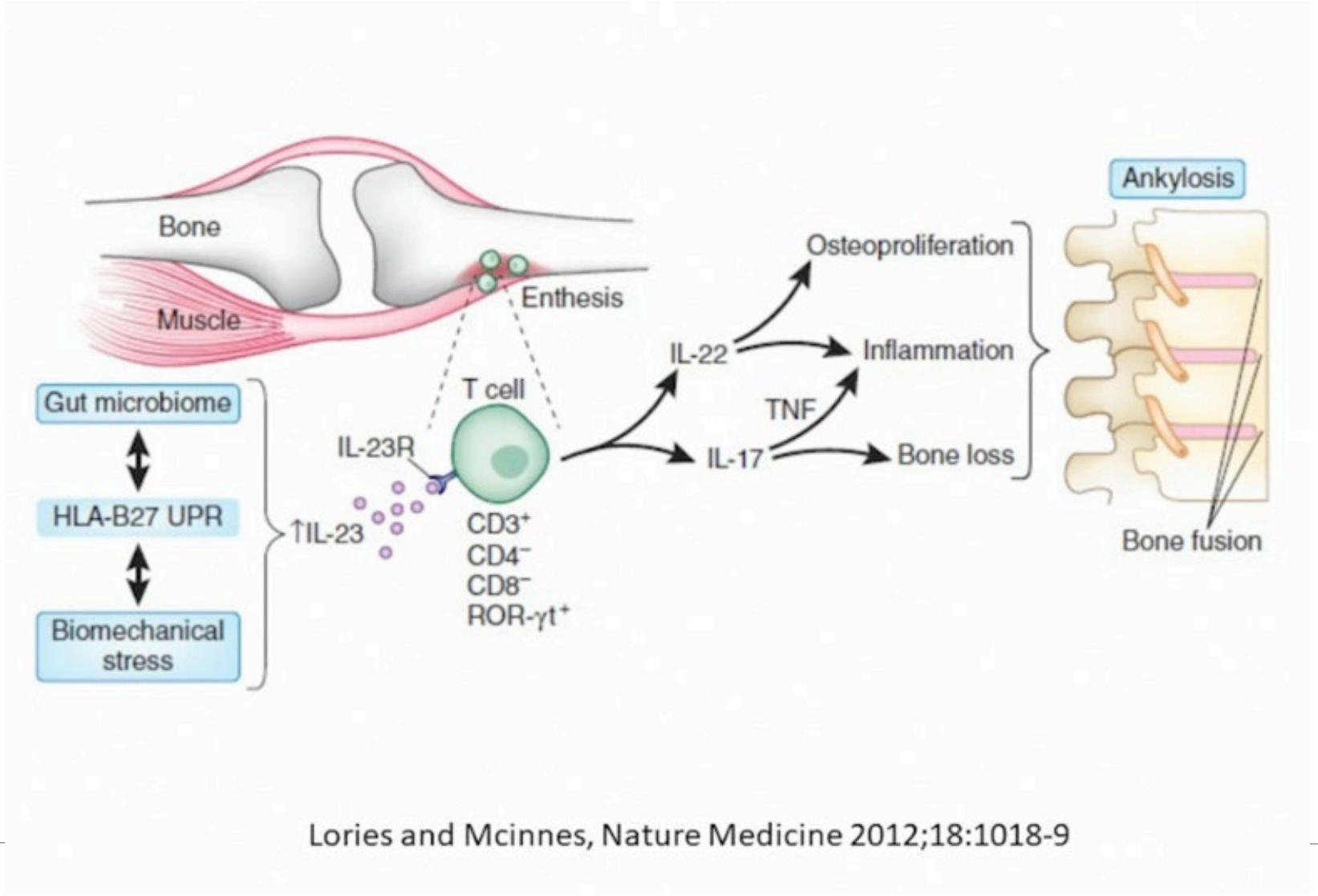
  AND/OR

- Radiographic: presence of sacroiliitis as of mNYc

Erfüllt in 295/1355 PsA Pat (22%)

