



Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): An international collaboration

Prof. Philip Helliwell
Co-chair Education, GRAPPA

Disclosures

- Received speaker fees from Novartis
- Served on advisory panel for Amgen

GRAPPA Membership 71 Countries

MEMBER TYPE	NORTH AMERICA	NON NORTH AMERICA	TOTAL
Dermatologist	120	194	314
Rheumatologist	183	515	698
Geneticist	6	5	11
Methodologist	3	11	14
Radiologist	2	5	7
Other/Scientist	39	79	118
GRAPPA PRP	5	7	12
TOTAL	358	816	1,174
EARLY CAREER MEMBERS	220	FULL GRAPPA MEMBERS	954
		TOTAL	1,174

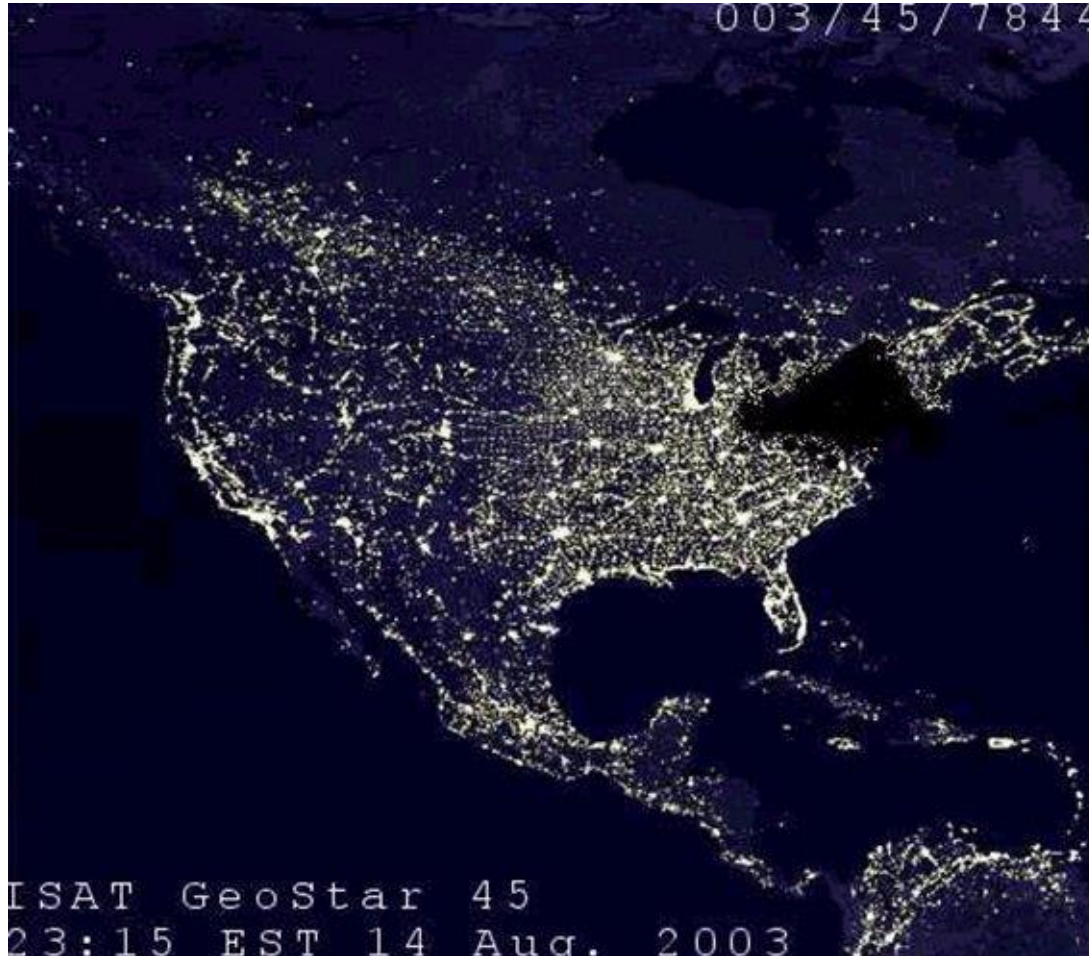
GRAPPA Achievements – 20 years

- How did GRAPPA start?
- GRAPPA Mission
- What have we achieved?
 - Annual meetings since 2003
 - Outcome measures 2005, 2007, 2015
 - Treatments recommendations 2009, 2015, 2021
 - Educational programs
 - Young GRAPPA

