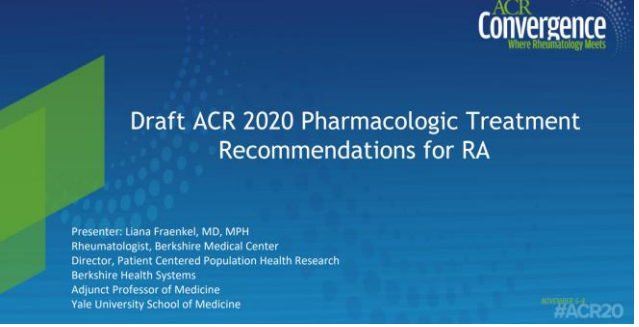
Αντώνης Φανουριάκης
2/12/2020



Overview

- DMARD naive with mod-high disease activity
- DMARD naive with low disease activity
- Administration of MTX
- Rx for patients not at target
- Tapering
- Specific populations

Glucocorticoids

- DMARDs without short-term (<3ms) GCs conditionally recommended over DMARD + short-term GCs
- DMARDs without longer-term (≥3ms) GCs strongly recommended over DMARD + longer-term GCs

Administering MTX

- When starting, oral conditionally recommended over SC
- If not tolerating oral, split dose or SC or increase folic acid, conditionally recommended over switch to new DMARD
- If not a target on oral, switch to SC MTX conditionally recommended over add/switch to new DMARD

Modification of DMARDs

- On maximally tolerated doses of MTX:
  - add biologic or tsDMARD conditionally recommended over add HCQ + SSZ (triple Rx)
- On biologic or tsDMARD:
  - switch to biologic or tsDMARD in different class conditionally recommended over same class

Tapering if at Target for ≥6ms

ACR Convergence
Where Rheumatology Meets

- Continuation all DMARDs at current dose conditionally recommended over dose reduction
- Dose reduction conditionally recommended over gradual discontinuation (i.e. gradually reduce dose → stop)
- Gradual discontinuation conditionally recommended over abruptly stopping

Patients Who Want to Discontinue

ACR Converge
Where Rheumatolog

- On triple therapy:
  - Gradual discontinuation SSZ conditionally recommended over HCQ
- On MTX + biologic or tsDMARD:
  - Gradual discontinuation MTX conditionally recommended over biologic or tsDMARD

Hepatitis B

- Prophylactic antiviral Rx strongly recommended:
  - anti-HBc+ starting RTX (even if HBsAG-)
  - HBsAG+ starting any biologic or tsDMARD
- Frequent monitoring conditionally recommended:
  - anti-HBc+ and HBsAG- starting non-RTX biologic or tsDMARD

Persistent Hypogammaglobulinemia without Infection

- On RTX and at target:
  - Continue RTX conditionally recommended over switch to different biologic or tsDMARD

Previous Serious Infection (within 12ms)

- Mod-high disease activity:
  - add/switch of DMARDs conditionally recommended over start/increase dose GCs
- Mod-high disease activity despite csDMARD monoRx:
  - add csDMARDs conditionally recommended over start biologic or tsDMARD

Selected abstracts

Efficacy of Tocilizumab in Patients Hospitalized with Covid-19

John H. Stone, M.D., M.P.H., for
The Boston Area COVID Consortium (BACC) Bay
Tocilizumab Trial Research Group

	Placebo (n=82)	Tocilizumab (n=161)	All (n=243)
Age (median)	56.5	61.6	59.8
Male (%)	55%	60%	58%
Hispanic ethnicity (%)	48%	43%	45%
BMI ≥ 30 kg/m² (%)	51%	50%	50%
Diabetes (%)	37%	28%	31%

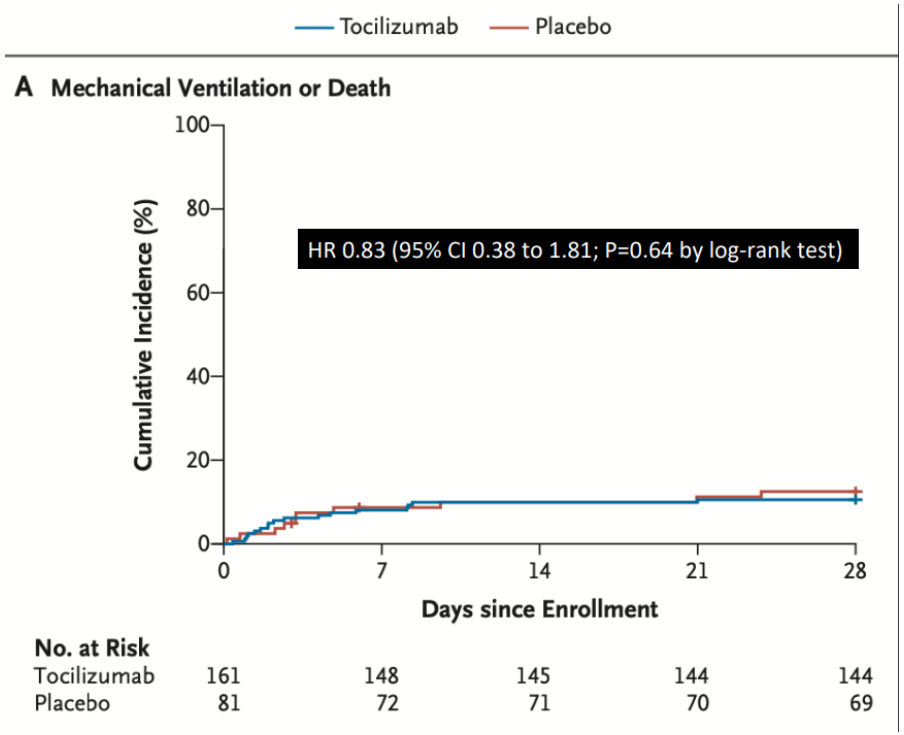
Outcomes

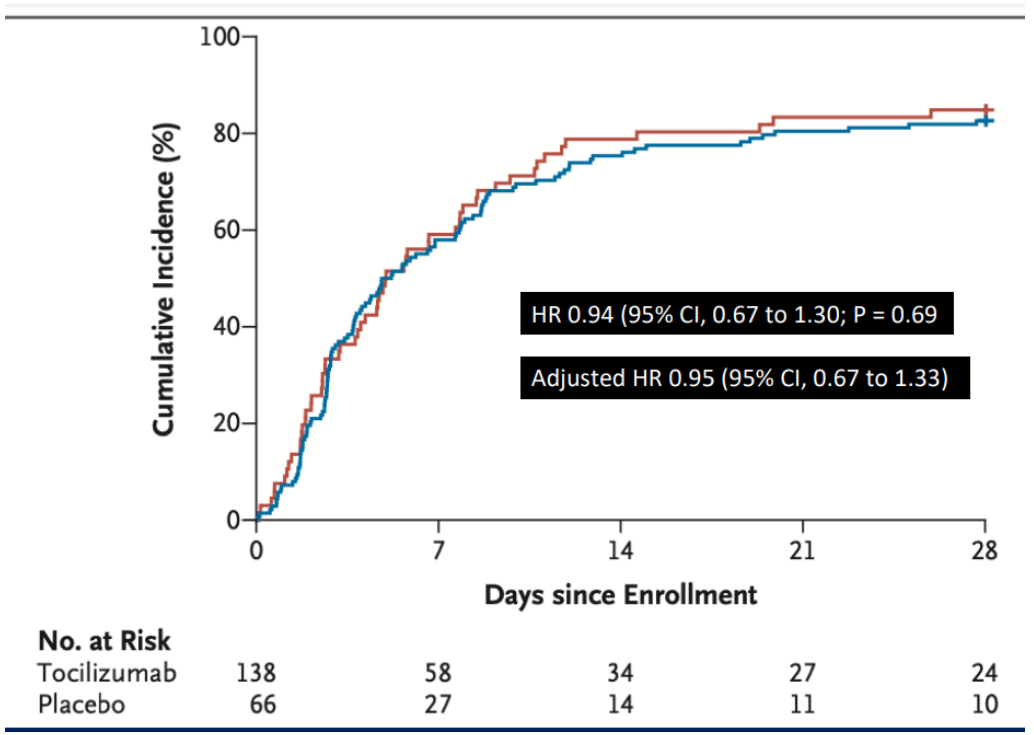
Primary

- Time to intubation (or death, for patients who died before intubation).

Secondary (both time-to-event)

- Clinical worsening, defined on an ordinal scale.
- Discontinuation of supplemental oxygen.





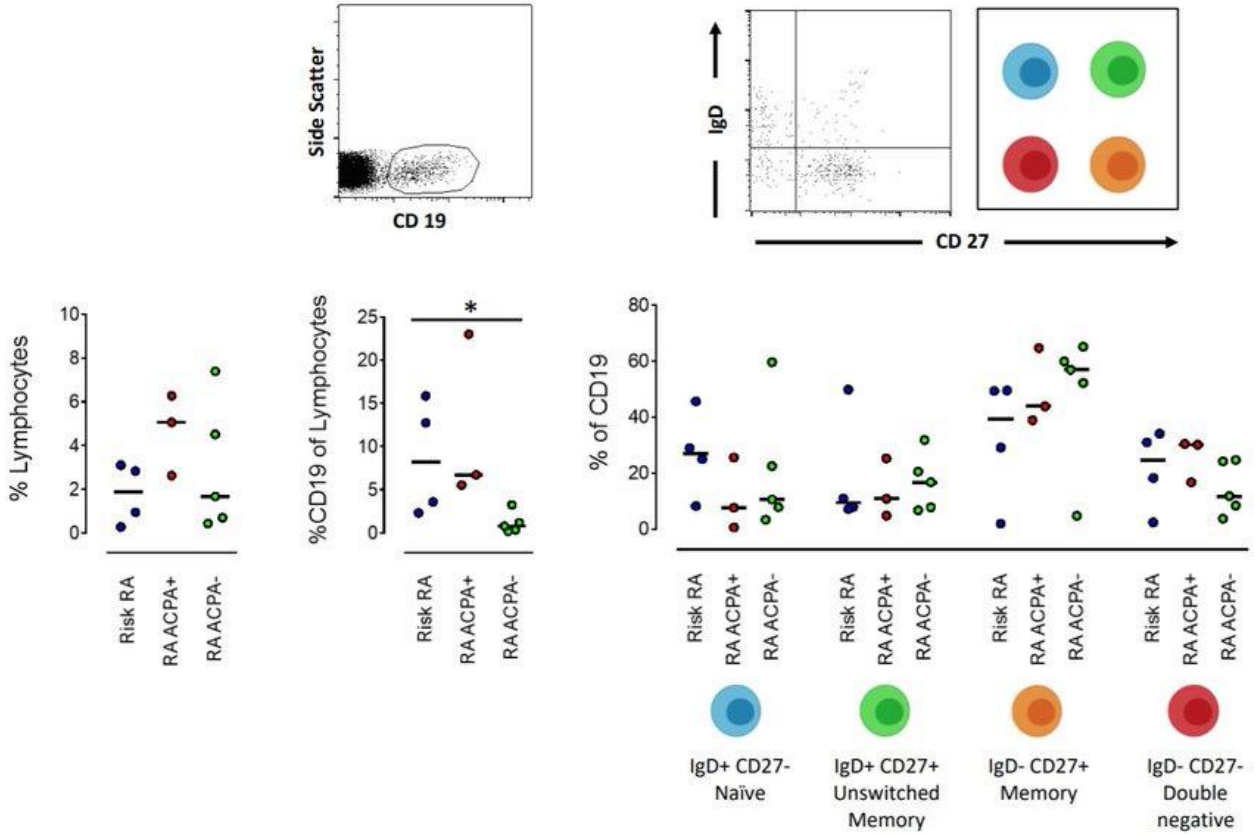
ABSTRACT NUMBER: 1445 • ACR Convergence 2020

Citrulline Reactive B Cells Are Present in the Lungs of Risk RA and Early Untreated RA

Vijay Joshua[1], Malena Loberg-Haarhaus[2], Akilan Krishnamurthy[1], Meng Sun[3], Christina Gerstner[4], Aase Hensvold[5], Khaled Amara[1], Lena Israelsson[1], Ragnhild Stålesen[6], Bence Rethi[7], Magnus Sköld[7], Johan Grunewald[1], Heidi Wähämaa[1], Caroline Grönwall[1], Vivianne Malmström[8] and Anca Catrina[5], [1]Karolinska

Higher proportion of CD19+ B cells are present in ACPA positive individuals (Risk RA and Early RA)

		Cells Sorted
Risk RA	L01	1248
	L02	1152
	L07	768
RA ACPA+	L04	1056
	L11	864
	L13	960
RA ACPA-	L05	960
	L06	288
	L08	96
	L09	384
	L12	960



Dr Joshua presents that citrulline-reactive B cells producing pathogenic ACPAs are present in the lungs of seropositive patients with arthralgia or early RA. **Supports lung as key site of initiation of RA**

Early DAS response after DMARD-start increases probability of achieving sustained DMARD-free remission in RA

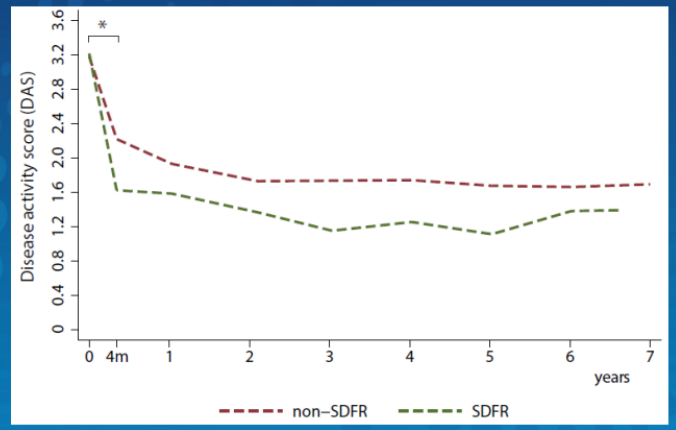
Marloes Verstappen
Department of Rheumatology
LEIDEN UNIVERSITY MEDICAL CENTER

NOVEMBER 5-9
#ACR20

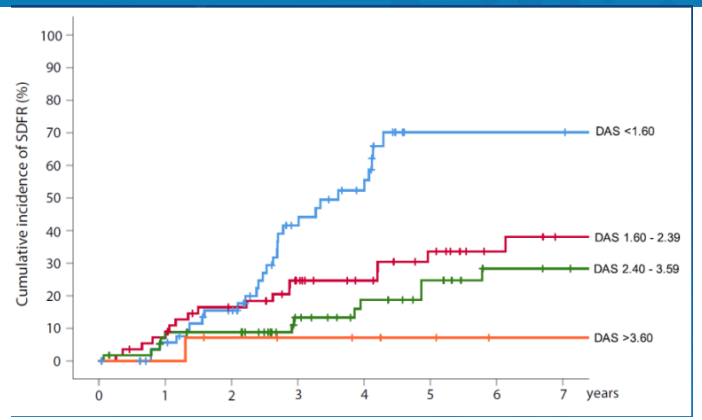
- **Understanding SDFR-development: is DAS-course related to SDFR?**
- **Can SDFR-development be predicted by DAS-course?**

Treatment	Prompt csDMARD-treatment (MTx first choice) DAS-steered adjustments ≥2005 Tapering/Discontinuation of all DMARDs (incl. GCs) when DAS<2.4 ***and*** no clinical arthritis
Outcome	Sustained DMARD-free remission (SDFR) = absence clinical arthritis for min. 1y after DMARD-stop & entire follow-up thereafter (SDFR+/- categorized after 7 years of follow-up)

SDFR-group: significant stronger DAS-decline within the first 4 months.

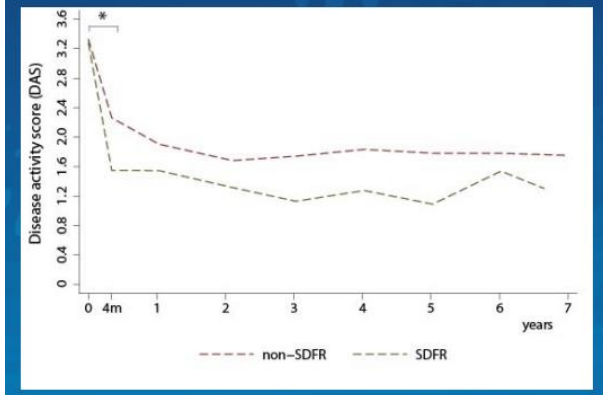


** Statistically significant different course of DAS between the SDFR-group and non-SDFR-group*



ACPA-negative RA

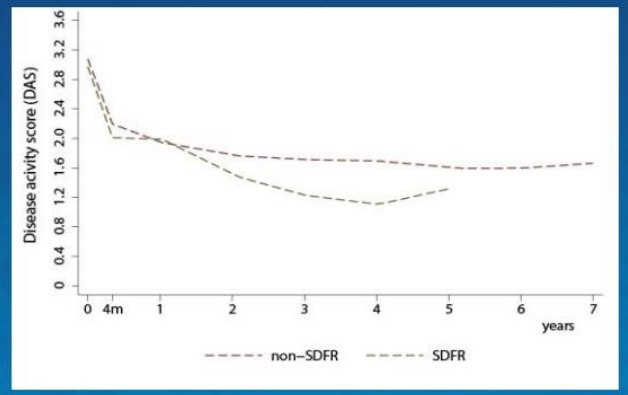
31.8% achieved SDFR (after median 3.2y)



SDFR-group: significant stronger DAS-decline in first 4 months

ACPA-positive RA

4.3% achieved SDFR (after median 3.3y)



No differences in DAS-course between both groups

Subclinical synovitis in arthralgia: how often does it result in clinical arthritis?

Reflecting on starting points for DMARD-treatment

Cleo Rogier
Department of Rheumatology
Erasmus Medical Center

NOVEMBER 5-9 #ACR2

To examine the frequency of non-progression to clinical inflammatory arthritis (IA) in patients with subclinical synovitis, also after considering the 2010-criteria.