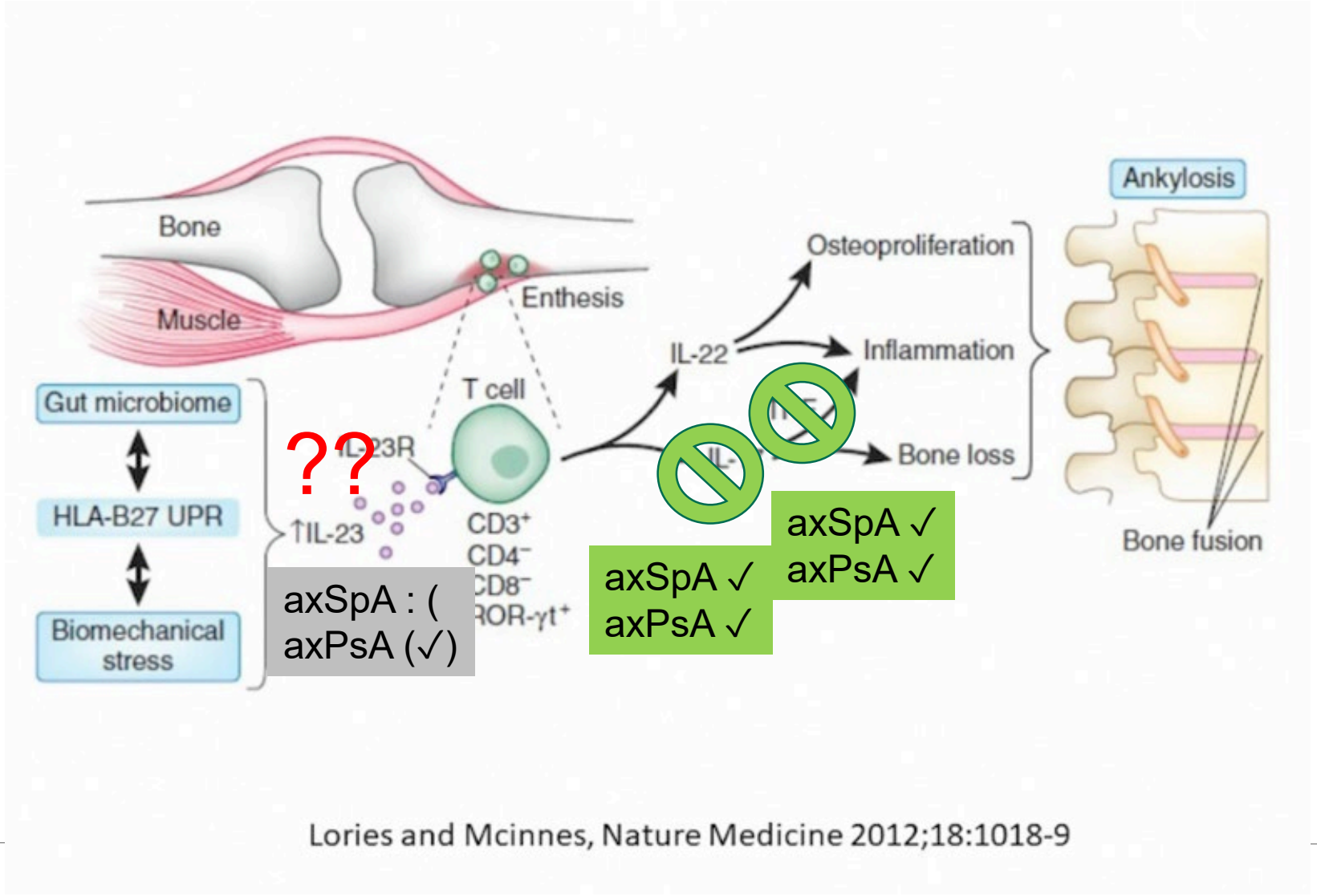
Ergebnisse	axSpA with PsO (n=182)	PsA with ax (clinical) (n=295)	PsA with ax (radiographic) (n=127)
Female gender, n (%)	80 (44)	178 (60)	80 (63)
Age, mean (SD)	47 (12.8)	51.1 (11.3) *	51.6 (11.4) *
HLA-B27 positive, n (%)	106 (67.1)	44 (23) *	28 (32.9) *
CRP mg/l, mean (SD)	9.9 (15.2)	8.5 (12.5)	6.9 (11.5)
CRP ≥5 mg/l, n (%)	70 (42)	106 (40) *	50 (45.9) *
Uveitis ever, n (%)	26 (14)	10 (3) *	7 (5.5) *
IBD ever, n (%)	13 (7)	14 (5) *	7 (5.5) *
Peripheral manifestations, n (%)	65 (36)	251 (85) *	109 (85.8) *
PhGA, mean (SD)	5.6 (2.1)	5.6 (1.9)	5.6 (2)
PtGA, mean (SD)	5.4 (2.6)	5.9 (2.3)	5.8 (2.2)
Pt: pain, mean (SD)	5.5 (2.6)	5.7 (2.3)	5.7 (2.2)

Pathomechanismen der axSpA



Lories and Mcinnes, Nature Medicine 2012;18:1018-9

Pathomechanismen axSpA versus axPsA



Lories and Mcinnes, Nature Medicine 2012;18:1018-9

POS0969

GENETIC AND MOLECULAR DISTINCTIONS BETWEEN AXIAL PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS

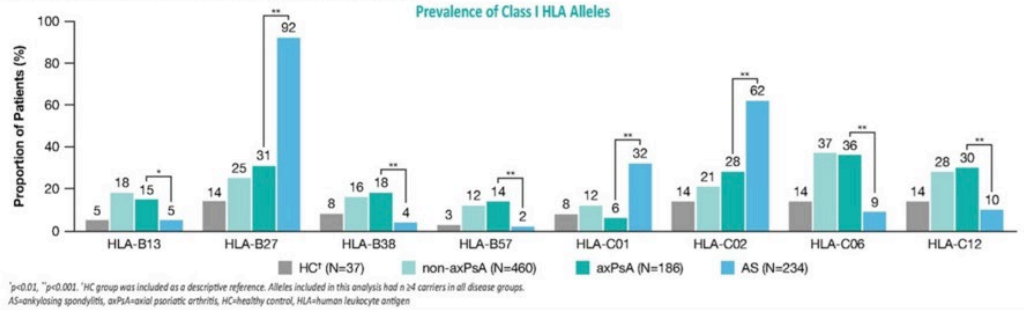
Arthur Kavanaugh[1*], Xenofon Baraliakos[2], Sheng Gao[3], Warner Chen[3], Kristen Sweet[3], Soumya D. Chakravarty[4,5], Qingxuan Song[3], May Shawi[6], Frank Behrens[7], Proton Rahman[8]

[1]University of California San Diego, San Diego, CA, USA; [2]Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Herne, Germany; [3]Janssen Research & Development, LLC, Spring House, PA, USA; [4]Janssen Scientific Affairs, LLC, Horsham, PA, USA; [5]Drexel University College of Medicine, Philadelphia, PA, USA; [6]Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson, Horsham, PA, USA; [7]Rheumatology and Fraunhofer ITMP - Translational Medicine and Pharmacology, Rheumatology, Goethe University, Frankfurt, Germany; [8]Memorial University of Newfoundland, St. John's, NL, Canada

*Presenting Author

Prevalence of class I HLA allele carriers differed significantly between axPsA and AS patients.

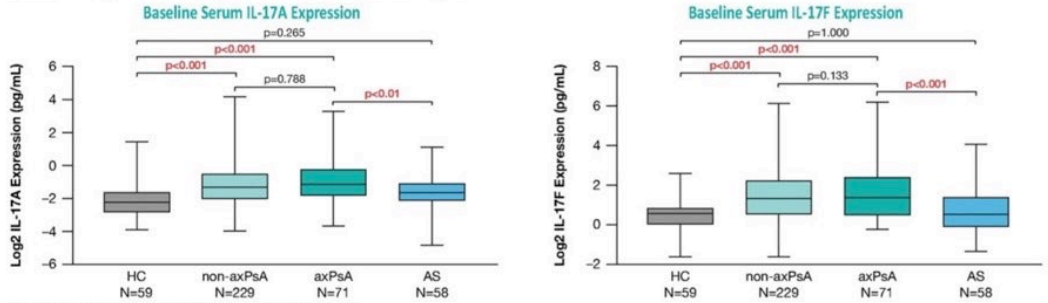
- Significantly fewer axPsA than AS patients were carriers of **HLA-B27 (30.7 vs 92.3%), -C01 (5.9 vs 31.6%), and -C02 (28.0 vs 62.0%)**, respectively
- Significantly more axPsA than AS patients were carriers of **HLA-B13 (15.1 vs 5.1%), -B38 (17.7 vs 4.3%), -B57 (14.0 vs 1.7%), -C06 (36.0 vs 8.6%),** and **-C12 (30.1 vs 9.8%)**, respectively
- Prevalence of HLA alleles was comparable between axPsA and non-axPsA cohorts



*p<0.01, **p<0.001. †HC group was included as a descriptive reference. Alleles included in this analysis had n ≥4 carriers in all disease groups.
AS=ankylosing spondylitis, axPsA=axial psoriatic arthritis, HC=healthy control, HLA=human leukocyte antigen

Baseline expression of IL-17A and IL-17F was significantly higher in axPsA vs AS patients.