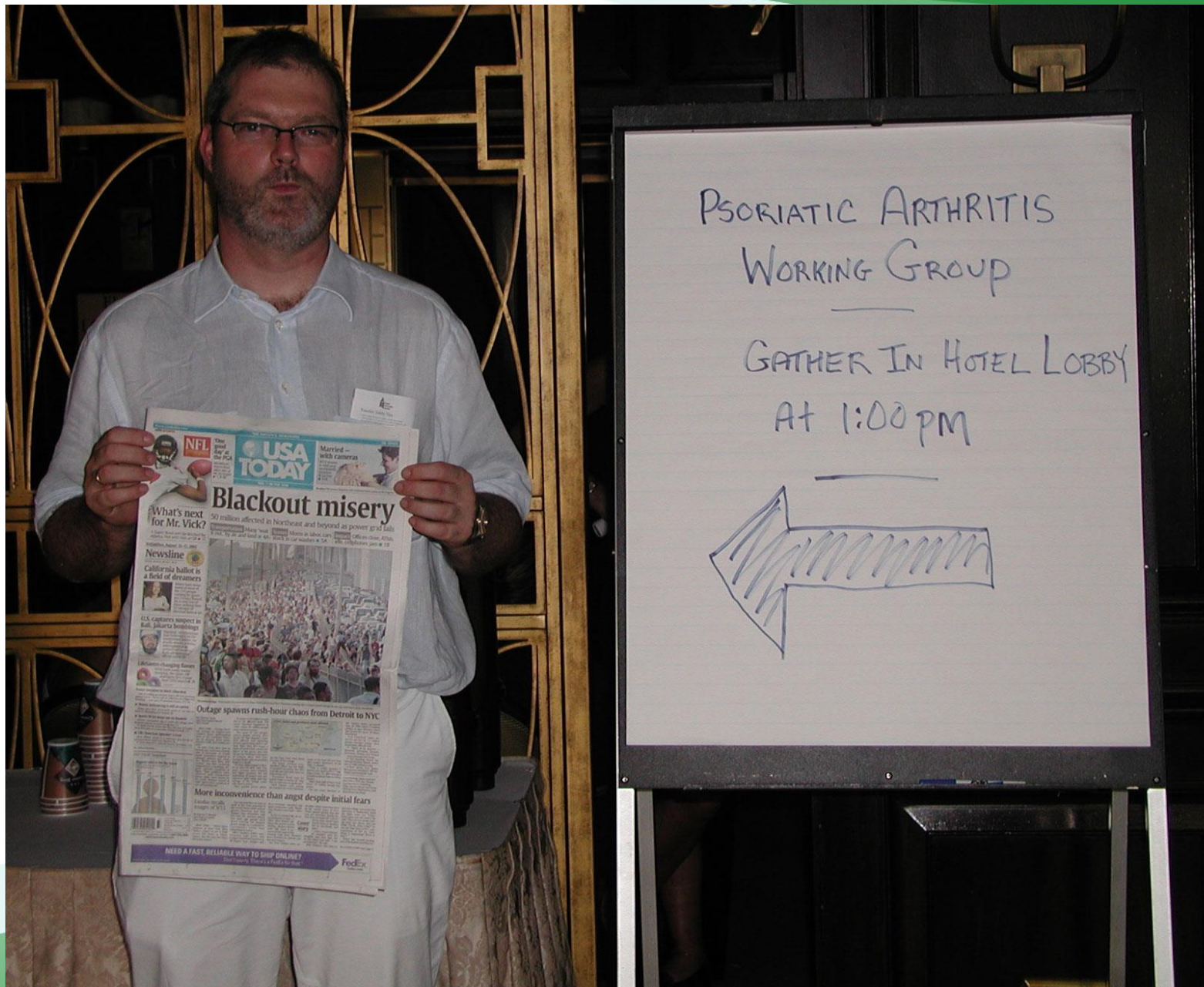


Where did GRAPPA emerge from?

- CASPAR criteria for classification, 1999
- 32 'expert' centres worldwide
- 590 patients with psoriatic arthritis
- 580 controls
- CASPAR criteria widely accepted and referenced (over 500 citations, 2013)
- To maintain collaboration, and model on ASAS, it was decided to form a new psoriatic arthritis and psoriasis focussed research group



Satellite image of North America on the evening of 14th August 2003





GRAPPA's Mission

GRAPPA is organized exclusively for non-profit, educational, and scientific purposes, specifically to facilitate sharing of information related to psoriasis and psoriatic arthritis, networking among different medical disciplines that see psoriasis and psoriatic arthritis patients, and to enhance research, diagnosis and treatment of psoriasis and psoriatic arthritis.



GRAPPA meetings

- Adjacent to the major rheumatology and dermatology meetings
 - EADV, AAD
 - ACR, EULAR
- An annual standalone meeting

GRAPPA – major projects

- CASPAR
- GRAPPA-OMERACT project on outcome measures in PsA
- GRACE project
- Treatment recommendations: 2015 and 2022
- Education
 - Combined dermatology/rheumatology meetings
 - Slide collection
 - App
 - Training videos
- GRAPPA-industry projects
- Collaborative Research Network (CRN)
 - Innovative Medicines Initiative (IMI) consortium HIPPOCRATES
 - Accelerating Medicines Partnership (AMP) – autoimmune and immune-mediated diseases: ELLIPSS consortium

Research Projects



COMPOSITION

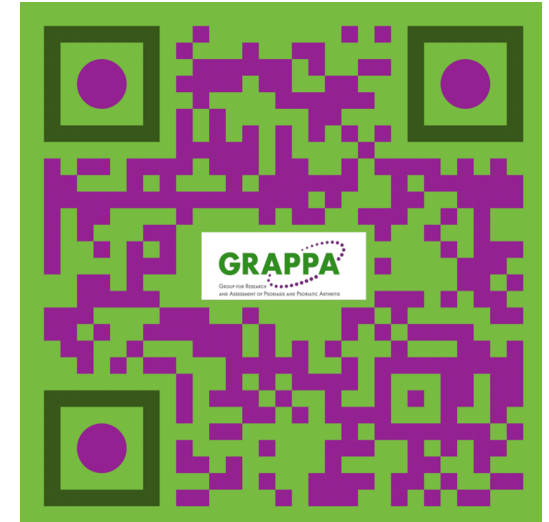
D2T/C2M

AXIAL PSA
MOLECULAR
STUDY



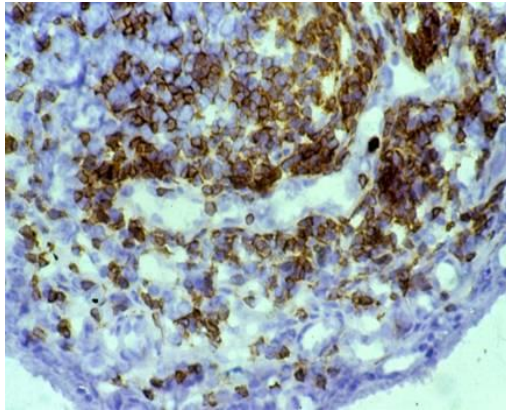
Educational Activities

- SPARTAN- GRAPPA
- NPF - GRAPPA
- GRAPPA Videos and GRAPPA slide library
- Training in joint and skin assessment
- European Educational Programs
- Individual Country Education – GRAPPA standalone meetings
- Patient Education