Patient selection Arthralgia-patients from three independent Dutch cohorts
Cohort 1 n= 166 (SONAR, Rotterdam)
Cohort 2 n= 473 (CSA cohort, Leiden)
Cohort 3 n= 162 (arthralgia cohort, Amsterdam)

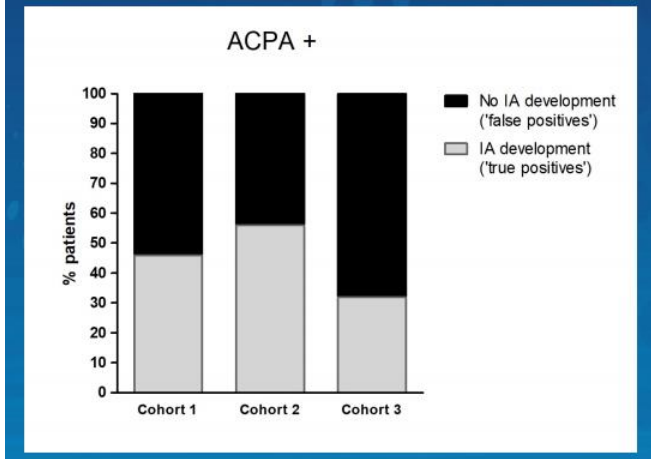
Measurement Determination of subclinical synovitis with ultrasound(US) (cohort 1 & 3) or MRI (cohort 2)
US subclinical synovitis; greyscale≥2 and/or power doppler≥1[1]
MRI subclinical synovitis; synovitis score ≥1 by two readers[2]

	All arthralgia patients		
	Cohort 1 (n=166)	Cohort 2 (n=473)	Cohort 3 (n=162)
Age in years, mean	45	44	51
Female, %	82	77	74
Symptom duration in weeks, median	29	19	57
TJC44, median	5	5	1
ACPA positivity, %	22	14	56
Presence of local subclinical synovitis [a], %	36	41	31
Development of IA after one-year, %	22	15	18

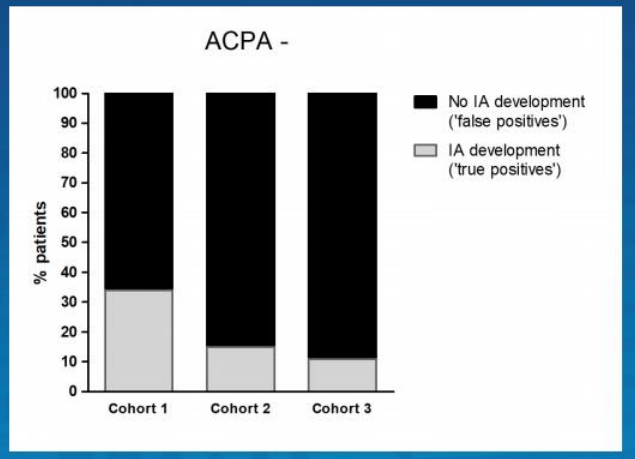
Non-progression to IA in patients with subclinical synovitis

ACR Convergence
Where Rheumatology Meets

1-year follow-up ACPA-positive



1-year follow-up ACPA-negative



Conclusion

- ACPA-positivity + subclinical synovitis ≠ clinical arthritis
- 44-68% non progression to IA after one-year
- DMARD-initiation in absence of clinical arthritis → overtreatment

Impact of targeting remission or low disease activity on 10-year severity in rheumatoid arthritis : data from ESPOIR cohort

DUPONT JULIA

UNIVERSITÉ TOULOUSE III PAUL SABATIER

Hôpitaux de Toulouse

Objectives

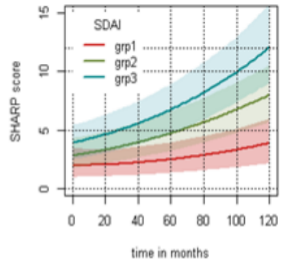
- To compare 10-year structural progression in patients with SDAI or DAS28 remission to patients with SDAI or DAS28 LDA in cohort ESPOIR
- To compare 10-year functional impairment in patients with SDAI or DAS28 remission to patients with SDAI or DAS28 LDA in cohort ESPOIR

Results : disease activity assessed by SDAI

10-year mTSS progression

	Wald test*	p-value
Group 1 VS Group 2	3.21	0.001
Group 2 VS Group 3	2.50	0.01
Group 1 VS Group 3	4.88	< 10^{-5}

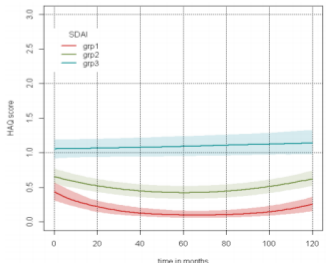
* Other covariables significantly associated : anti-CCP and baseline bone erosions



10-year HAQ

	Wald test*	p-value
Group 1 VS Group 2	5.24	< 10^{-5}
Group 2 VS Group 3	5.59	< 10^{-5}
Group 1 VS Group 3	9.01	< 10^{-5}

* Other covariables significantly associated : RF, corticoids, csDMARDs, bDMARDs

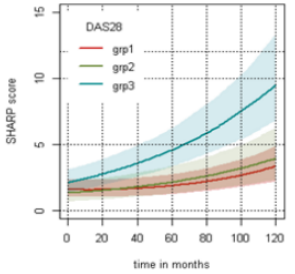


Results : disease activity assessed by DAS-28

10-year mTSS progression

	Wald test*	p-value
Group 1 VS Group 2	0.71	0.48
Group 2 VS Group 3	3.78	0.0002
Group 1 VS Group 3	5.01	< 10^{-5}

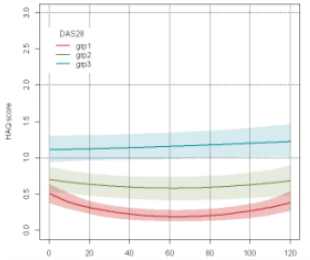
* Other covariables significantly associated : anti-CCP and baseline bone erosions



10-year HAQ

	Wald test*	p-value
Group 1 VS Group 2	3.36	0.0008
Group 2 VS Group 3	4.76	< 10^{-5}
Group 1 VS Group 3	8.53	< 10^{-5}

* Other covariables significantly associated : RF, ACPA, bone erosions, corticoids, csDMARDs, bDMARDs



Conclusion

- Sustained remission is rare in clinical practice
- We observed a clear benefit to target remission instead of LDA in long term structural progression and functional impairement
- SDAI should be prefered compared to DAS-28

Prevalence, Incidence, and Cause-Specific Mortality of Rheumatoid Arthritis-Associated Interstitial Lung Disease Among Older Patients with Rheumatoid Arthritis: A Nationwide Cohort Study

Jeffrey Sparks, Yinzhu Jin, Soo-Kyung Cho, Seanna Vine, Rishi Desai, Tracy Doyle, Seoyoung Kim

- To investigate the prevalence, incidence, and cause-specific mortality of RA-ILD among older US patients with RA using nationwide claims data from Medicare

Baseline characteristics (n=509,787)
Demographics, comorbidities, health care utilization

RA-ILD prevalence: 2.0%	Prevalent RA-ILD (n=10,306)	RA without ILD (n=499,481)
Mean age (SD), years	72.7 (6.5)	72.6 (6.8)
Male, %	27	24
Smoking, %	29	16
Asthma, %	27	11
COPD, %	56	17
Mean combined comorbidity score (SD)	3.3 (3.0)	1.2 (2.4)
Pulmonologist visit, %	94	11
Mean pulmonologist clinic visits (SD)	4.8 (4.7)	0.3 (1.3)
Mean physician visits (SD)	32.6 (29.9)	18.5 (17.0)

Incident RA-ILD results (n=499,481)

Median follow-up: 3.0 years/patient (IQR 1.4, 5.7)

Additional 2.7% developed incident RA-ILD

Cause-specific mortality results (n=509,787)
Prevalent RA-ILD vs. RA without ILD

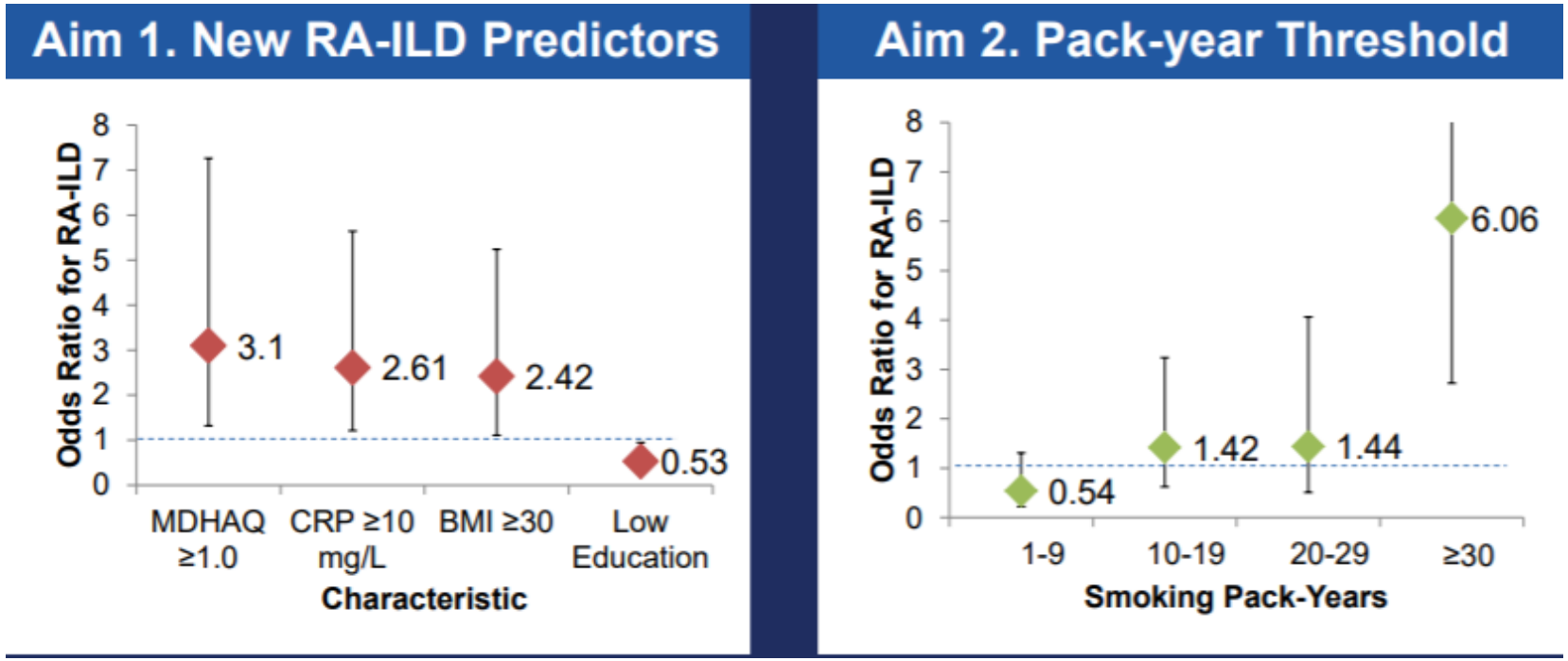
Total of 107,248 (21.0%) deaths
- 3,989 (38.7%) deaths in the prevalent RA-ILD group
- 103,259 (20.7%) deaths in the RA without ILD group

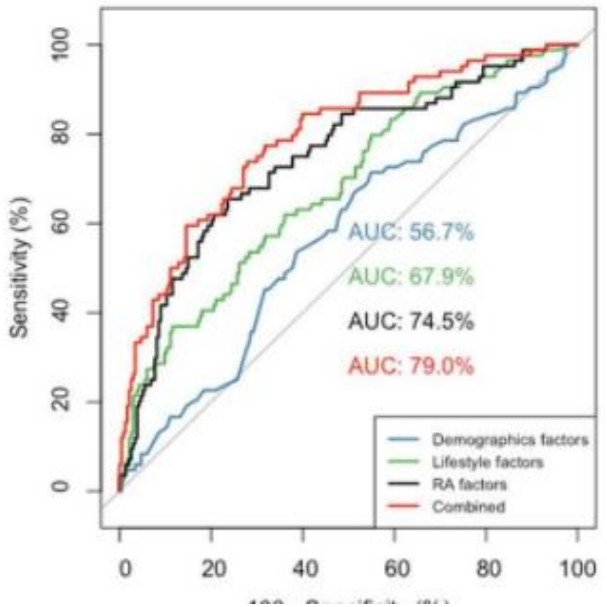
	Total mortality	CVD mortality	Cancer mortality	Respiratory mortality	Infection mortality	Other mortality
Unadjusted sdHR (95%CI)	2.36 (2.28-2.45)	1.42 (1.32-1.54)	2.08 (1.90-2.27)	7.08 (6.67-7.51)	1.89 (1.55-2.30)	1.78 (1.66-1.90)
Multivariable* sdHR (95%CI)	1.66 (1.60-1.72)	1.01 (0.93-1.09)	1.56 (1.43-1.71)	4.39 (4.13-4.67)	1.19 (0.97-1.45)	1.30 (1.21-1.40)

*Adjusted for age, sex, US region, smoking, methotrexate use, hydroxychloroquine use, TNF inhibitor use, other biologic or targeted synthetic DMARD use, glucocorticoid use, combined comorbidity score, and number of physician visits.

ABSTRACT NUMBER: 1198

Lifestyle and Clinical Risk Factors for Incident Rheumatoid Arthritis-Associated Interstitial Lung Disease Among Patients with Rheumatoid Arthritis





Dr Kronzer and @jeffsparks
presenting on lifestyle and clinical risk factors for RA-ILD. Obesity, CRP >=10mg/L, poor function, and high education level appear to be risks. Also threshold pk/yr effect for smoking

ABSTRACT NUMBER: 1199

Prevalence of Subclinical Interstitial Lung Disease After a Mean Rheumatoid Arthritis Duration of 13 Years: Results from the French ESPOIR Cohort

Dr Juge reports on prevalence of subclinical RA-ILD as identified by HRCT.

At mean disease duration of 13 years **18.2% of patients had subclinical RA-ILD**

Subclinical ILD with a HRCT extension of

- < 5%: 7 (4.1%)
- 5-10%: 15 (8.8%)
- >10%: 9 patients (5.3%)

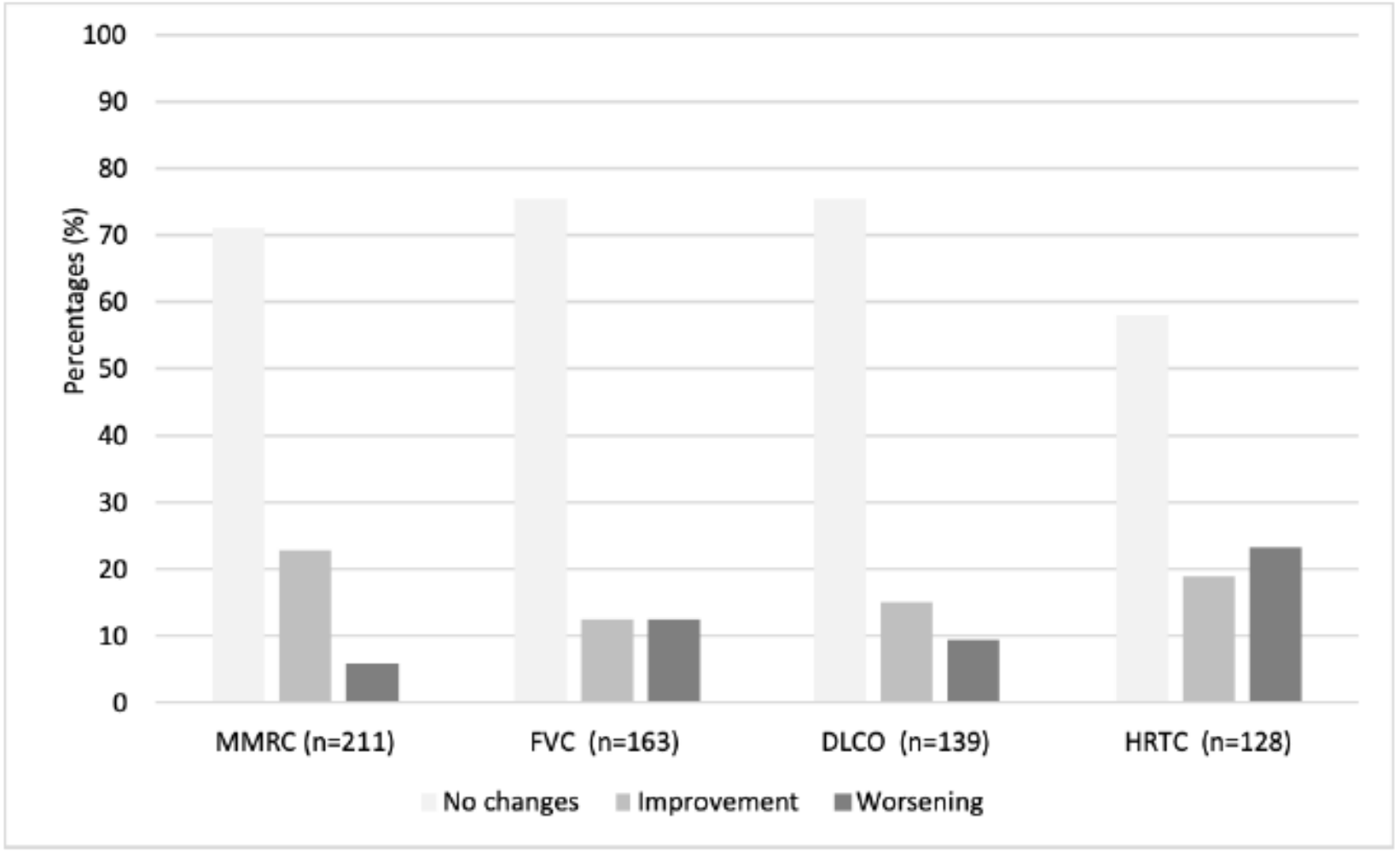
	RA-noILD (n=139)	RA-noILD (n=31)	P value
Patients characteristics			
Female, n (%)	114 (82.0)	19 (61.2)	**0.016**
Age at RA onset, y/o ± SD	46.1 ± 10.2	55.2 ± 9.0	**<0.001**
Age at HRCT, y/o ± SD	59.7 ± 10.1	67.9 ± 8.7	**<0.001**
RA duration, years ± SD	13.6 ± 1.1	13.9 ± 0.6	0.33
Body Mass Index at RA diagnosis, kg/m² ± SD	24.62 ± 4.56	25.65 ± 3.96	0.0829
Rheumatoid Factors positive, n (%)	75 (54.0)	23 (74.2)	0.0454
Rheumatoid Factors titers, U/mL ± SD	103.47 ± 159.38	303.97 ± 542.01	0.0055
ACPA positive, n (%)	84 (60.4)	21 (67.7)	0.5417
ACPA titers, U/mL ± SD	129.0 ± 491.3	219.3 ± 464.5	0.1080
Ever smoker, n (%)	60 (43.2)	18 (58.1)	0.1637
Smoking level at RA diagnosis, pack/year ± SD	13.6 ± 17.3	7.76 ± 13.6	0.0773
Sharp Score at RA diagnosis ± SD	3.0 ± 4.3	4.0 ± 6.8	0.5152
ILD characteristics			
Extension < 5%		7 (4.1)	
Extension 5-10%		15 (8.8)	
Extension >10%		9 (5.3)	
- UIP		4	
- NSIP		3	
- indeterminate		2	