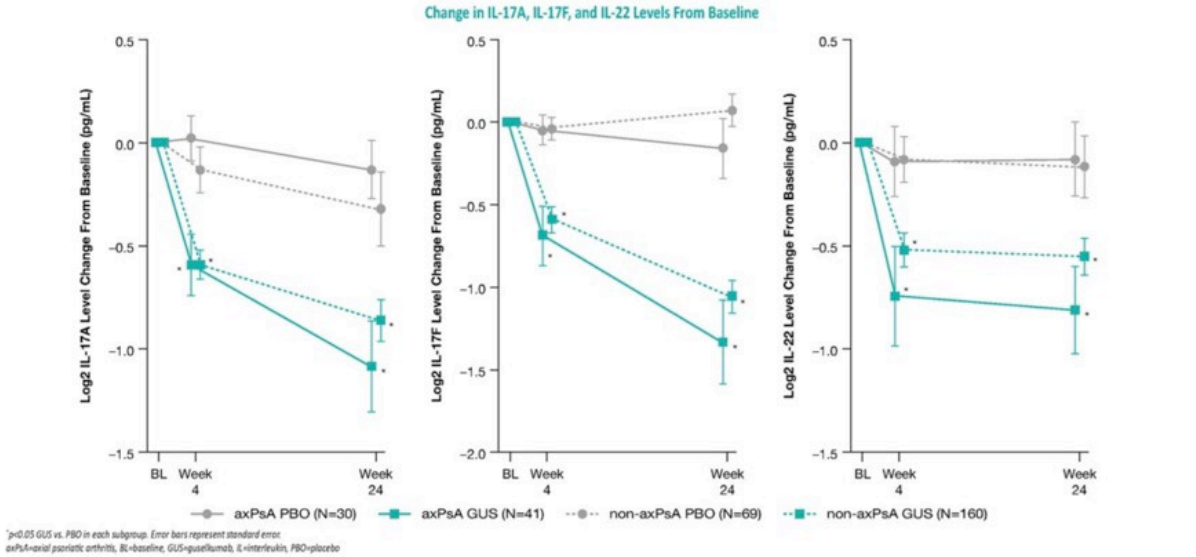
- Baseline IL-17A and -17F expression was comparable between non-axPsA vs axPsA patients



AS=ankylosing spondylitis, axPsA=axial psoriatic arthritis, HC=healthy control, IL=interleukin

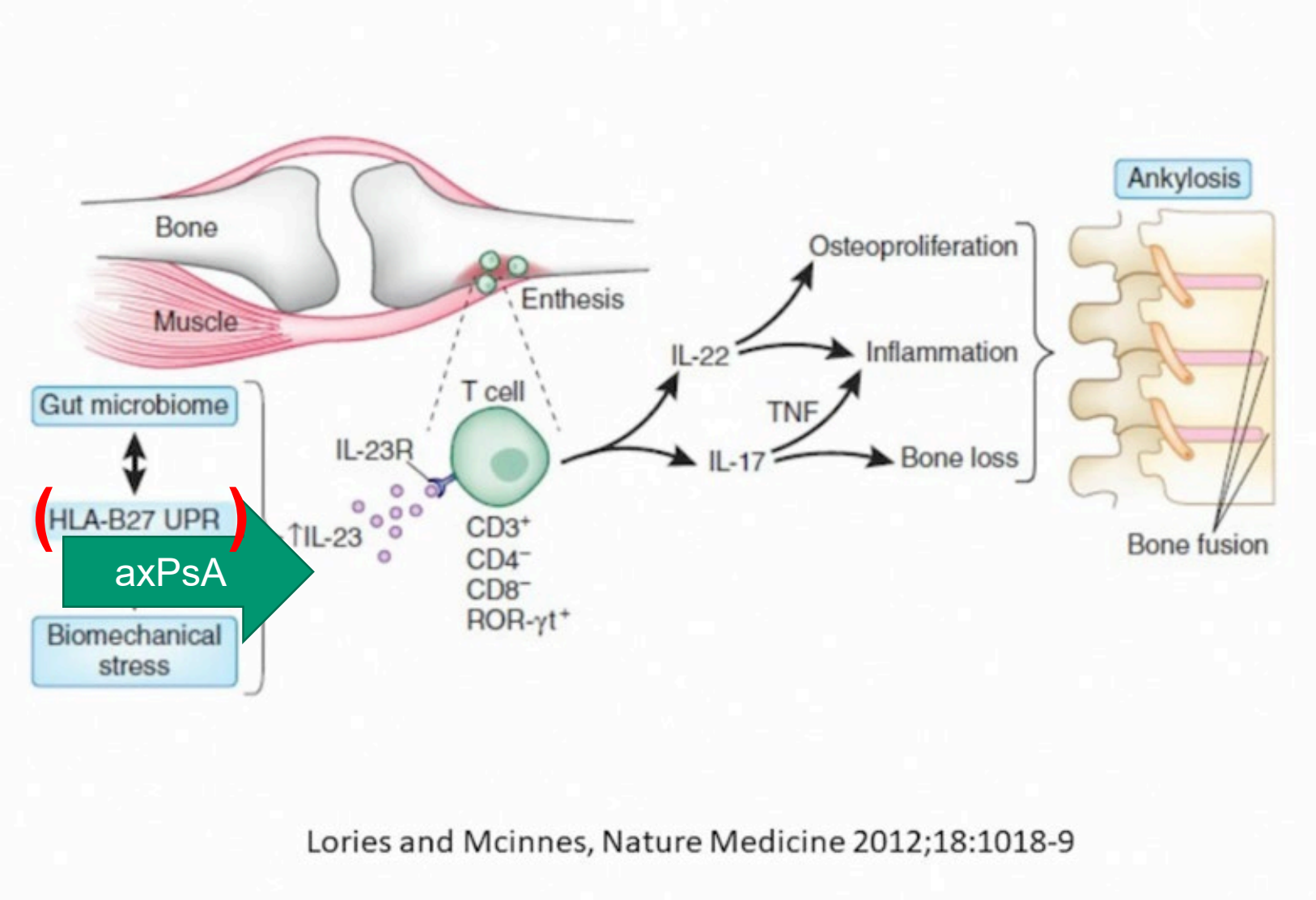
GUS treatment elicited significant reductions in serum IL-17A, IL-17F, and IL-22 levels in axPsA and non-axPsA patients vs PBO at both W4 and W24 (all p<0.05).