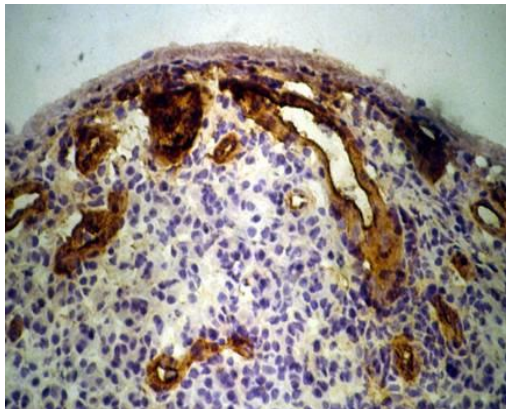


Synovial Immunopathology in PsA

CD4



FVIII



Mean no of cells/mm ² (SE)			
	PsA (15)	RA (15)	P-value
CD3	567.22 (151.12)	521.87 (94.33)	
CD8	186.72 (57.24)	250.78 (54.85)	
CD4	385.05 (101.16)	390.73 (47.57)	
CD45RO	432.04 (85.96)	306.11 (56.13)	
B cells	158.42 (34.72)	114.55 (43.27)	
MØ	169.40 (34.72)	358.91 (56.13)	<0.02
Vascularity (No. of vessels/mm ²)	244.82 (20.70)	131.90 (16.50)	<0.001
Lining layer mean cell depth (range)	3.56 (2–10)	9.02 (3–32)	<0.01

Patient Research Partners

- Developed through OMERACT work
- Initially few, now 12
- PRPs are assigned to each project
- PRPs contribute to publications



Niti Goel



Maarten DeWit



Young GRAPPA

- Get younger rheumatologists and dermatologists more engaged with GRAPPA
- Provide young rheumatologists and dermatologists mentorship
- Provide opportunities for young rheumatologists and dermatologists to collaborate in research



GRAPPA treatment recommendations 2022

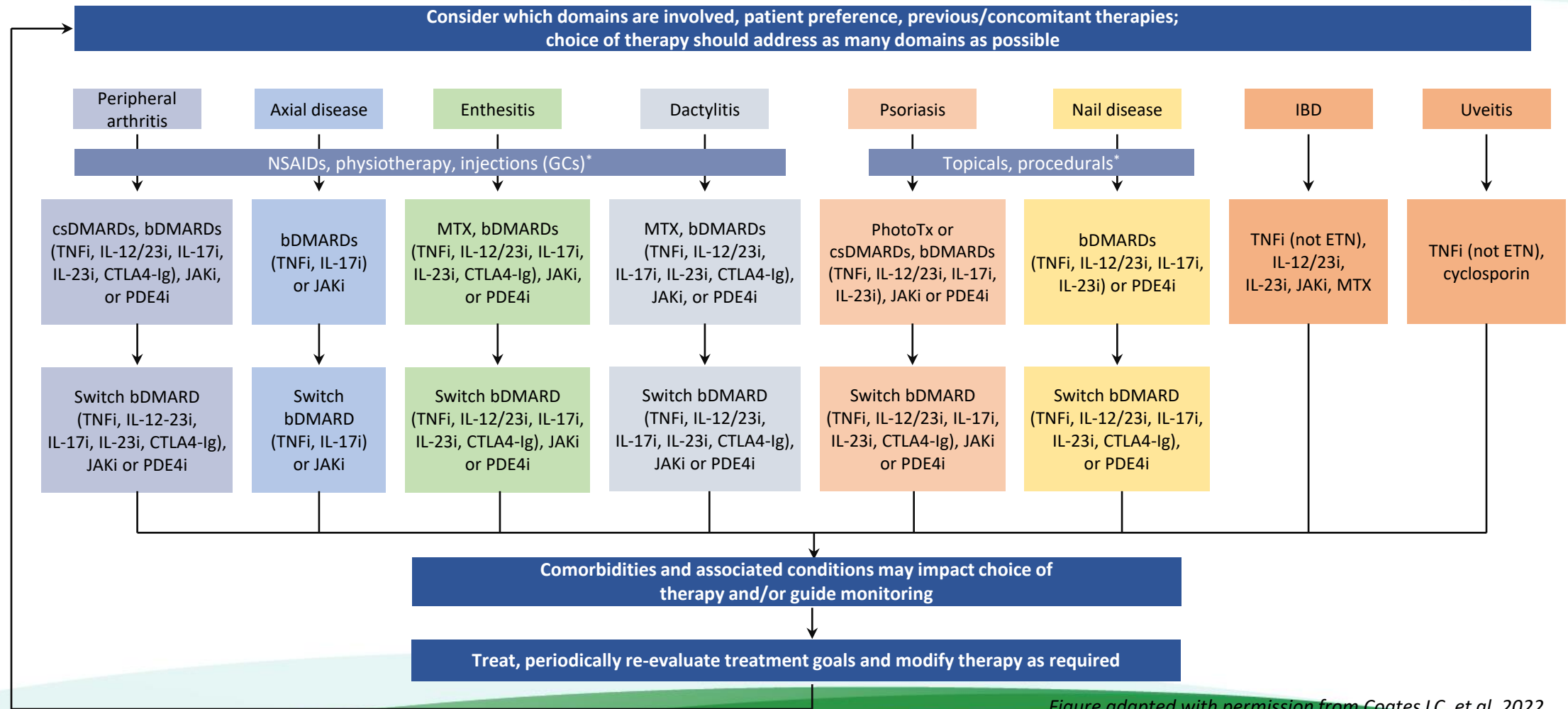


Figure adapted with permission from Coates LC, et al. 2022.

*Conditional recommendation based on data from abstracts only.

bDMARD, biological disease-modifying anti-rheumatic drug; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; CTLA4-Ig, cytotoxic T lymphocyte-associated antigen 4-Ig; ETN, etanercept; GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; GC, glucocorticoid; IBD, inflammatory bowel disease; IL, interleukin; JAKi, Janus kinase inhibitor; MTX, methotrexate; NSAID, non-steroidal anti-inflammatory drug; PDE4i, phosphodiesterase 4 inhibitor; photoTx, phototherapy; TNFi, tumour necrosis factor inhibitor.