Table 1. Characteristics of the included patients and RA-ILD

ABSTRACT NUMBER: 2345

Abatacept in Rheumatoid Arthritis with Interstitial Lung Disease: A Retrospective Multicenter Study of 263 Patients

Dr Fernandez-Diaz on abatacept in RA-ILD in 263 patients. Abatacept appears safe and effective. Equivalent to RTX. Good option as s/c admin

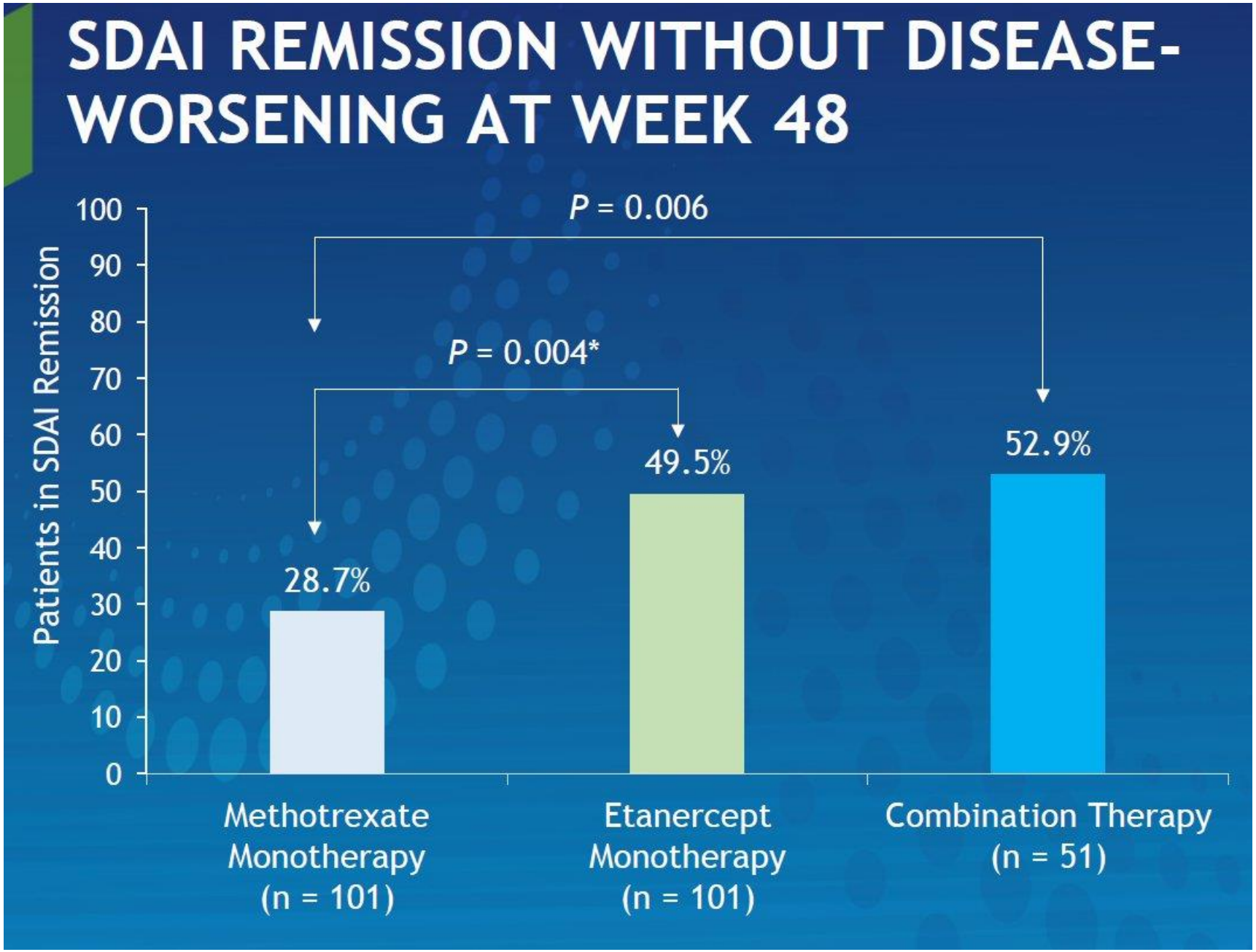


Abstr#939

MAINTENANCE OF REMISSION AFTER WITHDRAWAL OF ETANERCEPT OR METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SUSTAINED REMISSION ON COMBINATION THERAPY: RESULTS FROM A RANDOMIZED DOUBLE-BLIND, CONTROLLED TRIAL

Jeffrey R. Curtis,[1] Paul Emery,[2] Elaine Karis,[3] Boulos Haraoui,[4] Vivian P. Bykerk,[5] Priscilla K. Yen,[3] Gregory Kricorian,[3] James B. Chung[3]

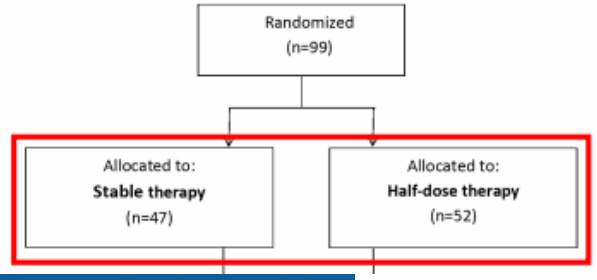
Dr Curtis presents **SEAM-RA RCT** of withdrawal of ETN or MTX in patients on combo therapy in sustained remission. 49.5% of ETN mono retained remission compared to 28.7% of MTX mono, and 52.9% who continued combo therapy.



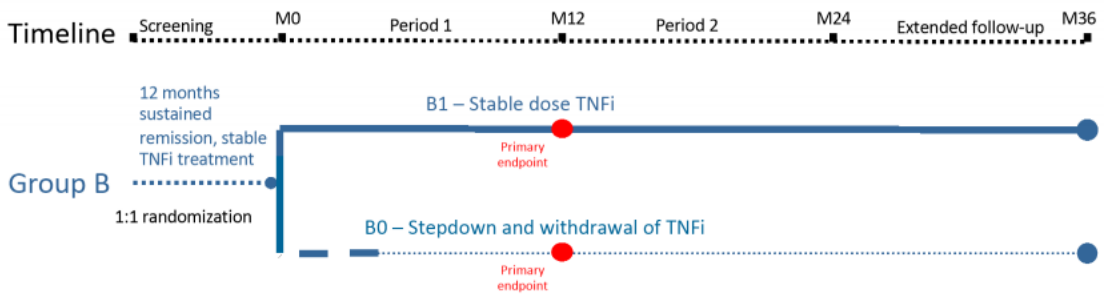
Stable versus Tapered and Withdrawn Treatment with Tumor Necrosis Factor Inhibitor in Rheumatoid Arthritis Remission: A Randomized, Open-Label, Phase 4, Non-Inferiority Trial

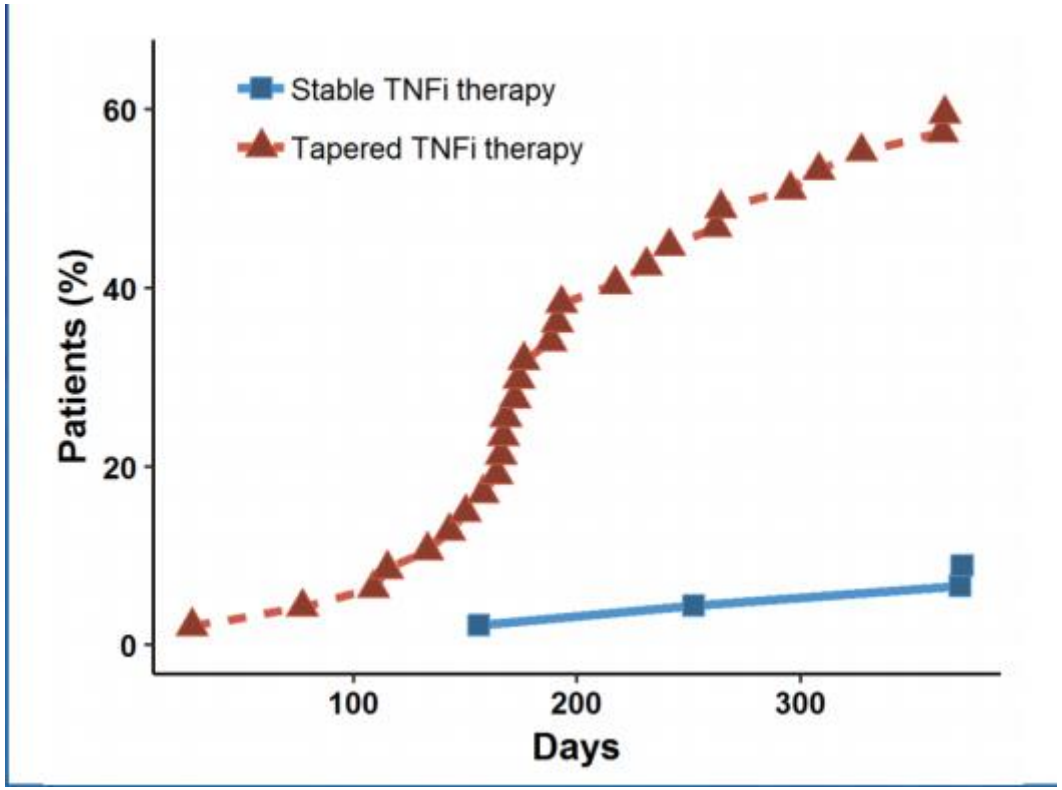
Siri Lillegraven, Nina Paulshus Sundlisæter, Anna-Birgitte Aga, Joseph Sexton, Inge C. Olsen, Åse Lexberg, Tor Magne Madland, Hallvard Fremstad, Christian A. Høili, Gunnstein Bakland, Cristina Spada, Hilde Haukeland, Inger Myrnes Hansen, Ellen Moholt, Till Uhlig, Daniel H. Solomon, Désirée van der Heijde, Tore K. Kvien, Espen A. Haavardsholm

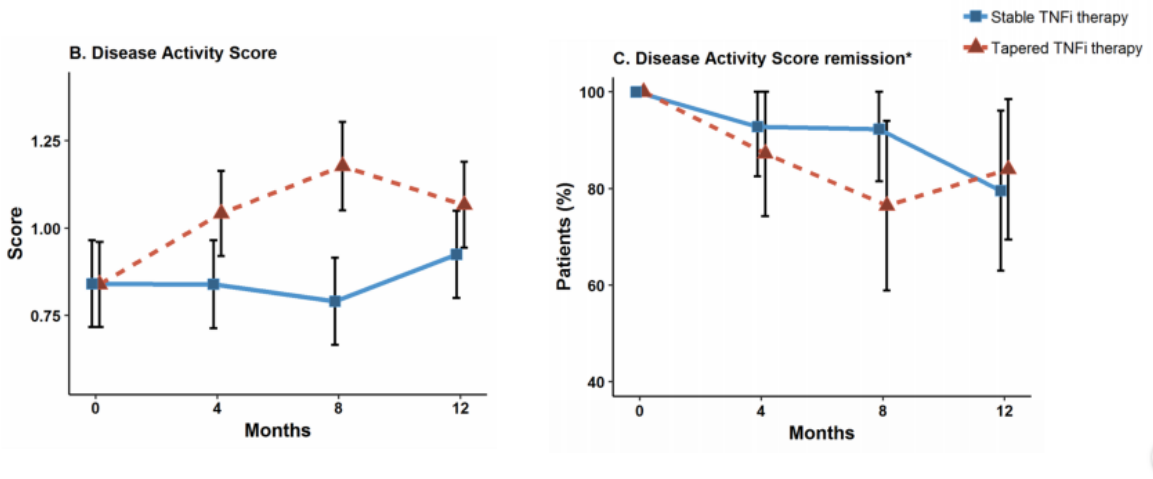
- To assess the effect of tapering and withdrawal of TNFi on the risk of flares in RA patients in sustained clinical remission, compared to continued stable TNFi treatment



- Inclusion criteria
  - RA according to 2010 ACR/EULAR criteria
  - Remission for at least 12 months, consecutive visits
  - DAS remission (based on ESR and 44 swollen joints) at inclusion with no swollen joints
- Stable TNFi/DMARD treatment for 12 months







ACR Convergence
Where Rheumatology Meets

TOFACITINIB FOR THE TREATMENT OF ADULT PATIENTS WITH ANKYLOSING SPONDYLITIS: PRIMARY ANALYSIS OF A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

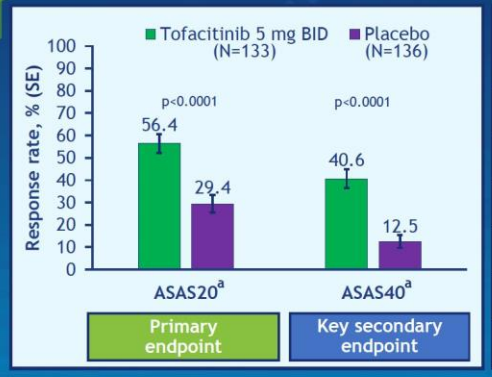
Atul Deodhar, MD
Oregon Health & Science University, Portland, OR, USA
Presentation No: L11

A Deodhar,[1] P Sliwinska-Stanczyk,[2] H Xu,[3] X Baraliakos,[4] LS Gensler,[5] D Fleishaker,[6] L Wang,[6] J Wu,[6] S Menon,[6] C Wang,[6] O Dina,[7] L Fallon,[8] KS Kanik,[6] D van der Heijde[9]

[1]Oregon Health & Science University, Portland, OR, USA; [2]Reumatika Centrum Reumatologii, Warsaw, Poland; [3]Shanghai Changzheng Hospital, Shanghai, China; [4]Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Herne, Germany; [5]University of California San Francisco, San Francisco, CA, USA; [6]Pfizer Inc, Groton, CT, USA; [7]Pfizer Inc, New York, NY, USA; [8]Pfizer Inc, Montreal, QC, Canada; [9]Leiden University Medical Centre, Leiden, The Netherlands

#ACR20

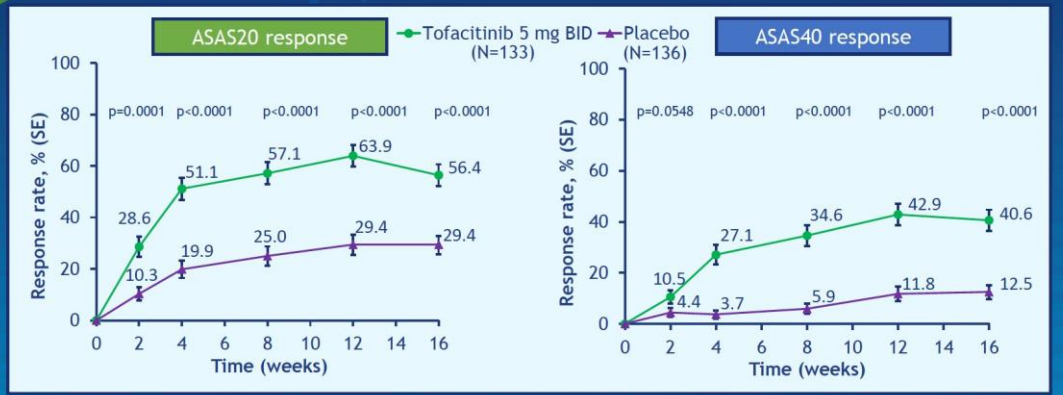
Efficacy at Week 16: global type I error-controlled endpoints



LS mean (SE) [N1]	Tofacitinib 5 mg BID (N=133)	Placebo (N=136)	p value
ΔASDAS[b]	-1.36 (0.07) [129]	-0.39 (0.07) [131]	<0.0001
ΔhsCRP[b] (mg/dL)	-1.05 (0.10) [129]	-0.09 (0.10) [131]	<0.0001
ΔASQoL[c]	-4.03 (0.40) [129]	-2.01 (0.41) [130]	0.0001
ΔSF-36v2 PCS[c]	6.69 (0.59) [129]	3.14 (0.59) [130]	<0.0001
ΔBASMI-linear method[b]	-0.63 (0.06) [129]	-0.11 (0.06) [131]	<0.0001
ΔFACIT-F total score[b]	6.54 (0.80) [129]	3.12 (0.79) [131]	0.0008

Data cut-off December 19, 2019; data snapshot January 29, 2020. Efficacy assessments used only on-drug data up to Week 16; efficacy data were final
To control for type I error, endpoints were tested in the following sequence: ASAS20 response at Week 16; ASAS40 response at Week 16; Δ to Week 16 in ASDAS, hsCRP, ASQoL, SF-36v2 PCS, BASMI-linear method, and FACIT-F total score
[a]Normal approximation adjusting for stratification factor (bDMARD naïve vs TNFi-IR or bDMARD use [non-IR]) derived from clinical database via Cochran-Mantel-Haenszel approach was used. Missing response was considered as non-response
[b]Mixed model for repeated measures included fixed effects of treatment group, visit, treatment group by visit interaction, stratification factor derived from clinical database, stratification factor by visit interaction, baseline value, and baseline value by visit interaction; an unstructured covariance matrix was used; missing values were not imputed
[c]Analysis of covariance model included fixed effects of treatment group, stratification factor derived from clinical database, and baseline value; missing values were not imputed
Δ , change from baseline; LS mean, least squares mean; N, number of patients in the full analysis set; N1, number of patients with observation at visit; SE, standard error

Efficacy over time up to Week 16



Data cut-off December 19, 2019; data snapshot January 29, 2020. Efficacy assessments used only on-drug data up to Week 16; efficacy data were final
To control for type I error, time points were tested in the following sequence: Week 16, Week 12, Week 8, Week 4, Week 2
Normal approximation adjusting for stratification factor (bDMARD naïve vs TNFi-IR or bDMARD use [non-IR]) derived from clinical database via Cochran-Mantel-Haenszel approach was used; missing response was considered as non-response
N, number of patients in the full analysis set

Lifetime risk of AS in HLA-B27 (+) FDRs of AS patients

Swiss Ankylosing Spondylitis Family Study 1985

358 AS Probands (mNY(+) 76%; HLA-B27(+) 86%; male 68%)

Mean Age of 672 FDRs of 305 HLA-B27(+) Probands: 26.9±8.2 yr

- 308 HLA-B27(+) FDR > 14 (4.5%) FDR had AS by mNY (7 males)
- 278 HLA-B27(-) FDRs > 0 FDR with AS by mNY

Mean Age of 83 FDRs of 50 HLA-B27(-) AS Probands: 27.4±6.0 yr

- *83* HLA-B27(-) FDRs > 0 FDR had AS by mNY

Follow-up after 35 yr of 1985 Swiss AS Family Study

462 Participants (124 AS Probands and 338 FDR)

152 HLA-B27(+) FDR >
36 HLA-B27(+) FDR report clinically defined AS/axSpA
(including 6 mNY(+) FDR diagnosed at the 1985 Family Study)
*> Lifetime Risk for HLA-B27(+) FDR 36/152 > 23.7%**

173 HLA-B27(-) FDR >
3 HLA-B27(-) FDR report clinically defined AS/axSpA
*> Lifetime Risk for HLA-B27(-) FDR 3/173 > 1.7%**

Mean Age in 2019 of all 39 FDR with AS: 58.4±8.7 yr

* $p = 1.2*10^{-9}$

ACR Convergence
Where Rheumatology Meets

Structural Entheseal Lesions in Psoriasis Patients Are Associated with an Increased Risk of progression to Psoriatic Arthritis - A Prospective Cohort Study

David Simon, Koray Tascilar, Arnd Kleyer, Sara Bayat, Eleni Kampylafka, Axel Hueber, Jürgen Rech, Louis Schuster, Klaus Engel, Michael Sticherling, Georg Schett

Objective

- To test whether the presence of structural entheseal lesions (SEL) and other signs of bone changes increases the risk for progression to PsA.