- Significant reductions in **IL-17A, IL-17F,** and **IL-22** were seen as early as **W4**, with continued normalization toward expression levels seen in **HC through W24**

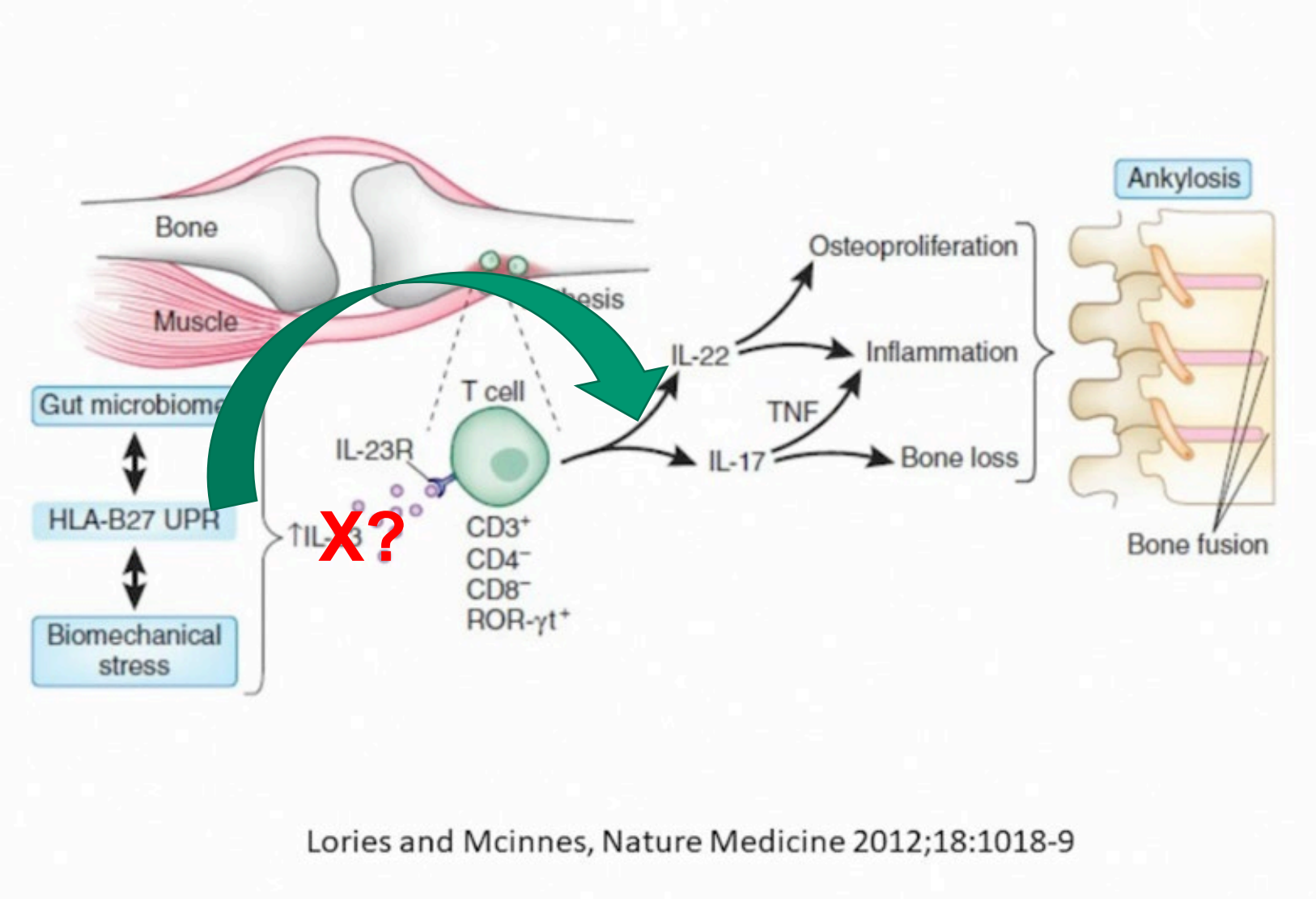


*p<0.05 GUS vs. PBO in each subgroup. Error bars represent standard error.
axPsA=axial psoriatic arthritis, BL=baseline, GUS=guselkumab, IL=interleukin, PBO=placebo

Hypothese axPsA



Hypothese axSpA




EUROSPA

Abstract #OP0020

Sex differences in the effectiveness of first-line tumor necrosis factor inhibitors in axial spondyloarthritis; results from the EuroSpA Research Collaboration Network

Presenting author: Pasoon Hellamand, MD

EULAR, 01-06-2022

P. Hellamand[1], M.G.H. van de Sande[1], L.M. Ørnbjerg[1], T. Klausch[1], D. Nordström[1], K. Eklund[1], N. Trokovic[1], A. Hokkanen[1], E. Sousa[1], A. G. Loft[1], B. Glintborg[1], M. L. Hetland[1], U. Lindström[1], J.K. Wallman[1], B. Michelsen[1], A. Ciurea[1], M. Nissen[1], M. T. Nurmohamed[1], R. F. van Vollenhoven[1], C. Codreanu[1], C. Mogosan[1], G. J. Macfarlane[1], G. T. Jones[1], K. Laas[1], Z. Rotar[1], M. Tomsic[1], I. Castrejon[1], M. Pombo-Suarez[1], B. Gudbjornsson[1], A.J. Geirsson[1], E.K. Kristianslund[1], J. Vencovský[1], L. Nekvindová[1], M. Østergaard[1], I.E. van der Horst – Bruinsma[1].