Coates LC, et al. *Nature Reviews Rheumatology* 2022; 18: 465–479.



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The GRAPPA app: What does it include?

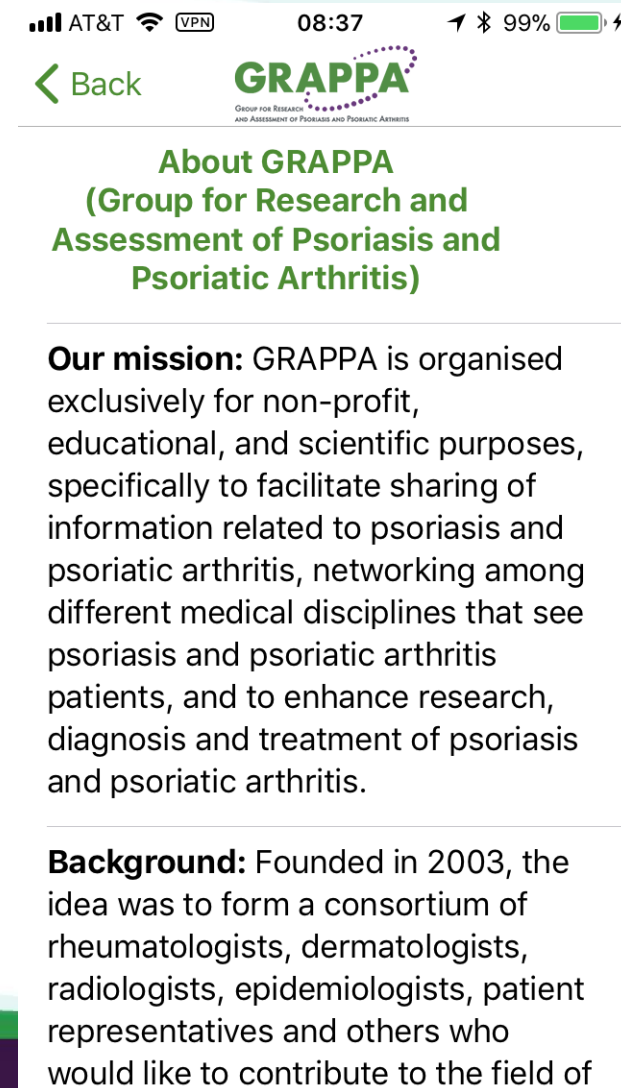
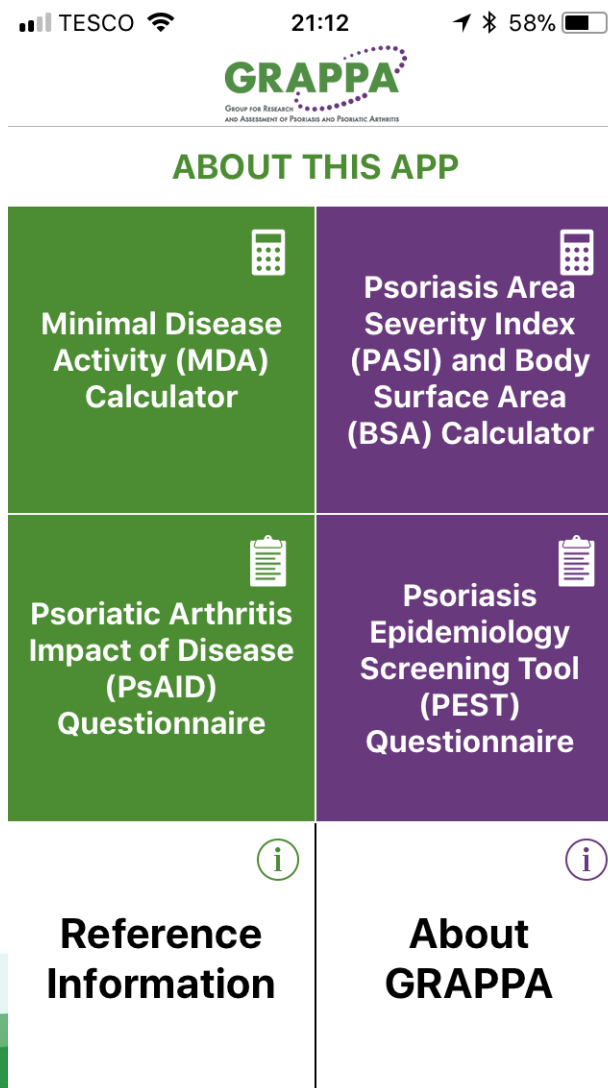
- ✓ About GRAPPA (*including website link and how to join*)
- ✓ VLDA/MDA treat-to-target calculator
- ✓ PsAID-12



- ✓ PASI/BSA calculator
- ✓ Screening questionnaire for dermatologists
- ✓ Key slides from GRAPPA slide set



Format of the app will be modular, allowing additions at a later date



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BSA, body surface area; GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; MDA, minimal disease activity; PASI, Psoriasis Area and Severity Index; PEST, Psoriasis Epidemiology Screening Tool;

PsAID, Psoriatic Arthritis Impact of Disease.