Methods

- Prospective cohort study on psoriasis patients without clinical evidence of MSK involvement
- Baseline
  - HR-pQCT:
    - structural entheseal lesions
    - volumetric bone mineral density (BMD) at entheseal and intra-articular sites
- Follow-Up
  - Until EOS
  - Until development of PsA

	Psoriasis N=90	PsA N=24
N, any entheseal lesion (%)	24 (**26.7**)	17 (**70.8**)
Entheseal lesion grade		
Mean (SD)	0.50 (1.18)	1.58 (1.69)
Median (IQR)	0 (0-1)	1 (0-2)

HR (95% CI)	
Unadjusted	Adjusted*
4.91 (2.03 to 11.89)	**5.10 (1.53 to 16.99)**

	Psoriasis N=90	PsA N=24
Intraarticular segment		
Total vBMD (mg HA/cm^3), mean (SD)	289.65 (35.70)	285.66 (43.38)
Entheseal segment		
Total vBMD (mg HA/cm^3), mean (SD)	281.18 (35.42)	265.47 (34.52)

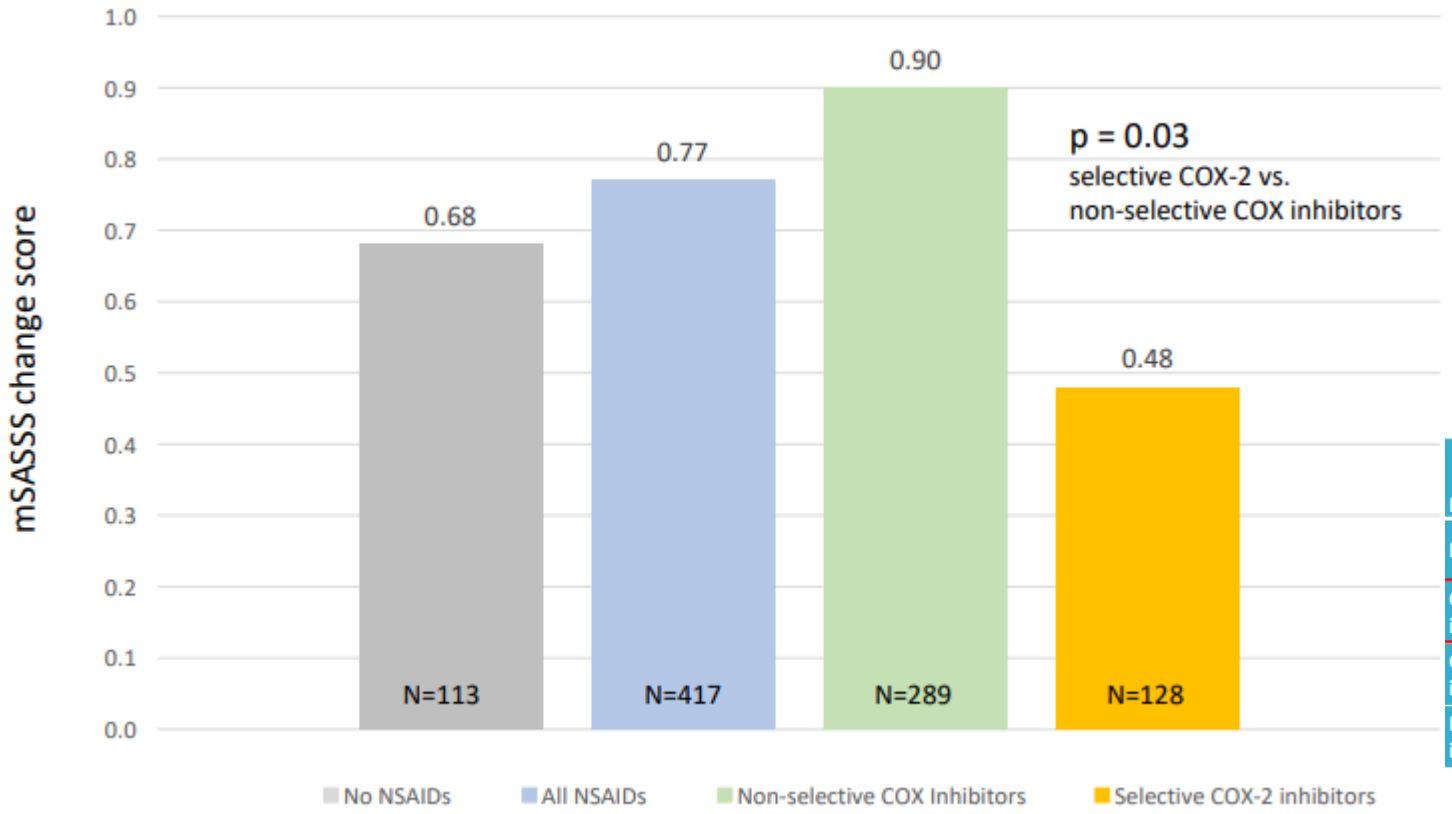
Total vBMD	Intra-articular	1.00 (0.61 to 1.63)	0.46 (0.20 to 1.10)
	Entheseal	0.69 (0.44 to 1.11)	**0.33 (0.13 to 0.83)**
Cortical vBMD	Intra-articular	0.80 (0.50 to 1.28)	0.51 (0.21 to 1.24)
	Entheseal	0.72 (0.46 to 1.12)	**0.32 (0.14 to 0.71)**

Treatment With Selective Cyclooxygenase-2 Inhibitors is Associated With Inhibition of Radiographic Spinal Progression in Patients With Axial Spondyloarthritis

Long-term Results From the German Spondyloarthritis Inception Cohort

- The aim of the current analysis was to evaluate the effect of NSAIDs including non-selective and selective COX-2 inhibitors on radiographic spinal progression in patients with axial SpA in a long-term inception cohort.

- **266 patients** contributed with a total of **542** 2-year **radiographic intervals**.



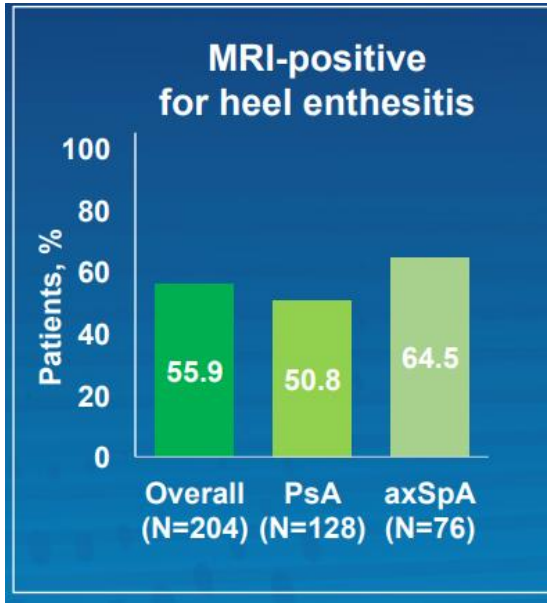
Parameter	Reference	Model 1 β (95% CI)*	Model 2 β (95% CI)*	Model 3 β (95% CI)*	Model 4 β (95% CI)*
NSAIDs intake	No NSAIDs	0.13 (-0.20 to 0.47)	-	-	-
COX-2-selective inhibitors	Non-selective inhibitors	-	**-0.30 (-0.58 to -0.01)**	-	-
COX-2-selective inhibitors	No NSAIDs	-	-	0.14 (-0.35 to 0.63)	-
Non-selective inhibitors	No NSAIDs	-	-	-	0.21 (-0.23 to 0.64)

Magnetic Resonance Imaging Characteristics in Patients with Spondyloarthritis and Clinical Diagnosis of Heel Enthesitis: Screening Data from a Phase 3 Trial

X Baraliakos[1], P Sewerin[2], E de Miguel[3], C Kleinmond[4], A Shekhawat[5], C Jentzsch[6], A Wiedon[6], and F Behrens[7] on behalf of the ACHILLES study group

- **ACHILLES** patients had to present with:
  - ✓Clinical diagnosis of Achilles tendon enthesitis according to swelling and tenderness at the insertional site of the Achilles tendon into the calcaneus

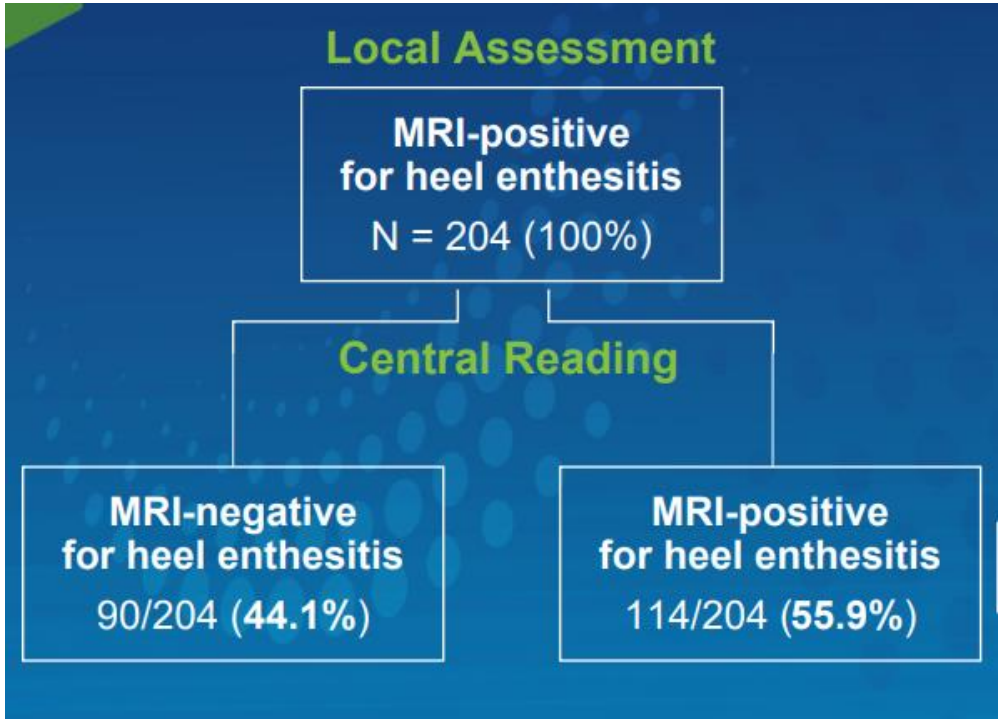
    AND
  - ✓Heel enthesitis that is MRI-positive according to the investigator`s judgment



MRI-positive heel enthesitis in ACHILLES:

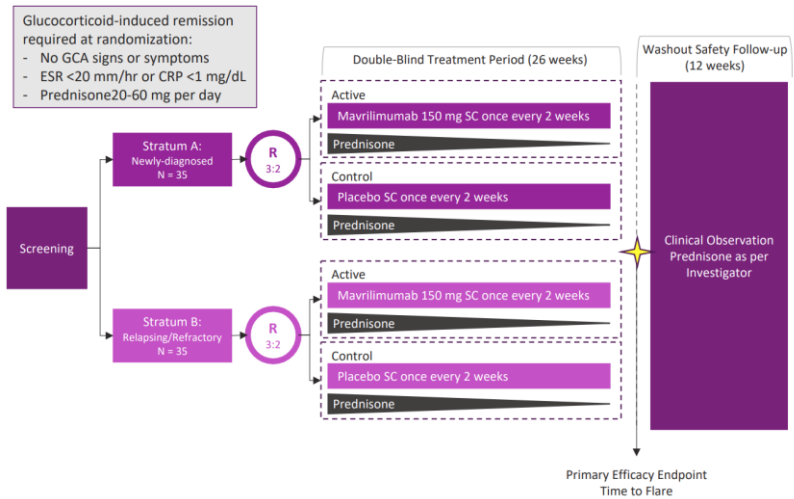
- **Tendinitis** and/or **bone marrow edema** in the area of the Achilles tendon and/or in the area of the plantar fascia

- Despite clinical assessment of enthesitis, only 56% of the ACHILLES patients presented with MRI-positive heel enthesitis according to central reading
- MRI screening results suggest that patients with HLA-B27 are more likely to be in the MRI-positive group



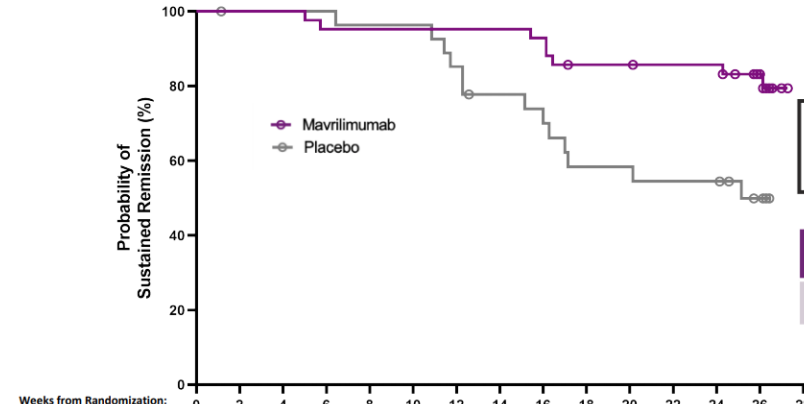
Mavrilimumab (anti GM-CSF receptor α monoclonal antibody) Reduces Risk of Flare and Increases Sustained Remission in a Phase 2 Trial of Patients with Giant Cell Arteritis

Maria C. Cid[1]*, Sebastian H. Unizony[2]*, Lara Pupim[3], Fang Fang[3], Joe Pirrello[3], Ai Ren[3], Manoj Samant[3], Teresa Zhou[3], John F. Paolini[3]



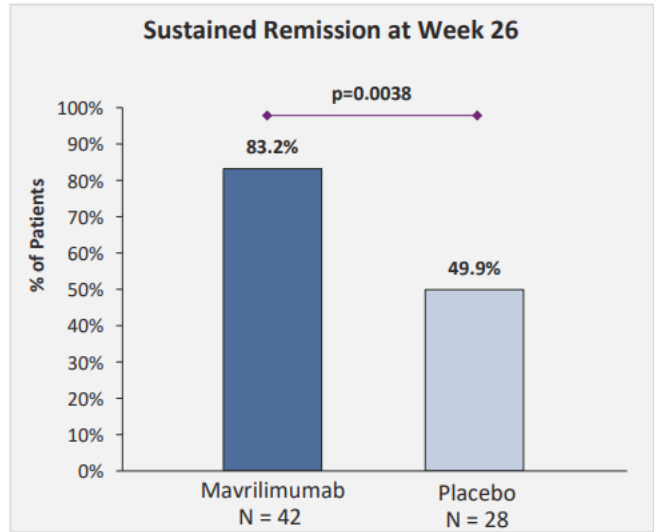
Mavrilimumab Significantly Reduced Risk of GCA Flare

Primary Efficacy Endpoint : Time to first adjudicated flare by Week 26 (All treated patients)



HR (95% CI) 0.38 (0.15, 0.92)
62% Risk Reduction
P = 0.0263

	Mavrilimumab (N=42)	Placebo (N=28)
Patients with Flare by Week 26, n (%)	8 (19)	13 (46.4)