- Ca 75% der AS Patienten in Studien sind männlich
- Neuere axSpa Epidemiologie zeigt mehr Richtung 50:50 Verhältnis in real world
- Unterschiedliches Schmerzempfinden/Wahrnehmung zwischen Männern und Frauen?
- Evidenz für geringere Effektivität von TNFi in Frauen

EuroSpA Register: 28608 Patienten, 15 Länder, 1999-2013

- Biologika-naive Patienten, CII nach 6 Monaten
- ASDAS-CRP und TNFi survival

Basischarakteristika

Characteristics	Female (n=2538)	Male (n=3913)
Age mean (SD)	42 (12.1)	41.4 (12.3)
HLA-B27+ (%)	72	83
TNFi start year (%)		
Start 1999-2008	4.5	7.1
Start 2009-2014	40	41
Start 2015-2020	56	52
ASDAS mean (SD)	3.5 (0.9)	3.5 (1.0)
CRP median (IQR)	6.7 (2.5 to 16)	12 (4.0 to 25)
BASDAI mean (SD)	59 (20)	54 (21)
VAS pain mean (SD)	63 (22)	59 (24)

Table 1. Excerpt of Baseline Table.

Männer versus Frauen

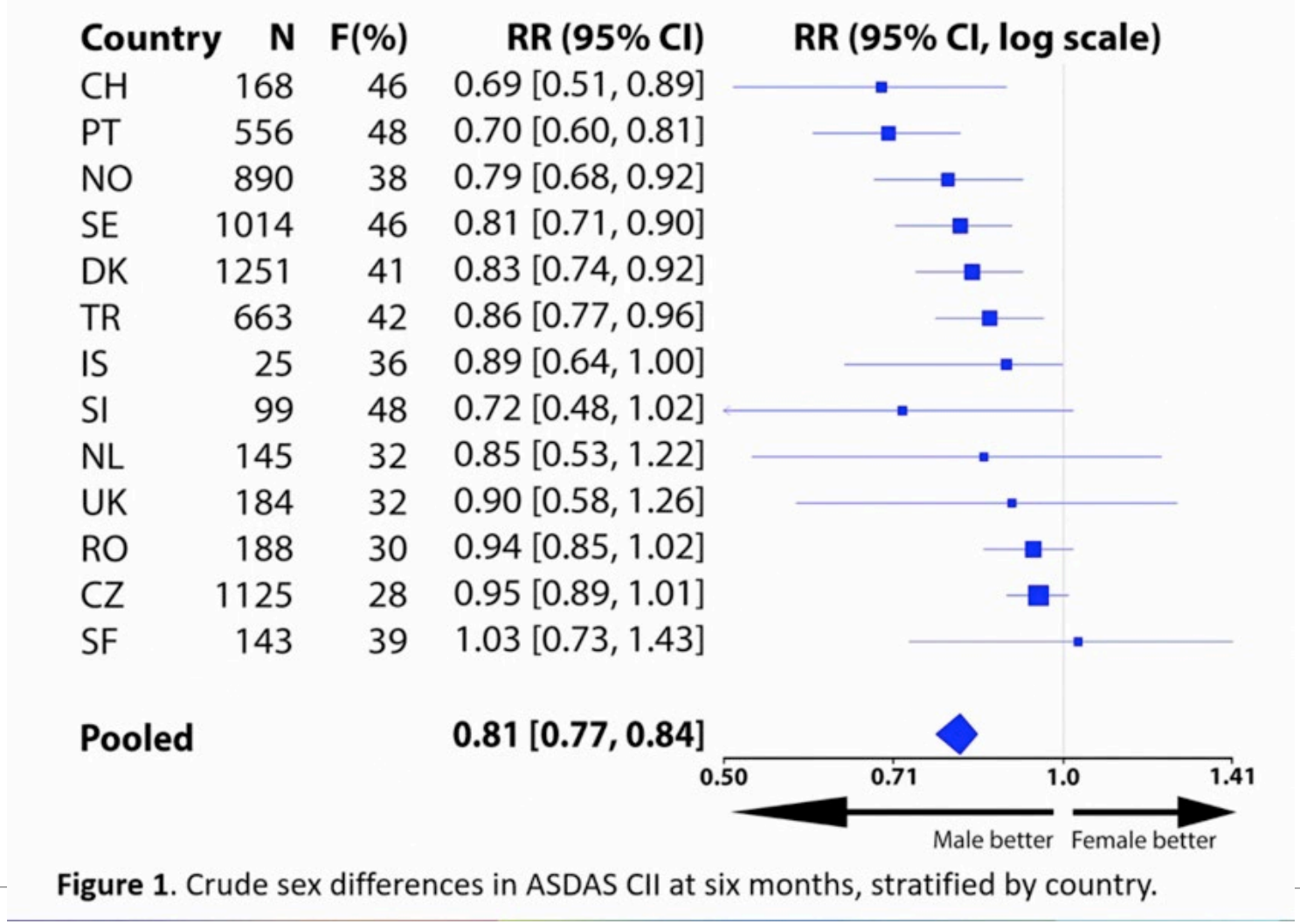


Figure 1. Crude sex differences in ASDAS CII at six months, stratified by country.