GRAPPA – a year in review

- HIPPOCRATES
- AXIS
- AGM – Dublin
- EDUCATION
- GOVERNANCE
- FUTURE

HIPPOCRATES background and objectives

Background:

- Psoriatic disease: Complex, polygenic autoimmune disease with diverse clinical features
- Current main therapies for PsA (anti-TNF, anti-IL-17) improve outcomes, but treatment gaps remain



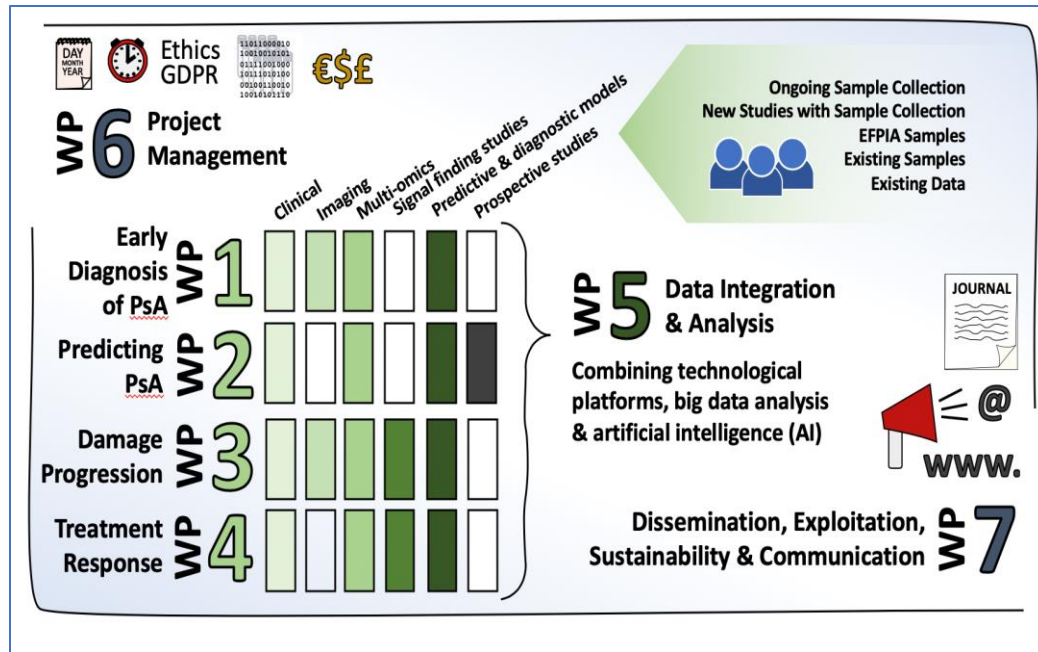
Objectives of HIPPOCRATES:

- Identification of **patients with psoriasis at risk of progression to PsA**
- Early **diagnosis of PsA**
- Identification of patients with PsA likely to experience **damage progression**
- Developing **precision medicine approaches** to treat PsA patient endotypes



To improve long-term outcomes for patients with psoriatic arthritis

Overview of the work packages and setup, enabling AI approaches from multiple cohorts to identify endotypes and respective biomarkers^{1,2}



- Collating data and biosamples from multiple cohorts to identify and validate biomarkers for PsA diagnosis, risk of developing PsA and of damage progression, as well as prediction of treatment response
- Using machine learning on real-world routinely collected data sets and RCTs from across Europe and via GRAPPA to identify predictive algorithms based on clinical data

Clinical phenotype

+

Imaging phenotype

+

Molecular phenotype

Endotype xyz

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AI, artificial intelligence; EFPIA, European Federation of Pharmaceutical Industries and Associations; GDPR, General Data Protection Regulation; GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; PsA, psoriatic arthritis; RCT, randomised controlled trial; WP, work packages.

1. HIPPOCRATES. Work Packages. Available at: <https://www.hippocrates-imi.eu/research/work-packages>. Last accessed: February 2023; 2. HIPPOCRATES. Impact. Available at: <https://www.hippocrates-imi.eu/impact>. Last accessed: February 2023.

Development of a Consensus Definition of Axial Involvement in Psoriatic Arthritis:

a joined ASAS – GRAPPA initiative



Do the radiological changes of classic ankylosing spondylitis differ from the changes found in the spondylitis associated with inflammatory bowel disease, psoriasis, and reactive arthritis?

P S Helliwell, P Hickling, V Wright*

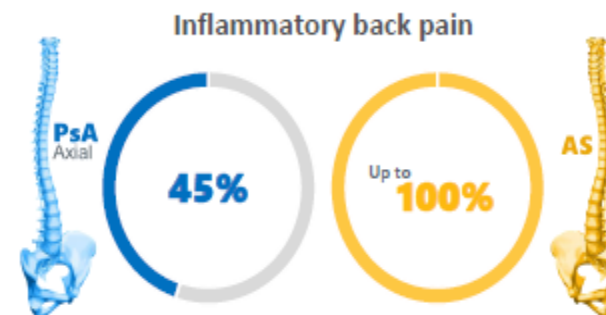
Table 1 Summary of radiological differences reported by McEwen et al⁶

<i>Feature</i>	<i>Ankylosing spondylitis and spondylitis of ulcerative colitis and regional enteritis</i>	<i>Spondylitis associated with psoriasis and reactive arthritis</i>
Sacroiliitis	Severe and symmetrical	Sacroiliitis sometimes unilateral or bilaterally asymmetrical
Symphysitis	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

PsA Axial Disease vs AS: Differing Clinical Presentations

Inflammatory back pain is reported by patients with PsA and by patients with AS, and includes¹:

- Pain in the hips or buttocks that improves with activity and worsens with rest
- Pain that occurs at night
- Pain that is responsive to NSAIDs
- Axial morning stiffness that lasts for more than 30 minutes



Compared to AS^{1,2}:

- Can be asymptomatic
- ✓ ✗ Asymmetrical sacroiliitis
- Worse degree of peripheral arthritis
- Spondylitis (w/ or w/o sacroiliitis)



Compared to PsA axial disease^{1,2}:

- ♂ Male
- ⌚ Younger
- More limitation of spinal mobility
- More back pain

Similar levels of self- perceived health status, which reflects pain, disease activity and quality of life, were reported for both diseases.

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.