Key Point

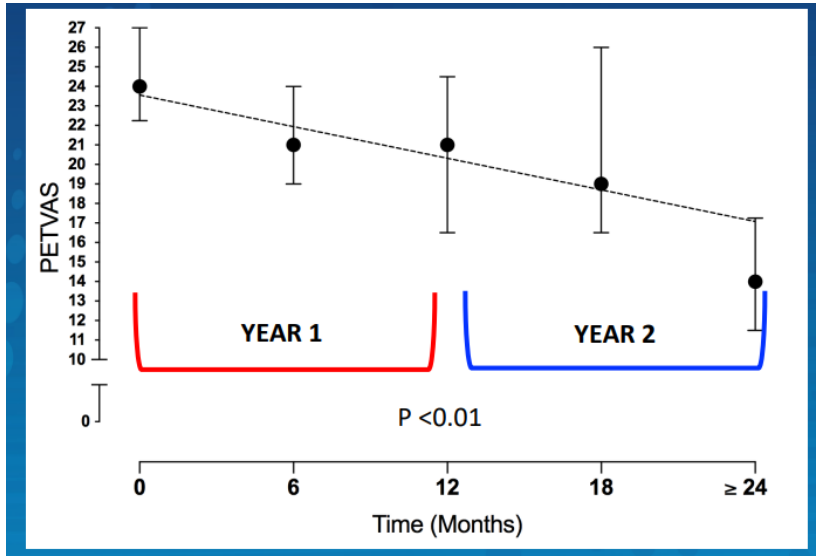
- The rate of sustained remission was 33.3 percentage points higher in the mavrilimumab than in the placebo group

Feasibility of 18F-fluorodeoxyglucose Positron Emission Tomography To Monitor the Effect of Tocilizumab on Vascular Inflammation in Giant Cell Arteritis: A Prospective, Longitudinal Study

Kaitlin A. Quinn, MD

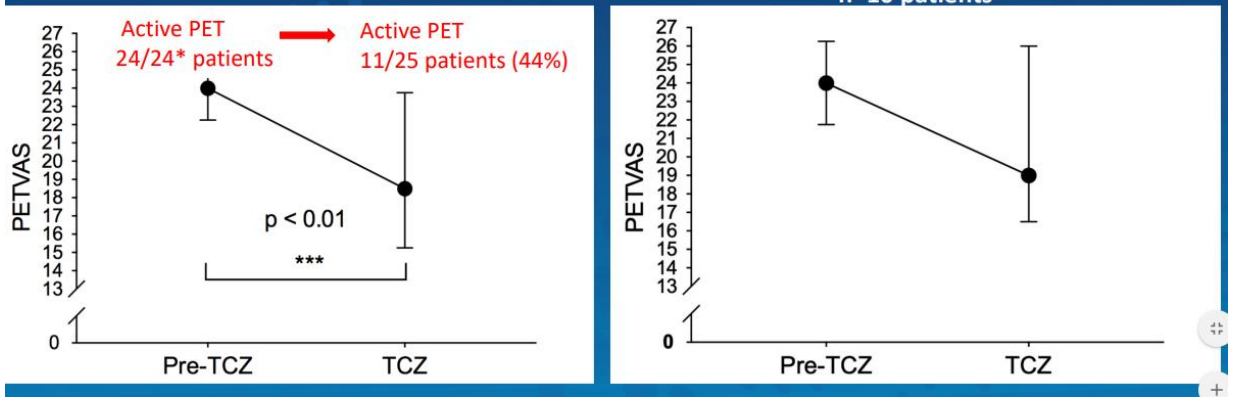
Objective

- Evaluate the time-dependent effects of tocilizumab on vascular inflammation as measured by FDG-PET in an observational cohort of patients with GCA

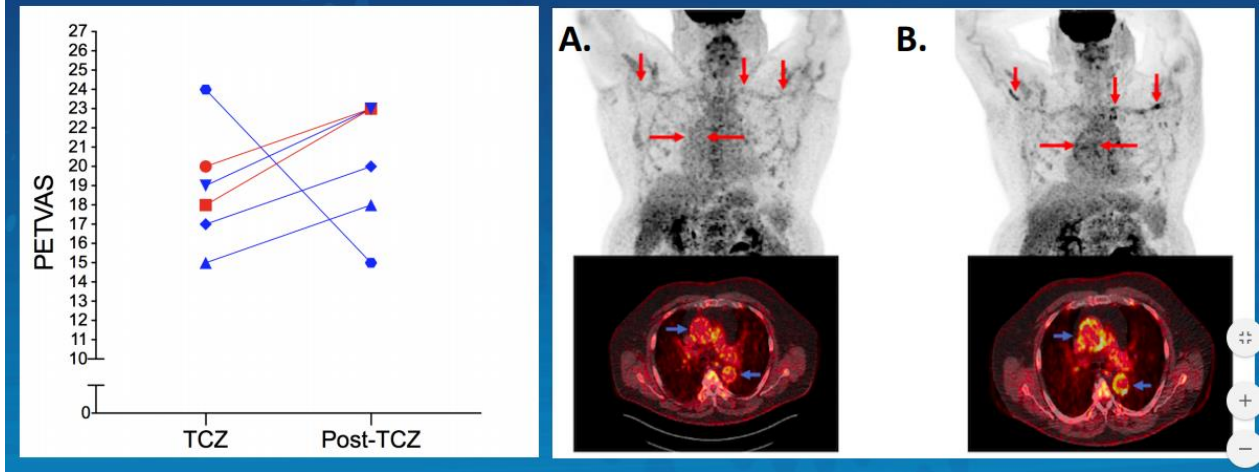


	Total (n=25 patients)
Age (years, IQR)	70.5 (63.7-75.9)
Gender (n, % female)	19 (76%)
Disease Duration (years, IQR)	1.5 (0.6-2.4)
Interpretation of PET* (n, % active)	24 (100%)
Clinical Disease Activity (n, % active)	25 (100%)
Temporal artery biopsy (n, % positive) LV-GCA (angiographic involvement) Both	10 (40%) 9 (36%) 6 (24%)
Methotrexate	14 (56%)
Prednisone (mg/day)	6 (0-23.8)

PET Activity in Response to Tocilizumab



PET Activity with Tocilizumab Discontinuation



Mass Spectrometry Identifies Novel Biomarkers in Giant Cell Arteritis (GCA)

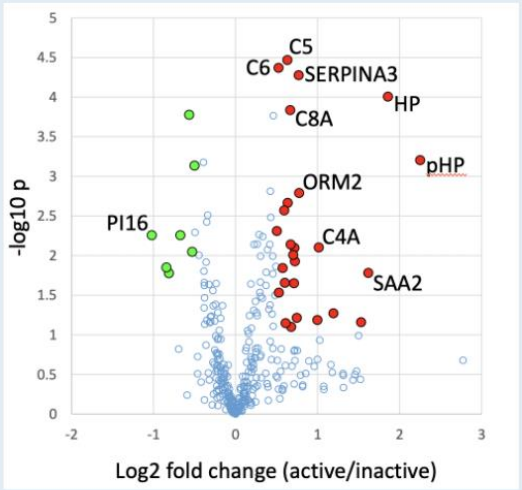
- Useful in Patients on Interleukin-6 Receptor Blockade -

Sebastian Unizony, Robert Morris, Johannes Kreuzer, Wilhelm Haas and John H Stone

- To identify biomarkers of disease activity in GCA patients treated with prednisone monotherapy
- To identify biomarkers of disease activity in GCA patients treated with prednisone in combination with TCZ

- 42 GCA patients with active and inactive disease were analyzed

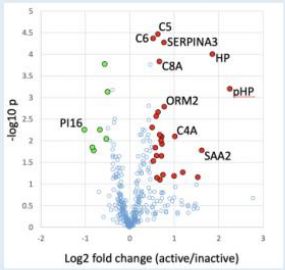
	PRED group		TCZ group	
	Active (n = 16)	Inactive (n = 5)	Active (n = 14)	Inactive (n = 7)
Age, mean (SD)	69 (9)	64 (9)	69 (9)	63 (8)
Time of sampling: weeks from baseline, mean (SD)	14 (12)	24 (0)	15 (10)	24 (0)
Prednisone dose at time of sampling: mg/d, mean (SD)	19 (23)	0.5 (0.5)	10 (11)	0 (0)
Tocilizumab weekly dosing, n (%)	NA	NA	9 (64)	7 (100)

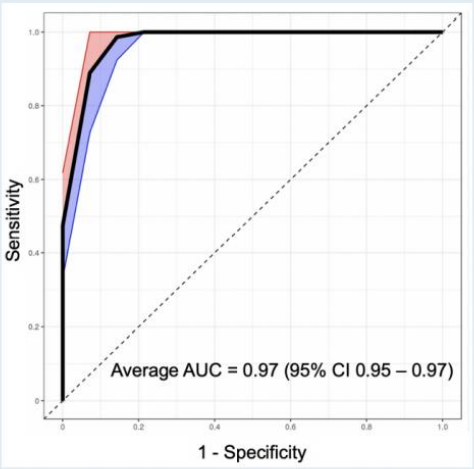


- Active TCZ-treated patients demonstrated overexpression of multiple biomarkers including haptoglobin, haptoglobin precursor, SSA2 and complement factors, and underexpression of peptidase inhibitor 16

	log2 fold change	P-value
Haptoglobin precursor (pHP)	2.3	0.0006
Haptoglobin (HP)	1.9	0.0001
Serum amyloid A2 (SAA2)	1.6	0.0165
Complement factor 4A (C4A)	1	0.0079
Alpha-1-acid glycoprotein 2 (ORM2)	0.8	0.0016
Alpha 1-antichymotrypsin (SERPINA3)	0.8	0.0001
Complement factor 8A (C8A)	0.7	0.0001
Complement factor 5 (C5)	0.6	<0.0001
Complement factor 6 (C6)	0.5	<0.0001
Peptidase Inhibitor 16 (PI16)	-1	0.0055

- Accuracy to discriminate active from inactive disease of the top 10 biomarkers in the TCZ group





- A signature of biomarkers classified disease activity status with high accuracy in each treatment group
- Haptoglobin, a readily available laboratory test, may be useful in monitoring disease activity in GCA patients receiving IL-6 blockade therapy

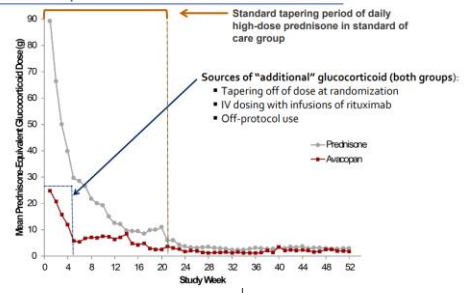
Are we saying goodbye to steroids in AAV?

The Effect on Renal Function of the Complement C5a Receptor Inhibitor Avacopan in ANCA-Associated Vasculitis: *Results from the ADVOCATE Trial*

Peter A. Merkel, Pirow Bekker, Huibin Yue, Catherine Kelleher, Thomas Schall, David Jayne, on behalf of the ADVOCATE investigators

November 6, 2020
American College of Rheumatology

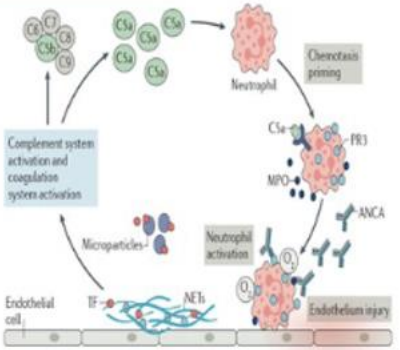
Average Weekly Glucocorticoid Usage Overtime by Treatment Groups



Background –AAV, Complement, and Avacopan

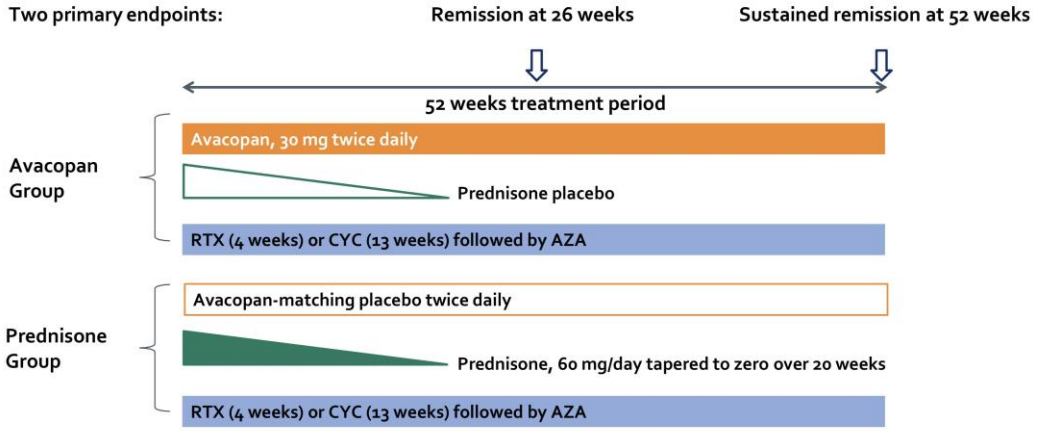
- **Pre-clinical data:**
  - C5a drives neutrophil activation in AAV via the C5a receptor
  - In an AAV animal model C5a receptor knock-out or antagonism stops the development of vasculitis
  - Avacopan is a highly selective oral inhibitor of the C5a receptor
- **Phase II trial data**
  - The CLEAR and CLASSIC Phase II trials in AAV demonstrated that avacopan has the potential to replace glucocorticoids, improve control of renal vasculitis, and reduce glucocorticoid toxicity, without additive toxicity

Jayne D et. al. *J Am Soc Nephrol* 2017; Merkel et. al. *ACR Open Rheum* (In Press)



Chen M et al. *Nat Rev Nephrol* 2017

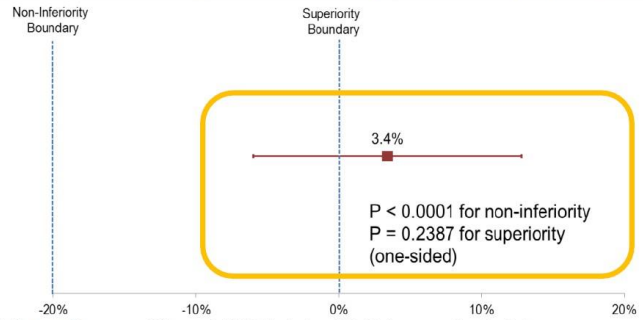
ADVOCATE Trial Design



Merkel P et al, *JIMR Res Protoc* 2020

Primary Endpoint, Disease Remission at Week 26

Treatment	n (%)	Estimate of Common Difference in Percentages	Two-Sided 95% CI	Non-Inferiority P-value*	Superiority P-value* (one sided)
Prednisone SOC (N=164)	115 (70%)				
Avacopan (N=166)	120 (72%)	3.4	(-6.0, 12.8)	<0.0001	0.2387

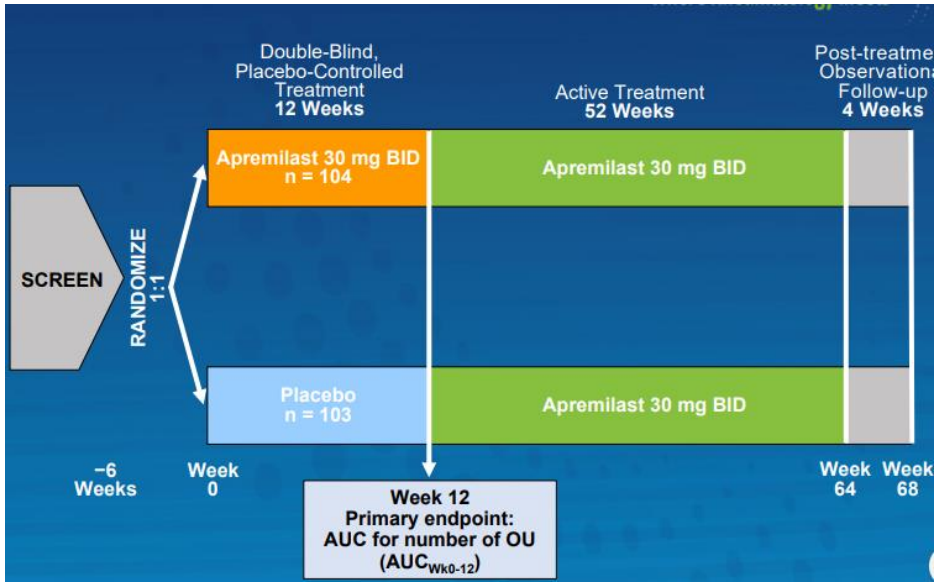


**Boundary for non-inferiority > -20% ; boundary for superiority > 0%*

Efficacy of Apremilast for the Treatment of Manifestations of Behçet's Syndrome Other Than Oral Ulcers, Including Skin Lesions and Arthritis

Gülen Hatemi[1]; Alfred Mahr[2]; Mitsuhiro Takeno[3]; Doyoung Kim[4]; Melike Melikoğlu[1]; Sue Cheng[5]; Sven Richter[5]; Michele Brunori[6]; Maria Paris[5]; Mindy Chen[5]; Yusuf Yazici[7]

Prof Hatemi report on apremilast in Behcets disease. We know it improves oral ulcers. Now shown to improve skin lesions and arthritis

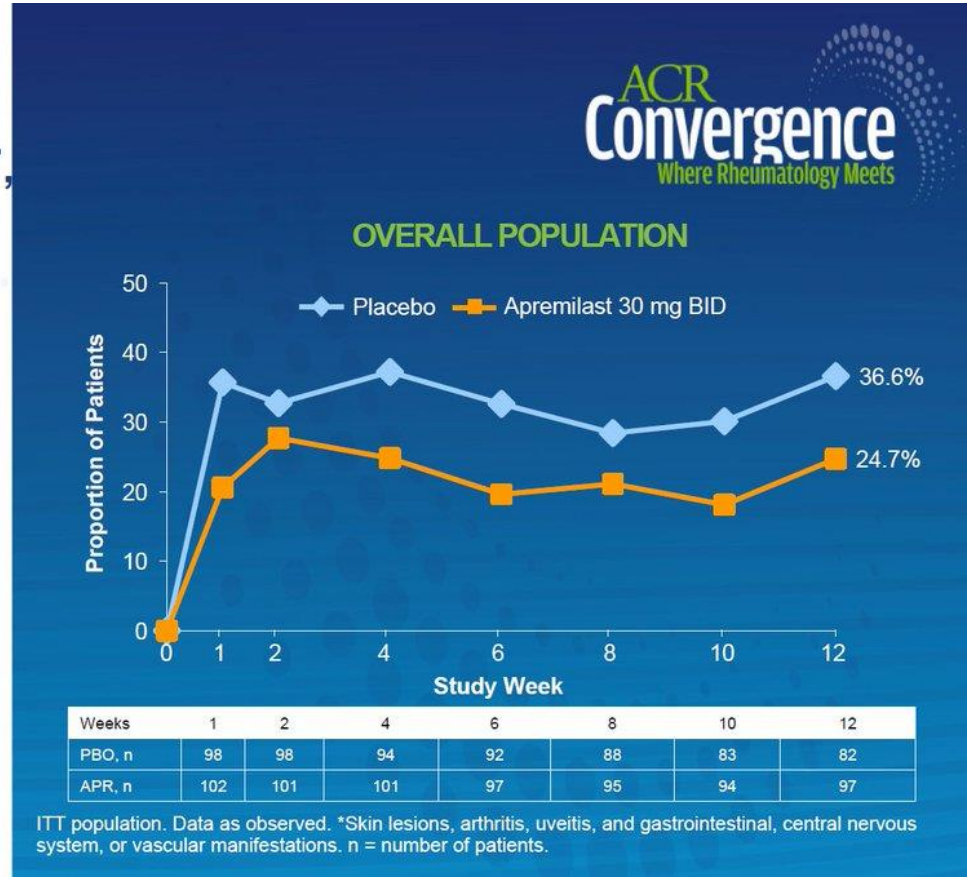


PATIENTS REPORTING ≥1 NEW, RECURRENT, WORSENING NON-OU MANIFESTATIONS*

New
Occurrence of manifestation absent at baseline

Recurrent
Manifestation not active at baseline but reported in the patient's disease history

Worsening
Worsening of manifestation from baseline



Weeks	1	2	4	6	8	10	12
PBO, n	98	98	94	92	88	83	82
APR, n	102	101	101	97	95	94	97

ITT population. Data as observed. *Skin lesions, arthritis, uveitis, and gastrointestinal, central nervous system, or vascular manifestations. n = number of patients.