TNFi survival

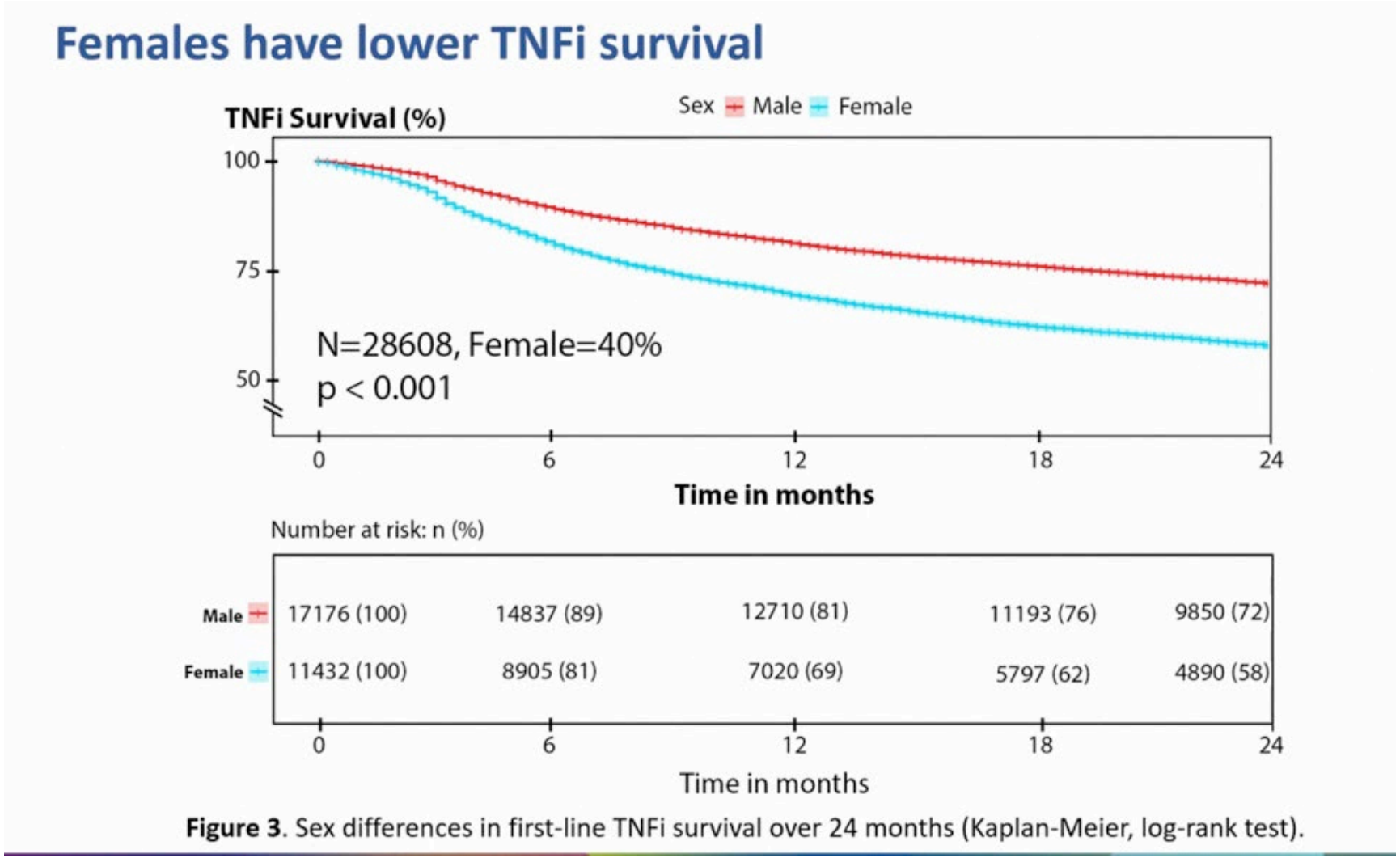


Figure 3. Sex differences in first-line TNFi survival over 24 months (Kaplan-Meier, log-rank test).

TNFi survival pro Land

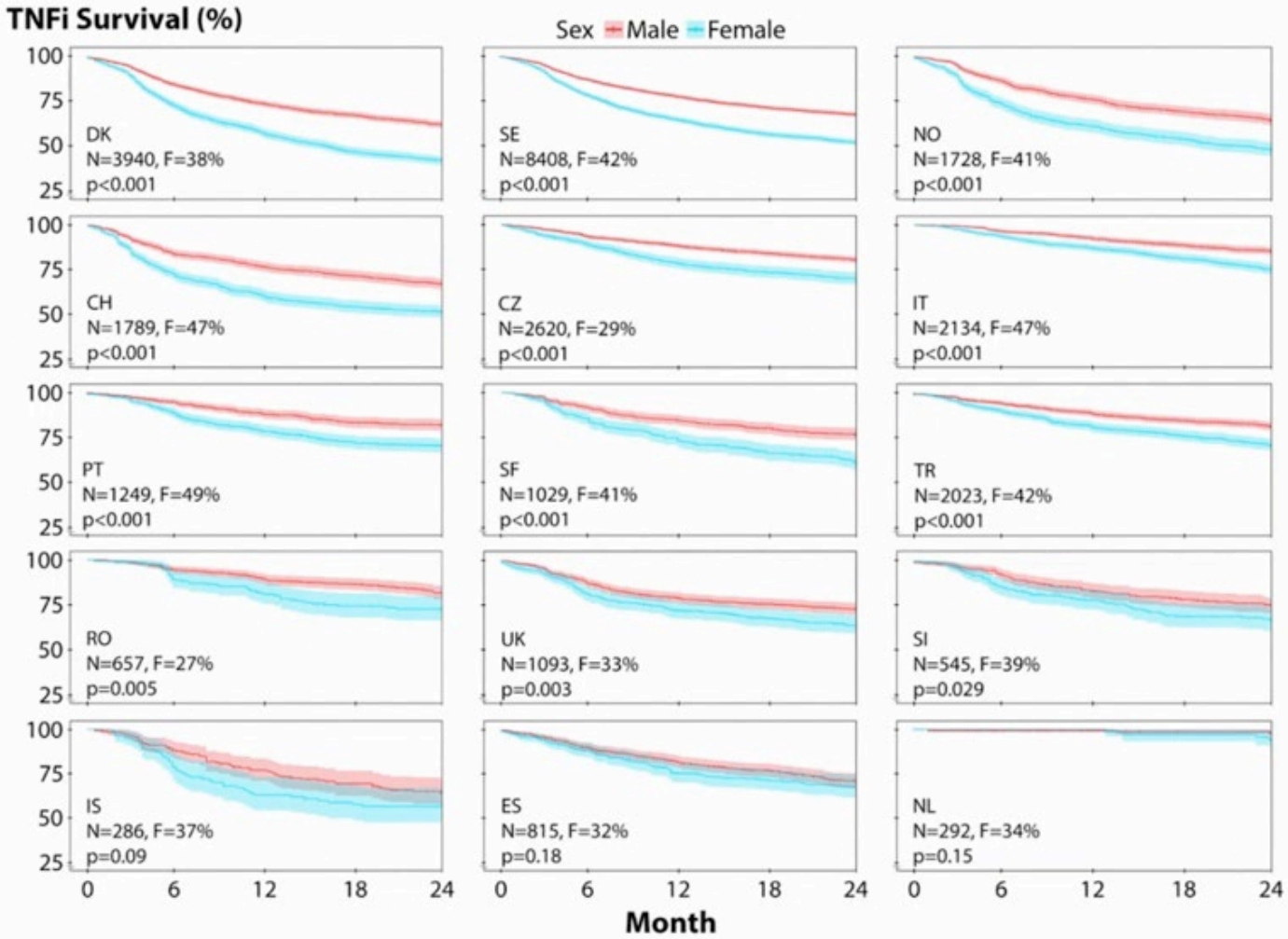


Figure 4. Sex differences in first-line TNFi survival over 24 months, stratified per country.