Genetics in PsA Axial Disease vs Ankylosing Spondylitis

HLA-B*39+ in axial PsA vs PsO

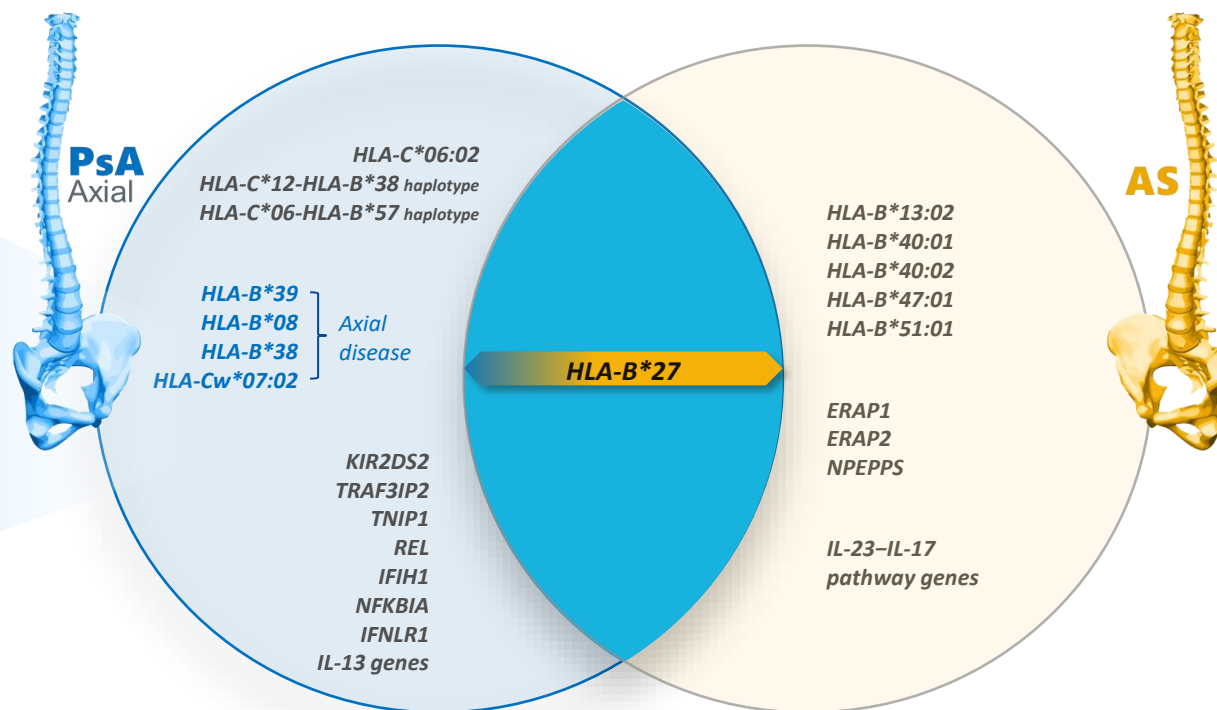
(OR 2.51, 95% CI 1.25–5.01, $P = 0.009$)¹

HLA-B*27, HLA-B*08 and HLA-B*38

Have specifically been linked to axial PsA¹

HLA-Cw*07:02

Associated with axial PsA in a Spanish cohort
(OR 5.0; 95% CI 1.4–25.0, $P = 0.01$)²



Feld J, et al. *Nat Rev Rheumatol*. 2018;14:363–371.

CI=confidence interval; HLA=human leukocyte antigen; ERAP=endoplasmic reticulum aminopeptidase; IFIH1=interferon induced with helicase C domain 1; IFNLR1=interferon lambda receptor 1; IL=interleukin; KIR=killer cell immunoglobulin like receptor, two Ig domains and short cytoplasmic tail 2; NFKB1A=nuclear factor kappa B inhibitor alpha; NPEPPS=aminopeptidase puromycin sensitive; PsA=psoriatic arthritis; PsO=psoriasis; OR=odds ratio; REL=reticuloendotheliosis; TRAF3IP2=Tumor necrosis factor receptor associated factor 3 interacting protein 2.

1. Eder L, et al. *Ann Rheum Dis*. 2012;71:50-55. 2. Queiro R, et al. *Arthritis Res Ther*. 2006;8(6):R185

The Phenotype of Axial Spondyloarthritis: Is It Dependent on HLA-B27 Status?

Laura C. Coates,¹ Xenofon Baraliakos,² Francisco J. Blanco,³ Elena Alonso Blanco-Morales,³ Jurgen Braun,² Vinod Chandran,⁴ Jose Luis Fernandez-Sueiro,⁴ Oliver FitzGerald,⁵ Phil Gallagher,⁵ Dafna D. Gladman,⁴ Elena Gubar,⁶ Tatiana Korotaeva,⁶ Elena Loginova,⁶ Ennio Lubrano,⁷ Juan Mulero,⁸ Jose Pinto-Tasende,³ Ruben Queiro,⁹ Jesús Sanz Sanz,⁹ Agnes Szentpetery,¹⁰ and Philip S. Helliwell¹¹

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

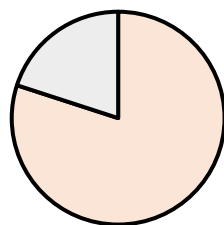
	HLA-B27 positive (n = 208)	HLA-B27 negative (n = 234)	Difference between B27+ and B27– (continuous data) and odds ratios (categorical data)	P
Age, mean ± SD years	49.1 ± 14.2	53.8 ± 13.8	–4.7 (–7.4, –2.1)†	< 0.0001
Male	152 (73)	138 (59)	1.9 (1.3, 2.8)‡	0.002
Duration of disease, mean ± SD years	13.6 ± 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