Abstr#512

Efficacy and Safety Results from a Phase 2, Randomized, Double-blind Trial of BIIB059, an Anti-Blood Dendritic Cell Antigen 2 Antibody, in Systemic Lupus Erythematosus

Furie RA,[1] van Vollenhoven RF,[2] Kalunian K,[3] Navarra S,[4] Romero-Diaz J,[5] Werth VP,[6] Huang X,[7] Carroll H,[7] Meyers A,[7] Musselli C,[7] Barbey C,[8] Franchimont N[7]

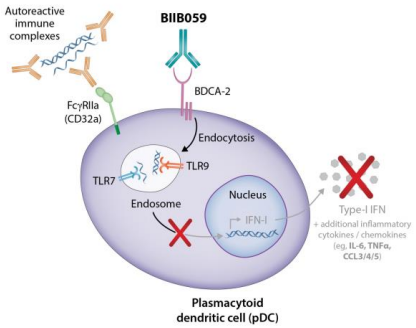
BIIB059 is a humanized IgG1 mAb that binds **BDCA2**[1]

- The **binding** of **BIIB059** to **BDCA2** leads to rapid internalization of BDCA2 from the cell surface of pDCs and **inhibits** the production of **pDC-derived IFN-Is,** cytokines, and chemokines[1]

In a **Phase 1 SLE study** (NCT02106897), BIIB059[2]:

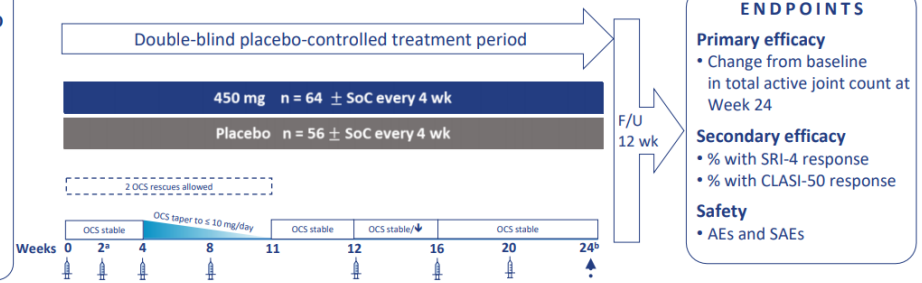
- Showed proof of biology with decreased expression of IFN-response genes in whole blood and IFN-modulated proteins, MxA, in lesional skin
- Reduced skin disease activity assessed by CLASI-A score
- Was associated with an acceptable safety profile

Proposed Role of BIIB059 in CLE/SLE



28-DAY SCREENING PERIOD

- ANA and/or anti-dsDNA antibody positive
- Stable lupus SoC
- Stable OCS (≤ 20 mg/day)
- Joint count:
  - ≥ 4 tender joints
  - ≥ 4 swollen joints
- Active skin disease (SLEDAI-2K)



ENDPOINTS

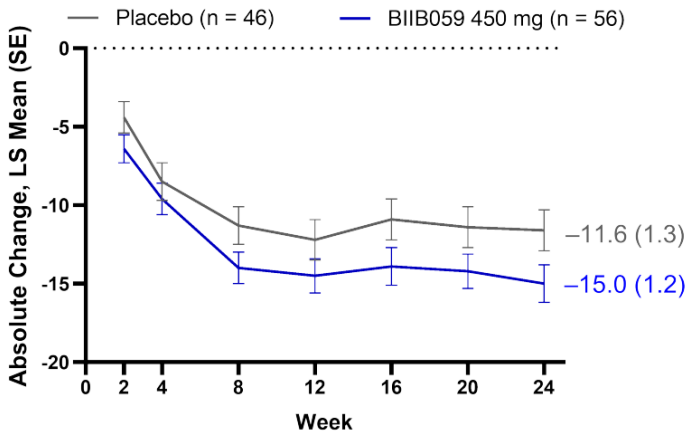
Primary efficacy
- Change from baseline in total active joint count at Week 24

Secondary efficacy
- % with SRI-4 response
- % with CLASI-50 response

Safety
- AEs and SAEs

Primary Endpoint: Change in Total Active Joint Count

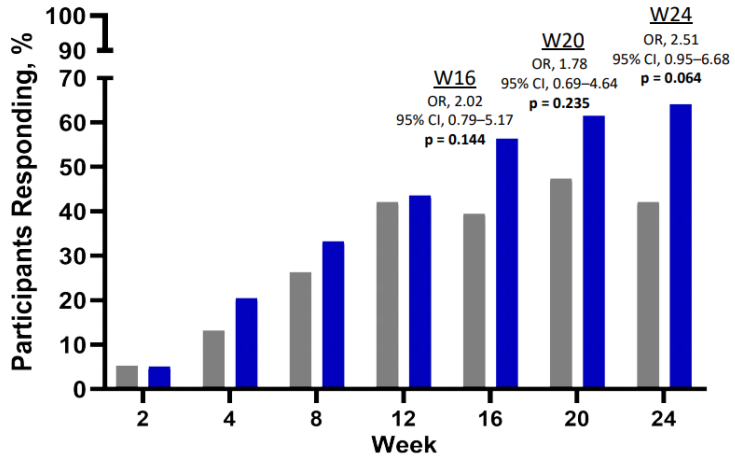
- At Week 24, the least-squares mean difference (95% CI) in **total active joint count**, defined as the sum of the tender joint count and swollen joint count, from baseline was:
  –3.4 (– 6.7 to – 0.2; p = 0.037)



Secondary Endpoint: CLASI-50 Response Rate

Treatment assignments of patients with baseline CLASI-A ≥ 8

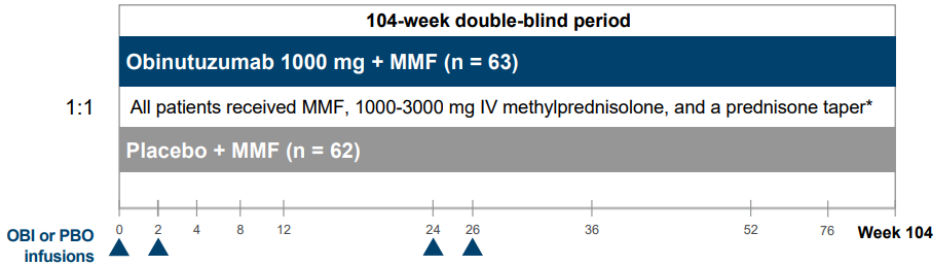
- Placebo (n = 38)
- BIIB059 450 mg (n = 39)



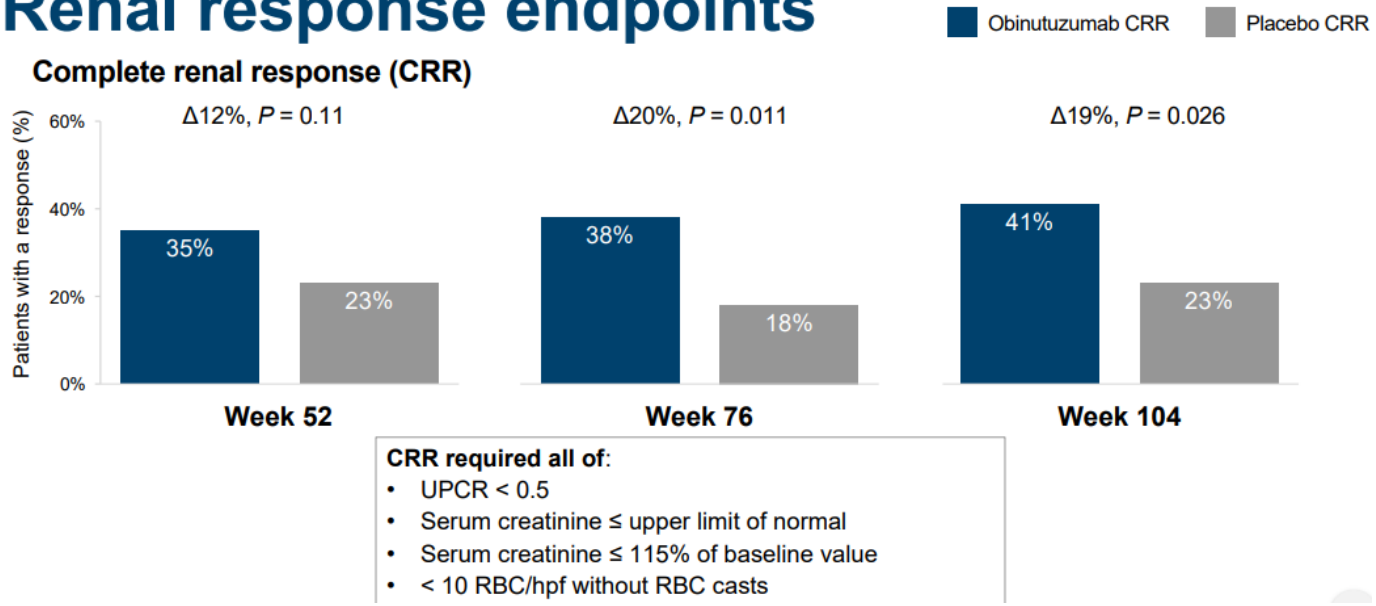
Two-Year Results from a Randomized, Controlled Study of Obinutuzumab for Proliferative Lupus Nephritis

Richard Furie[1], Gustavo Aroca[2], Analía Alvarez[3], Hilda Fragoso-Loyo[4], Elizabeth Zuta Santillán[5], Brad H. Rovin[6], Paul G. Brunetta[7], Thomas Schindler[8], Imran Hassan[9], Matthew D. Cascino[7], Jay P. Garg[7], Ana Malvar[10]

Phase 2 NOBILITY study design

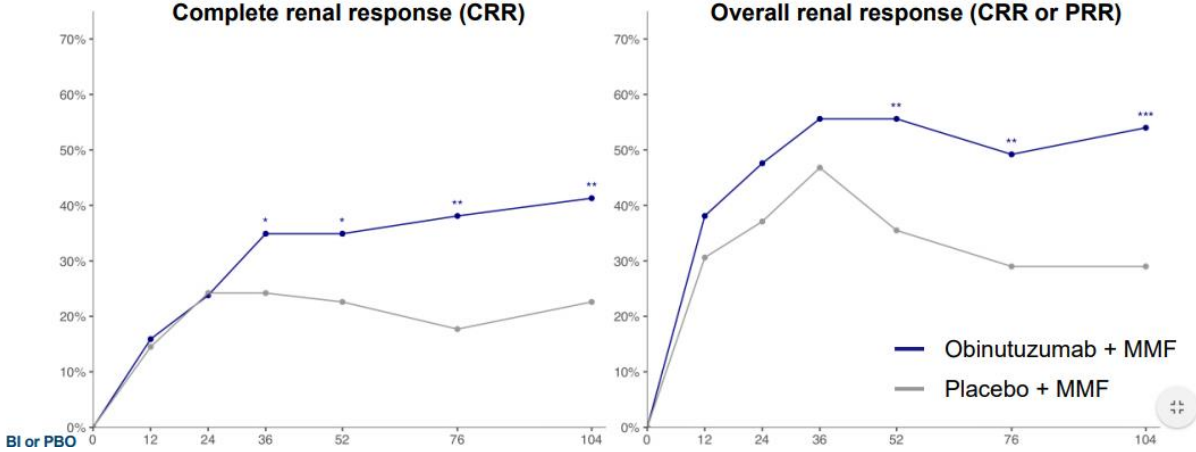


Renal response endpoints



	Obinutuzumab + MMF (n = 63)	Placebo + MMF (n = 62)
Female	55 (87%)	51 (82%)
Age	33.1 ± 9.8	31.9 ± 10.1
Race/ethnicity		
Hispanic	**42 (67%)**	**49 (79%)**
White	28 (44%)	26 (42%)
Black	**6 (10%)**	**5 (10%)**
Prior history of LN	40 (64%)	35 (57%)
Class IV LN	49 (78%)	44 (71%)
Concomitant class V LN	20 (32%)	17 (27%)
Serum creatinine – mg/dL	0.87 ± 0.34	0.80 ± 0.33
Serum creatinine ≤ ULN	51 (81%)	55 (89%)
UPCR	**3.3 ± 2.7**	**2.9 ± 2.5**
Anti-dsDNA positive	**31 (49%)**	**36 (58%)**
C3 < 90 mg/dL	**43 (68%)**	**37 (60%)**
C4 < 16 mg/dL	37 (59%)	44 (71%)

Renal responses over time



Plenary session 1 no#2F011

ACR Convergence
Where Rheumatology Meets

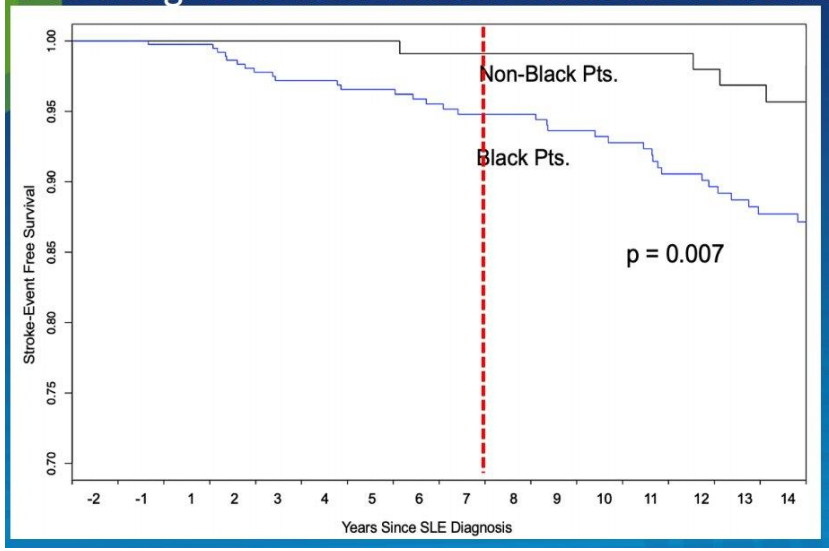
Racial Disparities and New SLE-Specific Predictors of Stroke and Ischemic Heart Disease in Patients with Lupus

Shivani Garg MD MS
Assistant Professor of Medicine, Division of Rheumatology
University of Wisconsin School of Medicine and Public Health
Co-authors: Christie M. Bartels[1], Gaobin Bao[2], Cristina Drenkard[2], S. Sam Lim[2]

School of Medicine and Public Health
UNIVERSITY OF WISCONSIN-MADISON [1]

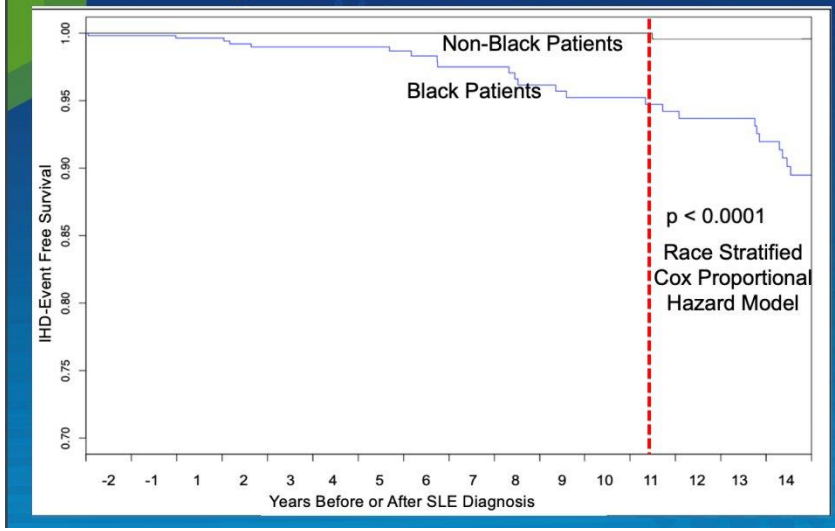
EMORY UNIVERSITY SCHOOL OF MEDICINE [2]