Schlussfolgerungen

- Bestätigt vorhergehende Studien in AS und nr-axSpA hinsichtlich schlechterem Ansprechen von Frauen

- Unterschiede zwischen den Ländern werden noch analysiert
  - Regionale Guideline Unterschiede...?
  - Einige Länder hatten im Jahr 2000 Zugang zu iTNF, andere erst 2013...?

- Andere Ideen für „Spitzenposition" der  ?

Disease activity-guided tapering of biologics in patients with inflammatory arthritis:
A randomised, open-label, equivalence trial
The BIODOPT Trial

Line Uhrenholt[1,2,3], Robin Christensen[3,4], Lene Dreyer[1,2], Ellen-Margrethe Hauge[5,6], Annette Schlemmer[1,6,7], Anne Gitte Loft[5,6], Mads Nyhuus Bendix Rasch[5], Hans Christian Horn[8], Katrine Hindborg Gade[1,8], René Østgård[9], Peter C. Taylor[10], Salome Kristensen[1,2]

- Metaanalysen zeigen, dass in RA und axSpA, dass Absetzen von DMARD versus tapering hat höheres Schubrisiko

→ Krankheits-Aktivität gesteuertes Tapering möglich?

Background

RHEUMATOLOGY
Rheumatology 2021;00:1–16
https://doi.org/10.1093/rheumatology/keab902
Advance access publication 3 December 2021

Systematic review and meta analysis

Risk of flare after tapering or withdrawal of biologic/ targeted synthetic disease-modifying anti-rheumatic drugs in patients with rheumatoid arthritis or axial spondyloarthritis: a systematic review and meta-analysis

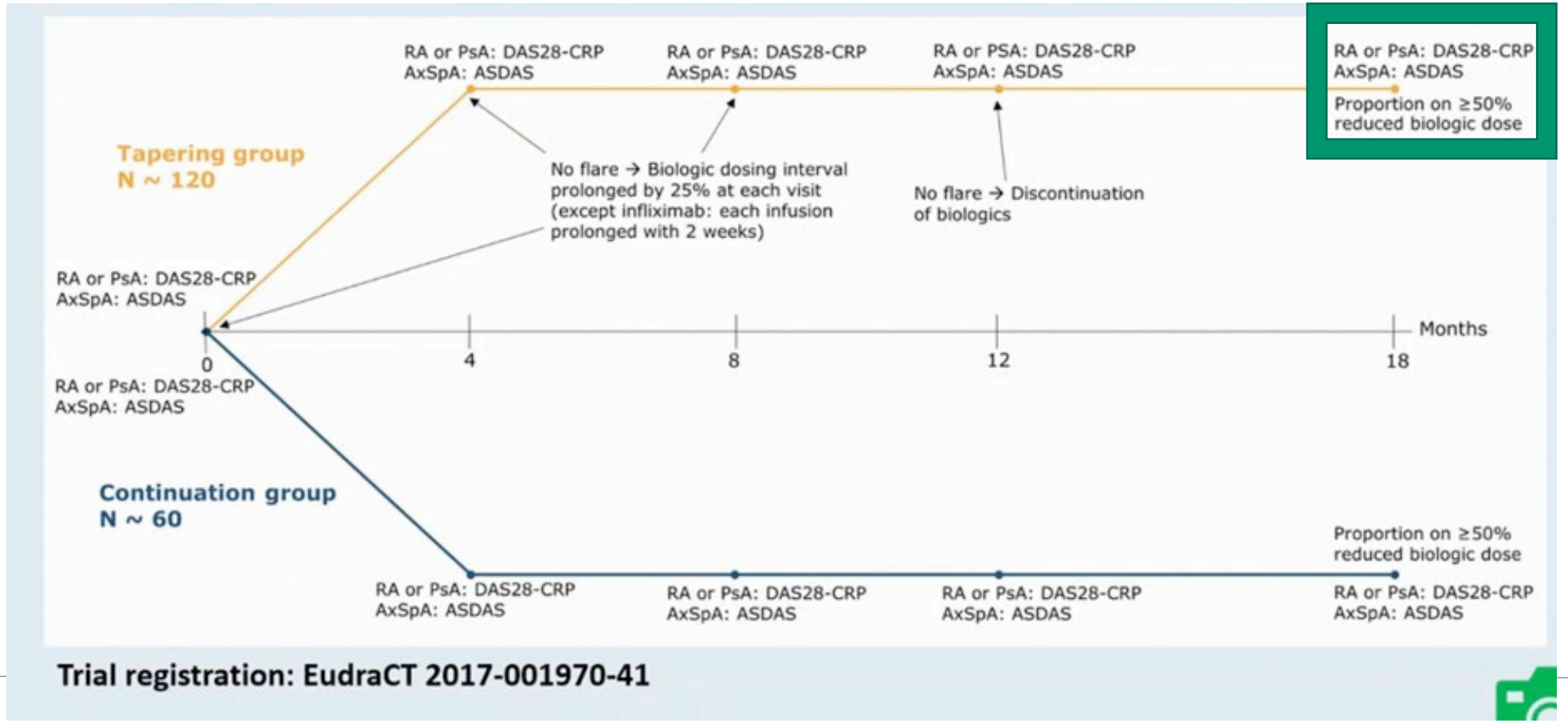
Line Uhrenholt [1,2,3], Robin Christensen[3,4], Wilfred K.H. Dinesen[2], Caroline H. Liboriussen[2], Stine S. Andersen[2], Lene Dreyer[1,2], Annette Schlemmer[1,5], Ellen-Margrethe Hauge[6,7], Conni Skrubbeltrang[8], Peter C. Taylor [9] and Salome Kristensen[1,2]

Outcome (N studies)	Withdrawal group n/N (%)	Tapering group n/N (%)	Odds ratio (95%CI)
Flare (22 studies)	830/1,500 (55.3%)	431/1,319 (32.7%)	5.62 (3.44 to 9.17)
Persistent flare (11 studies)	108/707 (15.3%)	50/1,035 (4.8%)	3.16 (1.49 to 6.67)

N: total number, n: number of patients with event, 95%CI: 95% confidence interval, NNT: number needed to treat.