Axial phenotypes

Classical

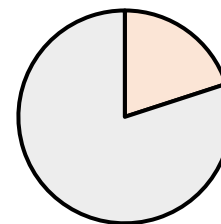
Atypical

axSpA



■ Classical ■ Atypical

axPsA



■ Classical ■ Atypical

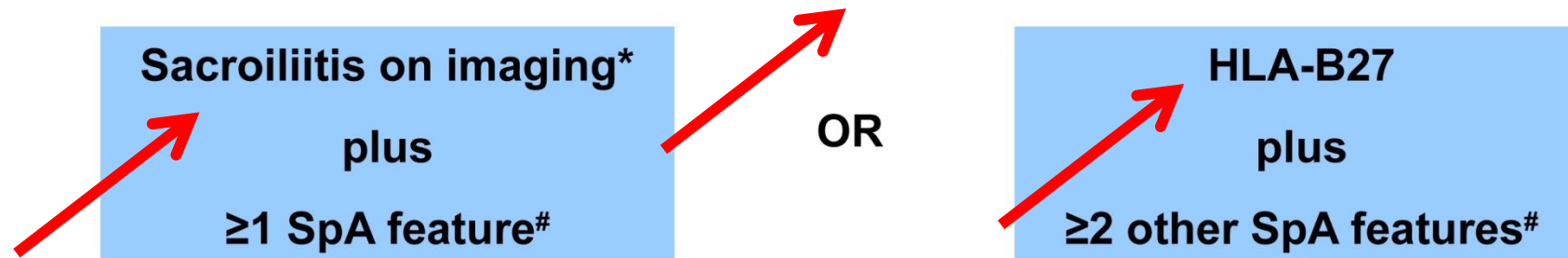
Does it really matter?

YES!

- Classification of disease
- Treatment

ASAS Classification Criteria for Axial Spondyloarthritis (SpA)

In patients with ≥ 3 months back pain and age at onset < 45 years



#SpA features

- inflammatory back pain
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn's/colitis
- good response to NSAIDs
- family history for SpA
- HLA-B27
- elevated CRP

*Sacroiliitis on imaging

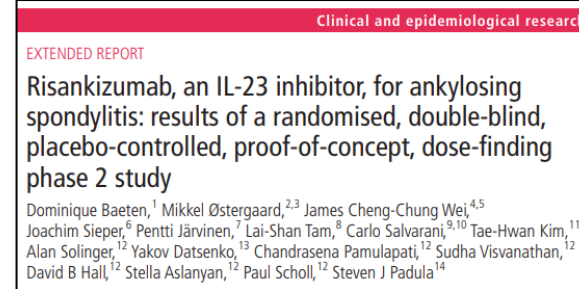
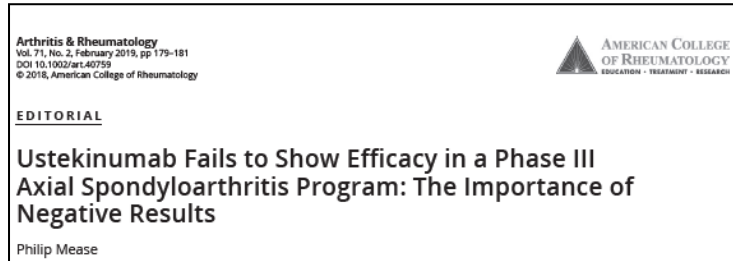
- active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
- definite radiographic sacroiliitis according to mod NY criteria

n=649 patients with back pain;
Sensitivity: 82.9%, Specificity: 84.4%
Imaging alone: Sensitivity: 66.2%, Specificity: 97.3%

Negative Results From Clinical Studies Question the Role of IL-23 in AS

IL-12/23

IL-23



Conclusions Treatment with risankizumab did not meet the study primary endpoint and showed no evidence of clinically meaningful improvements compared with placebo in patients with active AS, suggesting that IL-23 may not be a relevant driver of disease pathogenesis and symptoms in AS.

Efficacy and Safety Study of SUNPG1622 (tildrakizumab)

ClinicalTrials.gov Identifier: NCT02980705

Recruitment Status ⓘ : Terminated (Study terminated-Sponsor's decision)
First Posted ⓘ : December 2, 2016
Last Update Posted ⓘ : June 7, 2019



1. Mease P. *Arthritis & Rheum.* 2019;71(2):179-181. 2. Deodhar A et al. *Arthritis Rheumatol.* 2019;71:258-270. 3. Baeten D et al. *Rheum Dis.* 2018;77:1295-1302. 4. ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/study/NCT02980705>.

**RMD
Open**

Rheumatic &
Musculoskeletal
Diseases

ORIGINAL RESEARCH

Effects of ustekinumab on spondylitis-associated endpoints in TNFi-naïve active psoriatic arthritis patients with physician-reported spondylitis: pooled results from two phase 3, randomised, controlled trials

Philip S Helliwell ¹, Dafna D Gladman ², Soumya D Chakravarty,^{3,4}
Shelly Kafka,³ Chetan S Karyekar,⁵ Yin You,⁶ Kim Campbell,⁶ Kristen Sweet,⁶
Arthur Kavanaugh,⁷ Lianne S Gensler⁸

Development of the ASAS – GRAPPA consensus definition of axial involvement in psoriatic arthritis

Objective: development of a consensus definition for axial involvement in PsA to be used primarily in clinical trials.



The Survey

- Invitation sent to all ASAS (n=183) and GRAPPA (n=698) members 27.12.2018, reminder – 10.01.2019, survey closed – 14.01.2019.
- A total of 67 colleagues were members of both ASAS and GRAPPA (only one survey completion was allowed per person).
- The survey has been finally completed by 186 ASAS/GRAPPA members (106 ASAS, 123 GRAPPA, 43 both societies).