3-fold Higher STROKE Risk in Black SLE Patients



Race Stratified Cox Proportional Hazard Model

24-fold Higher IHD Risk in Black SLE Patients



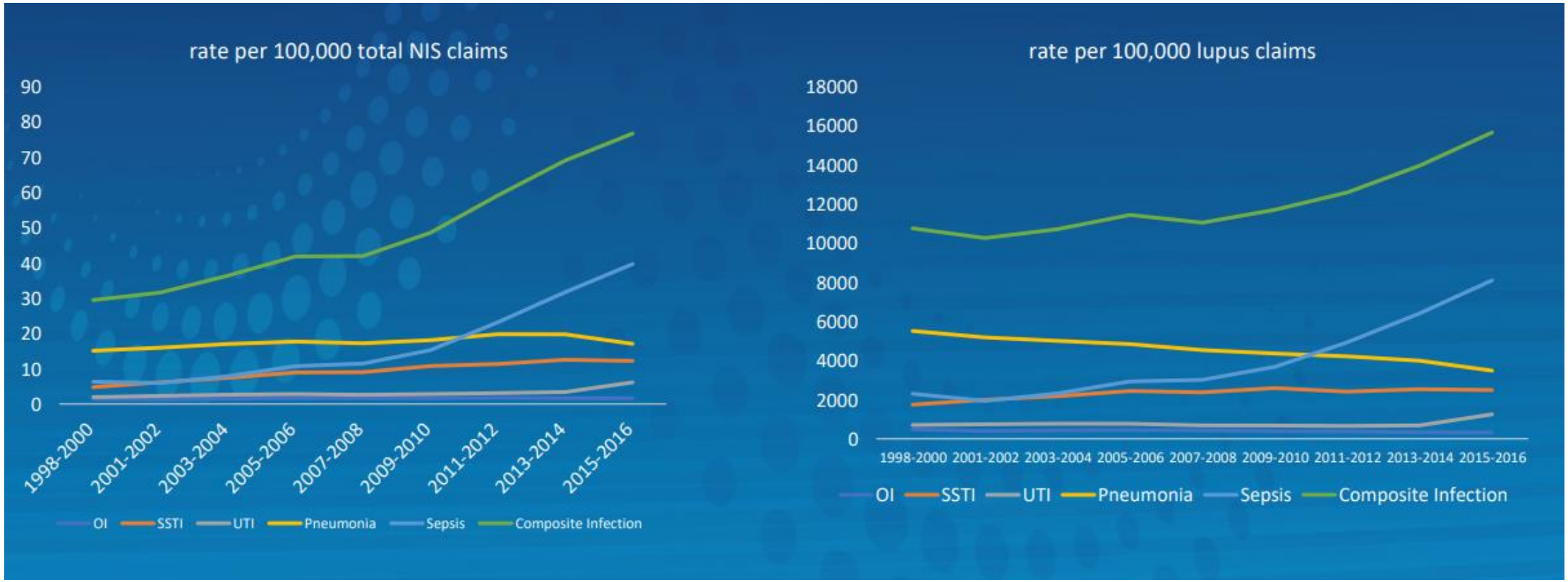
Hospitalized Infections in Lupus: A Nationwide Study of Types of Infections, Time-trends, Healthcare Utilization and In-Hospital Mortality

Jasvinder A. Singh, John D. Cleveland
2020 American College of Rheumatology Convergence Annual Meeting
SLE: Diagnosis, Manifestations, & Outcomes 1: Morbidity
Saturday, November 7, 2020; 4:30 PM - 6:00 PM

- (1) To examine the differences by lupus in hospitalized infections;
- (2) To assess the incidence and time-trends in five common hospitalized infections and associated health care utilization in people with lupus from 1998 to 2016; and
- (3) To analyze the predictors of health care utilizatio and in-hospital mortality in patients with lupus hospitalized with infections.

- We used the U.S. Nationwide Inpatient Sample (NIS) data from 1998-2016, a 20% stratified sample of all discharge records (17)
- 5 types of hospitalized infections identified by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes in the primary position:

(1) pneumonia (003.22, 481.0, 513.0, 480.xx, 482.xx, 483.xx, 485.xx, and 486.xx);
(2) sepsis/bacteremia (referred to as sepsis from here onwards; 038.xx and 790.7);
(3) urinary tract infection (UTI; 590.xx);
(4) skin and soft tissue infections (SSTI; 040.0, 569.61, 681.xx, 682.xx, 785.4, 728.8 035.xx);
(5) opportunistic infections (OI; 010.xx –018.xx, 031.xx, 078.5, 075.xx, 053.xx, 112.4 112.5, 112.81, 112.83, 130.xx, 136.3, 117.5, 027.0, 039.xx, 117.3, 114.xx, 115.xx, 116.0), as previously (15, 18).



Sepsis surpassed pneumonia in 2011-12

Hydroxychloroquine Use Was Not Associated With QTc Length in a Large Cohort of SLE and RA Patients

Elizabeth Park[1], Jon T. Giles[1], Thania Perez-Recio[1], Paloma Pina[2], Christopher Depender[1], Joan Bathon[1], Laura Geraldino-Pardilla[1]

1 Columbia University Medical Center; New York, New York

2 Northwestern Medicine; Chicago, IL

N=530

Clinical Characteristics	HCQ (n=371)	NO HCQ (n=159)	p-value
Female n (%)	329 (89)	136 (87)	0.51
Age (Mean ± SD)	**46.3 (14.1)**	**55.3 (13.1)**	**<0.005**
Race			
White n (%)	**83 (23)**	**57 (37)**	**0.001**
Black n (%)	**107 (29)**	**33 (21)**	**0.052**
Hispanic n (%)	166 (46)	60 (38)	0.13
Other n (%)	8 (2)	6 (3.8)	0.29
Disease Duration Years (Mean ± SD)	12.4 (9.03)	11.5 (12.3)	0.43
Biologics n (%)	67 (28.1)	59 (37.1)	0.060
Steroids n (%)	**293 (86.2)**	**61 (38.4)**	**<0.005**
HTN n (%)	170 (46.1)	76 (49)	0.54
DM n (%)	**25 (6.7)**	**20 (12.5)**	**0.02**
Smoking n (%)	23 (6.2)	15 (9.5)	0.18
Statin n (%)	**79 (32.4)**	**30 (18.9)**	**0.003**
ASA n (%)	**147 (57.2)**	**31 (19.5)**	**<0.005**

Adjusted QTc Was Comparable Between HCQ vs. NO HCQ

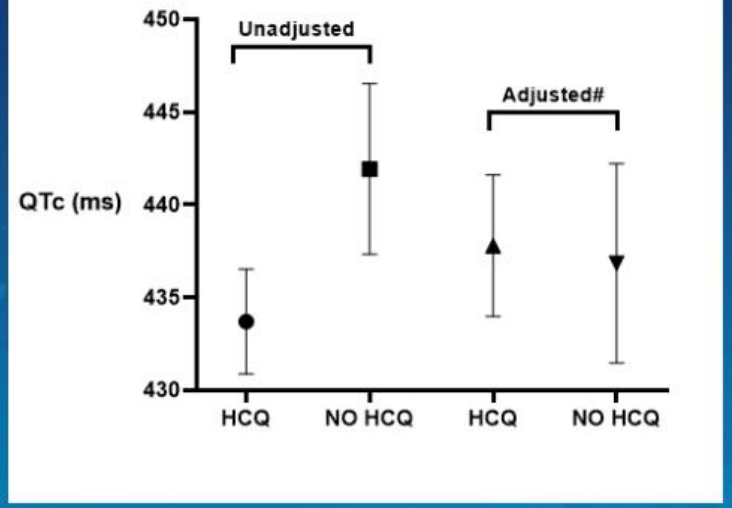


Figure 1. QTc length and 95% CI in HCQ vs. NO HCQ in combined SLE/RA cohorts

#Adjusting for age, race, current prednisone use, hypertension, current smoking, diabetes, and aspirin use, anti-microbial use

- Hydroxychloroquine use was **NOT ASSOCIATED** with QTc length in a large cohort of SLE and RA patients, while adjusting for important confounders

Outcomes Following Antimalarial Withdrawal in Patients with Quiescent Systemic Lupus Erythematosus

Danaë Papachristos, Jiandong Su, Dafna D Gladman, Murray B Urowitz

Centre for Prognosis Studies in Rheumatic Diseases, Toronto Lupus Clinic, University Health Network, Toronto, Ontario, Canada

NOVEMBER 5-9

- Case-control study
- University of Toronto Lupus Clinic long-term observational cohort study
  - Prospectively collected data
- Cases: achieved clinical remission ≥1yr then ceased AM (index date)
- Controls: achieved clinical remission ≥1yr and continued AM

- 1573 lupus patients ever treated with AM
- 165 cases had at least 1yr clinical remission, of whom 96 had 2yrs F/U
- Of 96 cases, 88 matched to one control, 85 to a second control (near 2:1 match)
- Total: 88 cases, 173 controls

RESULTS

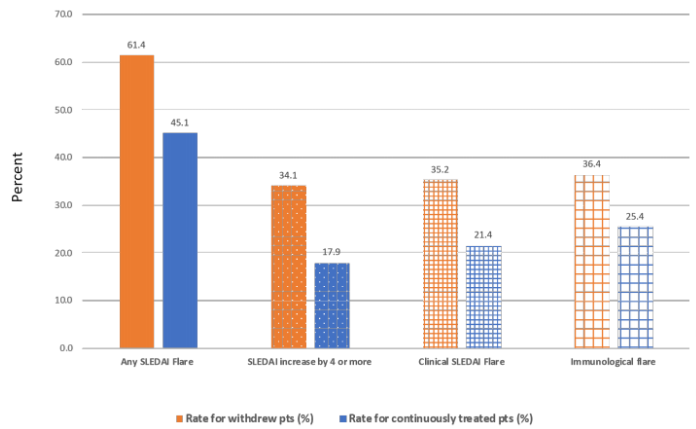
AM withdrawn vs. continued

Multivariate analysis:

- Adjusted for demographics, disease activity, treatment
- OR for flare if AM ceased vs. continued = 2.26 (95%CI: 1.24-4.11, p = 0.008)

ACR Convergence Where Rheumatology Meets

Rates of Flare for Patients who Withdrew vs. Continued AM



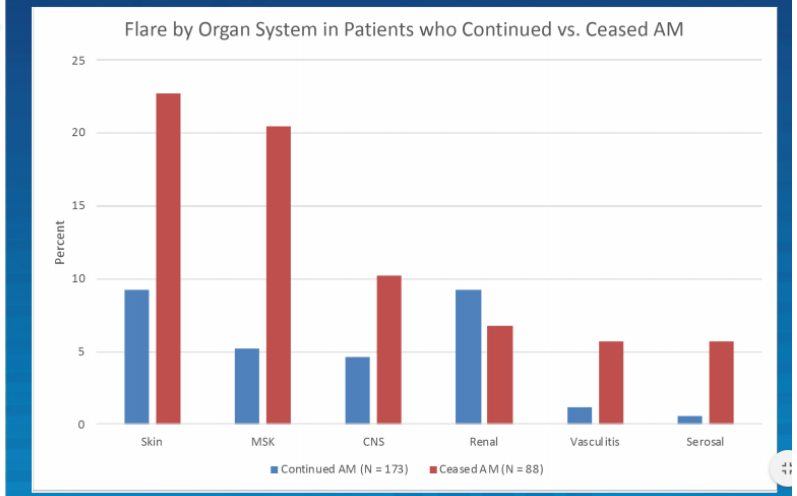
FLARE BY ORGAN SYSTEM

Most common clinical flare types:

- Cutaneous
- Musculoskeletal

ACR Convergence Where Rheumatology Meets

Flare by Organ System in Patients who Continued vs. Ceased AM



Outcomes Following Antimalarial Withdrawal in Patients with Quiescent Systemic Lupus Erythematosus

Danaë Papachristos, Jiandong Su, Dafna D Gladman, Murray B Urowitz

Centre for Prognosis Studies in Rheumatic Diseases, Toronto Lupus Clinic, University Health Network, Toronto, Ontario, Canada

NOVEMBER 5-9

RESULTS

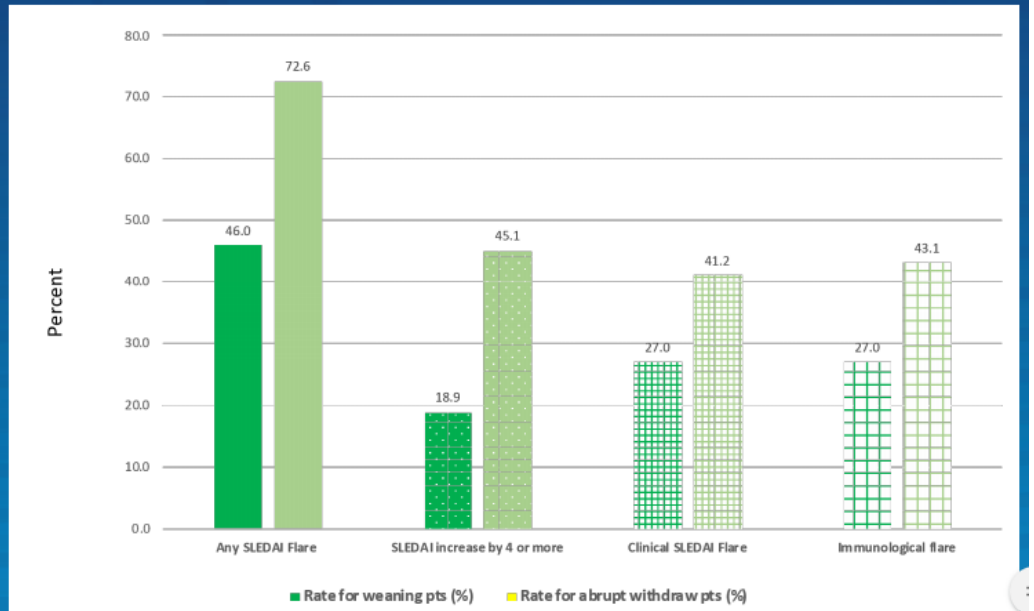
Taper vs. abrupt cessation

Multivariate analysis:

- OR flare (abrupt vs. taper withdrawal) 3.42 (95% CI: 1.26-9.26, p = 0.016)

ACR Convergence
Where Rheumatology Meets

Rates of Flare for Taper vs. Abrupt Withdrawal of AM



- AMs aid in preventing flare, even for patients in prolonged clinical remission
- If therapy is withdrawn, taper results in lower rates of flare
  - Similar to rates seen in those who continue

The Value of Renal Biopsy at Lower Levels of Proteinuria in Patients Enrolled in The Lupus Accelerating Medicines Partnership

American College of Rheumatology
November 8, 2020

Philip Carlucci, Kristina Deonaraine, Andrea Fava, Jessica Li, David Wofsy, Judith A. James, Chaim Putterman, Betty Diamond, Derek Fine, Jose Monroy-Trujillo, Kristin Haag, William Apruzzese, H. Michael Belmont, Peter Izmirly, Sean Connery, Fernanda Payan-Schober, Richard Furie, Celine Berthier, Maria Dall'Era, Kerry Cho, Diane Kamen, Kenneth Kalunian, the Accelerating Medicines Partnership in SLE network, Michelle Petri and Jill Buyon

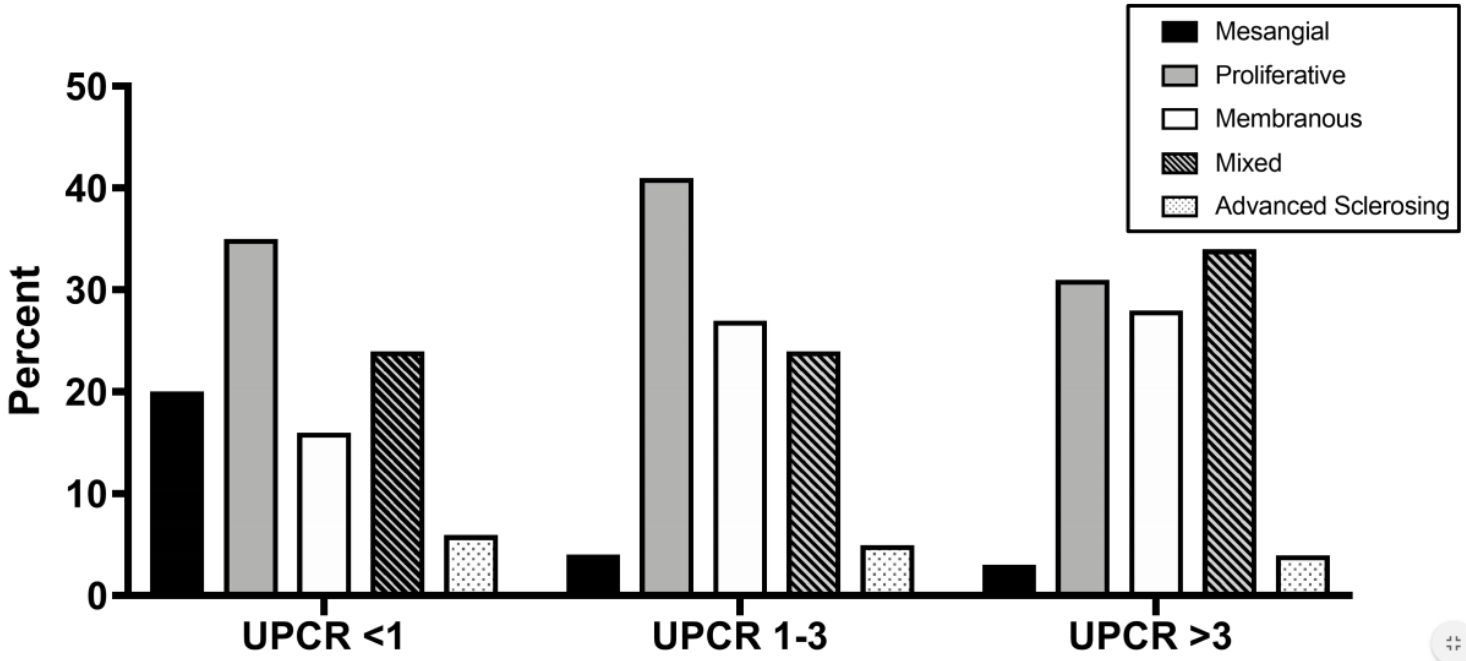
Objective:

To leverage the well-characterized AMP lupus nephritis cohort, to address whether urine protein to creatinine ratios (UPCR) between .5 and 1 differ from higher ratios with regard to clinical, serologic and histologic variables and whether clinical characteristics can distinguish patients with UPCR less than 1 based on renal pathology

Increased Proteinuria Associated with Active Urinary Sediment

Baseline Characteristics	UPCR < 1 N=55	UPCR 1 - 3 N=128	UPCR > 3 N=100	<1 vs >3 p-value
Hematuria (> 5 RBC)	13 (25%)	54 (43%)	50 (51%)	**0.003**
Pyuria (> 5 WBC)	14 (26%)	51 (41%)	50 (51%)	**0.007**
Casts	0 (0%)	3 (3%)	1 (1%)	1.00
No Sediment	25 (53%)	43 (37%)	32 (34%)	**0.04**

UPCR <1 is Not a Reliable Predictor of Biopsy Class



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The Absence of an Active Sediment in Patients with UPCR <1 Does Not Reassure Mild Disease

Baseline Characteristics	I or II N=11	III, IV, V, Mixed N=41
No Sediment, (N%)	7 (88%)	15 (42%)
Hematuria, N (%)	1 (11%)	12 (29%)
Pyuria, N (%)	0 (0%)	14 (34%)
Casts, N (%)	0 (0%)	0 (0%)

- Patients with UPCR >3 were more likely to have relapsed disease
- Patients with UPCR <1 had increased mesangial histology but frequencies of other classes and activity/chronicity were similar among all proteinuria levels
- No serologic variables distinguished patients with UPCR <1 with mesangial histology, from those with UPCR <1 and proliferative or membranous histology
- Nearly half of patients with UPCR <1 and proliferative or membranous histology had no active sediment

Renal Responder Status and Associated Clinical Variables in the Lupus Accelerating Medicines Partnership cohort

American College of Rheumatology
November 8, 2020

Philip Carlucci, Andrea Fava, Kristina Deonaraine, Jessica Li, David Wofsy, Judith A. James, Chaim Putterman, Betty Diamond, Derek Fine, Jose Monroy-Trujillo, Kristin Haag, William Apruzzese, H. Michael Belmont, Peter Izmirly, Sean Connery, Fernanda Payan-Schober, Richard Furie, Celine Berthier, Maria Dall'Era, Kerry Cho, Diane Kamen, Kenneth Kalunian, the Accelerating Medicines Partnership in SLE network, Michelle Petri and Jill Buyon

Objective:

To leverage the well-characterized multi-center AMP cohort to evaluate renal responses of provider chosen standard of care in a real-world setting that is not impacted by the controlled environment of a clinical trial.