BIODOPT Design

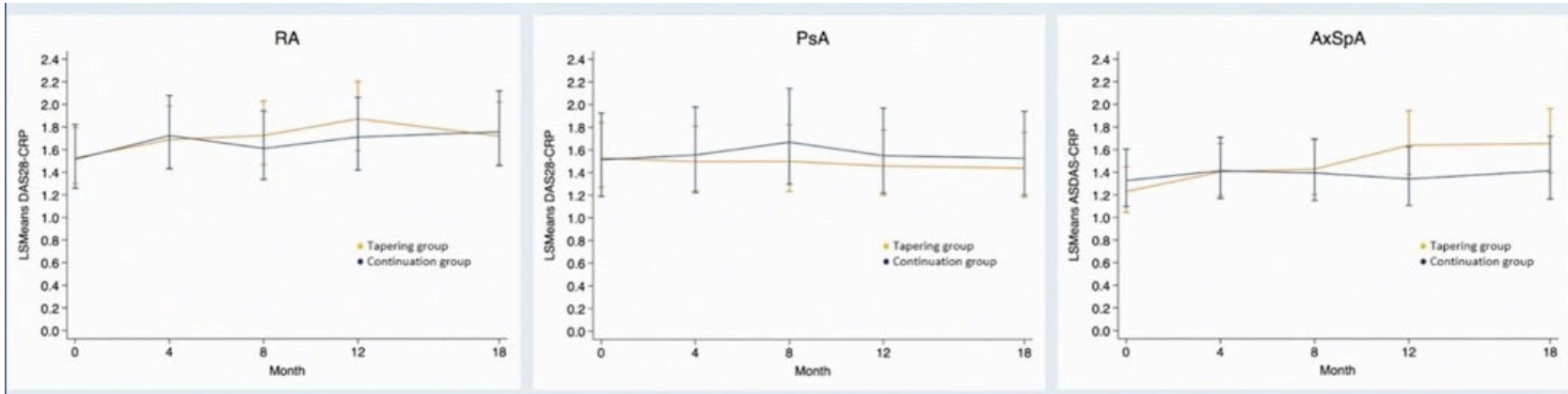
- Drei Erkrankungen: RA, PsA, axSpA mit LDA ≥ 12 Monate
- Über 18 Monate: Tapering um 25% alle 4 Monate bis zum Schub oder vollständigem Absetzen (ab Monat 12)



Baselinecharakteristika

	Tapering group, N = 95	Continuation group, N = 47
Female, n (%)	52 (55%)	20 (43%)
Age (years), mean (SD)	51.9 (15.4)	52.3 (15.9)
Diagnosis:		
RA, n (%)	41 (43%)	20 (43%)
PsA, n (%)	18 (19%)	8 (17%)
AxSpA, n (%)	36 (38%)	19 (40%)
Disease duration (years), median (IQR)	11.3 (6.3;17.9)	12.4 (6.4;19.9)
In remission, n (%)	82 (86%)	40 (85%)
On csDMARDs, n (%)	41 (43%)	22 (47%)
Current biological therapy:		
TNF-α inhibitor, n (%)	88 (93%)	41 (87%)
IL-6 inhibitor, n (%)	6 (6%)	3 (6%)
T-cell co-stimulation blocker, n (%)	1 (1%)	3 (6%)

Resultate



Outcome	Tapering group N = 95	Continuation group N = 47	Group difference (95%CI)	p-value
Primary outcome				
Biologic dose reduced ≥50%, n (%)	35 (37%)	1 (2%)	35% (24% to 45%)	<0.001
Disease activity, LSMeans (SE)	1.84 (0.15)	1.75 (0.16)	0.08 (-0.12 to 0.29)	0.428
Key secondary outcomes				
Remission[1], n (%)	63 (66%)	33 (70%)	-4% (-20% to 12%)	0.637
Low disease activity[2], n (%)	79 (83%)	41 (87%)	-4% (-16% to 8%)	0.511

N: number, CI: confidence interval, LSMeans: Least squares means, SE: Standard error.
[1]: RA or PsA: DAS28-CRP <2.6. AxSpA: ASDAS <1.3.
[2]: RA or PsA: DAS28-CRP ≤3.2. AxSpA: ASDAS <2.1.

	Tapering group N = 95	Continuation group N = 47	Risk difference[1] (95% CI)
Total flares:	77/95 (81%)	16/47 (34%)	47% (31% to 63%)
Fulfil flare criteria, n/N (%)	39/95 (41%)	10/47 (21%)	20% (4% to 35%)
Symptoms of flare, n/N (%)	38/95 (40%)	6/47 (13%)	27% (14% to 41%)
Rescue therapy due to flare:			
Biologic dose escalation, n/N (%)	66/77 (86%)	6/16 (38%)	..
Glucocorticoid treatment[2], n/N (%)	24/77 (31%)	10/16 (63%)	..
NSAIDs, n/N (%)	23/77 (30%)	8/16 (44%)	..
Biologic switch due to flare, n/N (%)	1/95 (1%)	3/47 (6%)	-5% (-13% to 2%)

Schlussfolgerungen

- Tapern erlaubt Reduktion der Biologika ≥ 50% über 18 Monate über verschiedene Indikationen in ca. jedem dritten Patienten

- Volle Studiengrösse wurde nicht erreicht
- DAS28:CRP nicht für PsA validiert

- Subanalysen abwarten:
  - Wieviele Patienten konnten Biologikum komplett absetzen?
  - Wieviele Patienten im Tapering Arm mit Sekundärversagen
  - Wie identifiziere ich den richtigen „dritten Patienten“?

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Vielen Dank für die Aufmerksamkeit.

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