Results: criterion ranking (all, n=186)

		Median	Mean
1	Presence of structural damage on an X-ray of sacroiliac joints	2	2,8
2	Presence of structural damage on an X-ray of spine	3,5	4,1
3	Presence of subchondral bone marrow edema / osteitis on magnetic resonance imaging (MRI) of sacroiliac joints (SIJ) compatible with spondyloarthritis	4	4,5
4	Presence of bone marrow edema / osteitis on magnetic resonance imaging (MRI) of spine compatible with spondyloarthritis (presence of anterior/posterior spondylitis in ≥ 3 sites)	4	5,0
5	History or current presence of back pain (entire spine including neck)	5,5	5,8
6	History of or current presence of inflammatory back pain (IBP)	5,5	6,0
7	Good response of back pain to non-steroidal anti-inflammatory drugs - NSAIDs	8	7,8
8	HLA-B27	8	8,1
9	Family history (first- or second degree relatives) for spondyloarthritis	9,5	9,0
10	Elevated C-reactive protein - CRP (above upper normal limit, after exclusion of other causes for elevation)	10	9,3
11	Presence of peripheral arthritis and/or enthesitis and/or dactylitis (past or present, diagnosed by a physician)	10	9,4
12	Presence of anterior uveitis (past or present, diagnosed by an ophthalmologist)	10	9,5
13	Presence of inflammatory bowel disease - IBD (past or present, diagnosed by a physician)	10	9,6

GRAPPA Annual meeting in Dublin July 2023



Pre-meeting workshops – US, IDEOM, CRN
Trainee symposium
Workshops – axial lesions on MRI, co-morbidities
Debates – MTX as 1st line? Biologics for mild psoriasis.
Enthesitis as primary lesion
Breakouts – dermatology/rheumatology collaboration
Plenary sessions – difficult to treat PsA

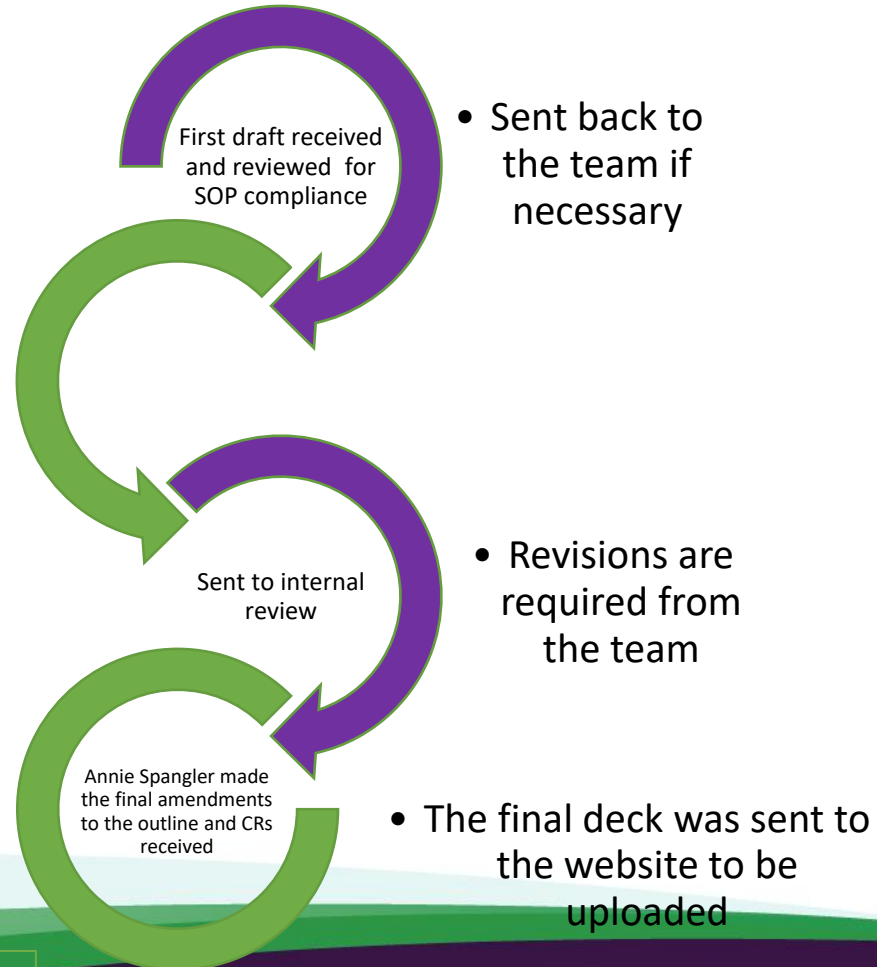
Educational meetings this year

- Leeds GRAPPA Feb 2024
- Latin America Regional Course: Cartagena, Colombia – May 4, 2024
- Cairo, Egypt – May 24, 2024
- Curitiba, Brazil – August 16-17, 2024
- APLAR: Singapore – August 2024
- Sardinia, Italy - September 2024
- GRAPPA Scientific Standalone on Psoriatic Disease: Dubai, UAE, October 18-29, 2024
- GRAPPA UK Webinar/Workshop – 2-part online miniseries in October and November 2024
- Bangladesh – Potential meeting in the works.
- Sri Lanka GRAPPA Workshop – October 23, 2024
- GRAPPA Workshop Adjacent to the Indian Rheumatology Association Meeting – November 2024
- SPARTAN-GRAPPA-ASAS Symposium – November 2024
- Mexico SPARTAN-GRAPPA Educational Symposium – February 2025

MAY 2022



JUNE 2023



Annie Spangler



Suggested for you

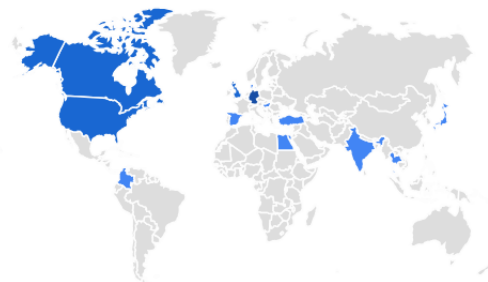
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Insights & recommendations

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COMMITTEES & RESPONSIBILITIES



GRAPPA – future developments?

The future is bright

Real chance of early intervention to prevent progression (if not prevention) from psoriasis to PsA

Better care of psoriatic disease patients with collaborative working

Better treatment algorithms – the right treatment for the right patient at the right time

The role of GRAPPA

- World-wide collaboration with over 1300 members
- Opportunity to develop collaboration between dermatology and rheumatology
- Research will answer some major questions – Hippocrates and Ellipss
- Education
 - multidisciplinary meetings like this
 - On line educational symposia (allow much greater exposure)
 - Slide collection



Thank you!