Phase 2: Overall Response Rates for First and Repeat Biopsies

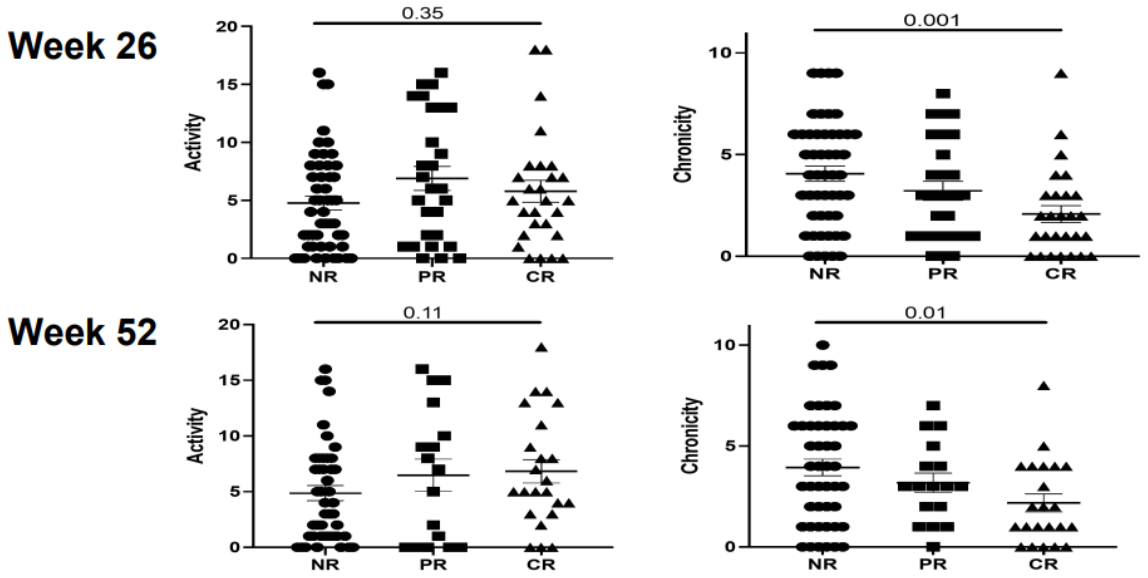
Response at 26 weeks	All patients N=136	First Biopsy N=49	Repeat Biopsy N=87
CR	36 (26%)	18 (37%)	18 (21%)
PR	33 (24%)	15 (31%)	18 (21%)
NR	67 (49%)	16 (33%)	51 (59%)

Response at 52 weeks	All patients N=118	First Biopsy N=40	Repeat Biopsy N=78
CR	31 (26%)	16 (40%)	15 (19%)
PR	26 (22%)	8 (20%)	18 (23%)
NR	61 (52%)	16 (40%)	45 (58%)

Phase 2: Greater Proportion of Complete Responders at 26 weeks were Taking MMF and/or prednisone at 12 weeks

Medications at 12 weeks	CR at 26 weeks N=34	PR at 26 weeks N=33	NR at 26 weeks N=64	CR vs NR p-value
Hydroxychloroquine	26 (77%)	27 (82%)	54 (86%)	0.39
Azathioprine	1 (3%)	0 (0%)	7 (11%)	0.31
Tacrolimus	3 (9%)	3 (9%)	8 (13%)	0.78
Mycophenolate Mofetil	28 (82%)	24 (73%)	38 (60%)	0.07
Rituximab	1 (3%)	1 (3%)	2 (3%)	0.99
Cyclophosphamide	3 (9%)	3 (9%)	8 (13%)	0.78
Pulse steroids	0 (0%)	0 (0%)	0 (0%)	-
Prednisone	27 (80%)	24 (73%)	34 (54%)	0.02

Phase 2: Lower Chronicity Index at Baseline Associated with Complete Response at 26 and 52 weeks



Renal Responder Status and Associated Clinical Variables in the Lupus Accelerating Medicines Partnership cohort

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November 8, 2020

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Phase 2 : Greater Number of Complete Responders have Proliferative Compared to Membranous Histology

Week 26

Class	CR N=36	PR N=33	NR N=67	NR vs CR P-value
Membranous	6 (17%)	7 (21%)	25 (37%)	**0.03**
Mixed	11 (31%)	13 (39%)	18 (27%)	0.69
Proliferative	19 (53%)	13 (39%)	24 (36%)	0.09

Week 52

Class	CR N=31	PR N=26	NR N=61	NR vs CR P-value
Membranous	4 (13%)	8 (31%)	22 (36%)	**0.02**
Mixed	11 (36%)	11 (42%)	19 (31%)	0.67
Proliferative	16 (52%)	7 (27%)	20 (33%)	0.08

- Complete response in the AMP SLE cohort was 26% and early responses were generally sustained over time
- First biopsy patients had higher response rates than relapsed patients
- Lower chronicity but not activity index associated with complete response
- Proliferative histology associated with complete response

Abstr#938

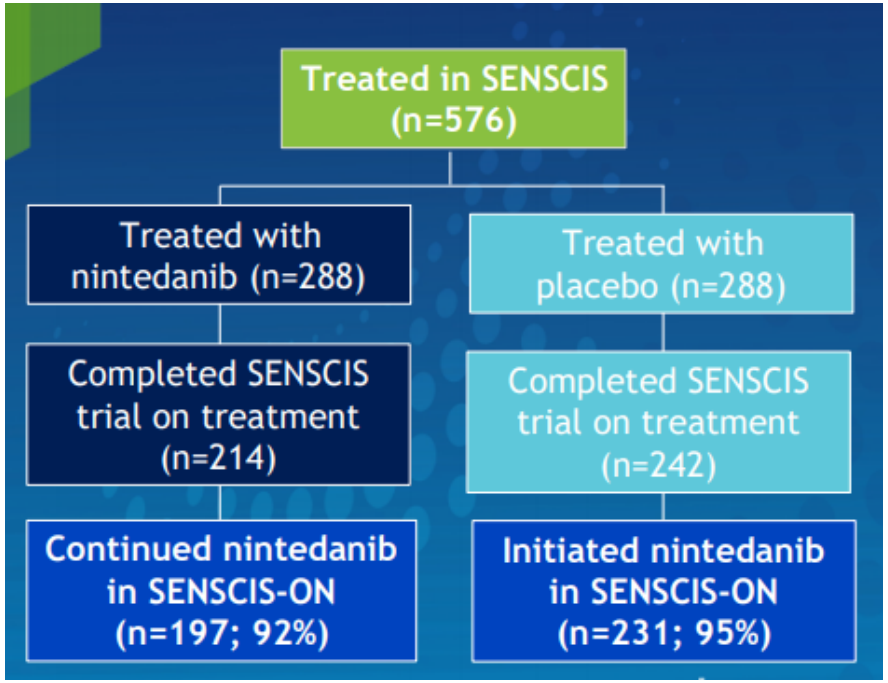
We performed a multicentric study (461 pregnancies from 10 Italian Centers and 1 Russian Center were included) and collected retrospectively data on pregnancies in women with **primary APS** (n=293) and **aPL carriers** with persistent positivity(n=168).

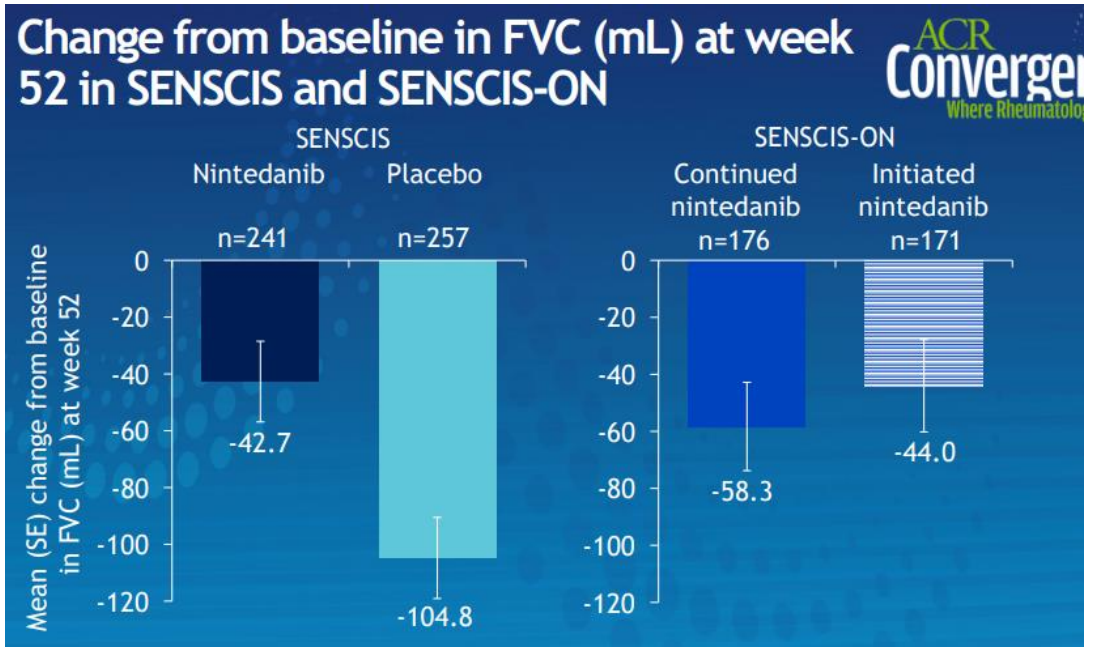
	All pregnancies		p
Gestational outcome	Low C3/C4 (n=97)	Normal C3/C4 (n=134)	
Term live birth (≥37w)	59 (60%)	96 (72%)	ns
Preterm live birth (<37w)	19 (20%)	27 (20%)	ns
Pregnancy losses (abortion and miscarriages)	19 (20%)	11 (8%)	0.01
Maternal complications			
PE	5 (5%)	4 (3%)	ns
DVT	1 (1%)	0 (0%)	ns
thrombocytopenia	1 (1%)	0 (0%)	ns

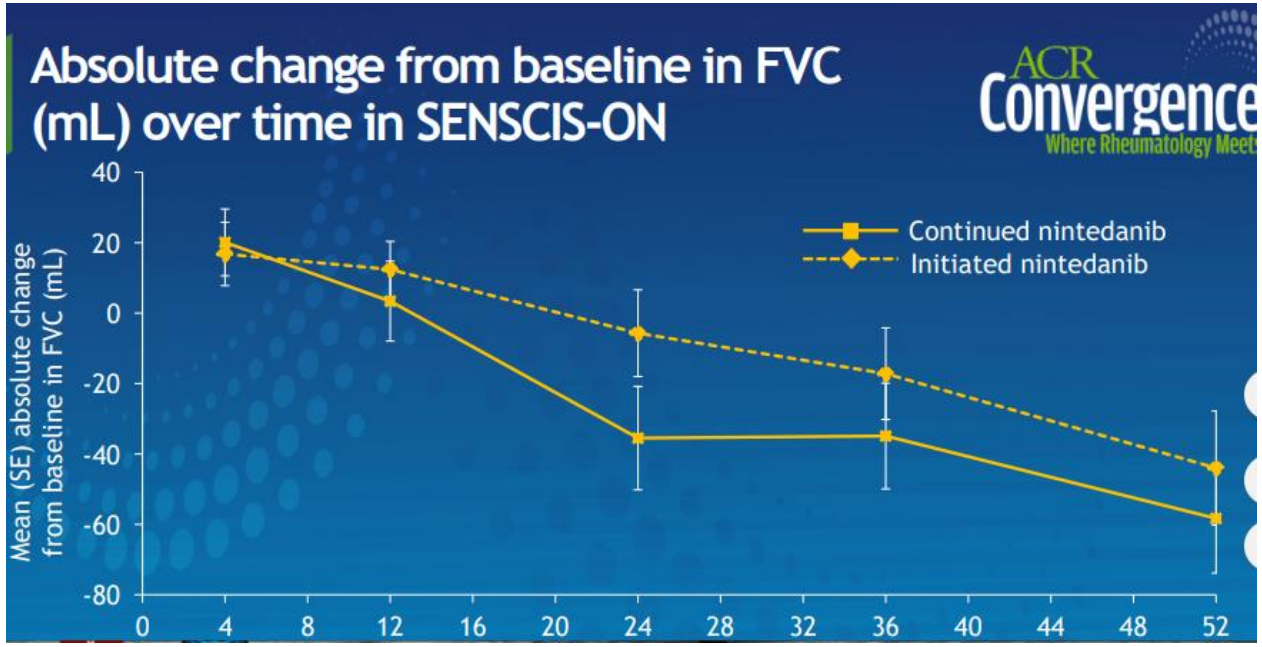
	Triple aPL positivity		p	One or double aPL positivity		p
Gestational outcome	Low C3/C4 (n=32)	Normal C3/C4 (n=16)		Low C3/C4 (n=65)	Normal C3/C4 (n=118)	
Term live birth (≥37w)	16 (50%)	10 (63%)	ns	15 (23%)	20 (17%)	ns
Preterm live birth (<37w)	7 (22%)	6 (37%)	ns	11 (17%)	19 (16%)	ns
Pregnancy losses (abortion and miscarriages)	9 (28%)	0 (0%)	0.04	39 (60%)	79 (67%)	ns

Continued Treatment with Nintedanib in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD): Interim Analysis of SENSCIS-ON

Yannick Allanore,[1] Madelon C Vonk,[2] Arata Azuma,[3] Maureen D Mayes,[4] Martina Gahlemann,[5] Alexandra James,[6] Veronika Kohlbrenner,[7] Susanne Stowasser,[5] Kristin B Highland[8] on behalf of the SENSCIS-ON trial investigators







The change in FVC in patients who received nintedanib over 52 weeks of SENSCIS-ON was similar to the change in FVC in patients who received nintedanib over 52 weeks of the SENSCIS trial.

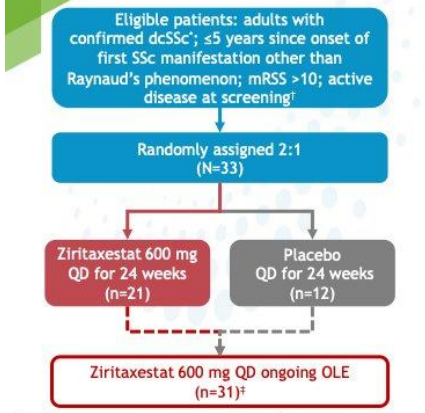
A Phase 2a Randomized, Double-blind, Placebo-controlled Study of Ziritaxestat in Early Diffuse Cutaneous Systemic Sclerosis (NOVESA)

Dinesh Khanna,[1] Christopher P. Denton,[2] Daniel E. Furst,[3] Maureen Mayes,[4] Marco Matucci-Cerinic,[5] Vanessa Smith,[6] Dick de Vries,[7] Liesbeth Deberdt,[8] Pieter-Jan Stiers,[8] Niyati Prasad,[8] Sohail Ahmed[9*]

- Lysophosphatidic acid (LPA) is a well-known pro-fibrotic and pro-inflammatory lysophospholipid that has been implicated in the pathogenesis of SSc[4,5]
- LPA is generated at sites of inflammation by autotaxin-mediated hydrolysis of lysophosphatidylcholine and other lysophospholipids[6,7]
- Previous studies have demonstrated that targeting the autotaxin/LPA pathway could be promising for modulating the skin pathology of SSc[4,7-9]
- Ziritaxestat (GLPG1690) is a small-molecule, selective autotaxin inhibitor with a novel mechanism of action that is under clinical investigation for SSc

METHODS

NOVESA study



*ACR/EULAR/Van den Hoogen/LeRoy 2013 criteria[1]; †Defined as worsening of skin thickening (≥2 mRSS points) or new areas of skin involvement or new-onset SSc with signs other than Raynaud's phenomenon, or ≥1 tendon friction rub. ‡1 placebo patient lost to follow-up, 1 placebo patient chose not to enter OLE. 1. van den Hoogen F, et al. Arthritis Rheum 2013;65:2737-47

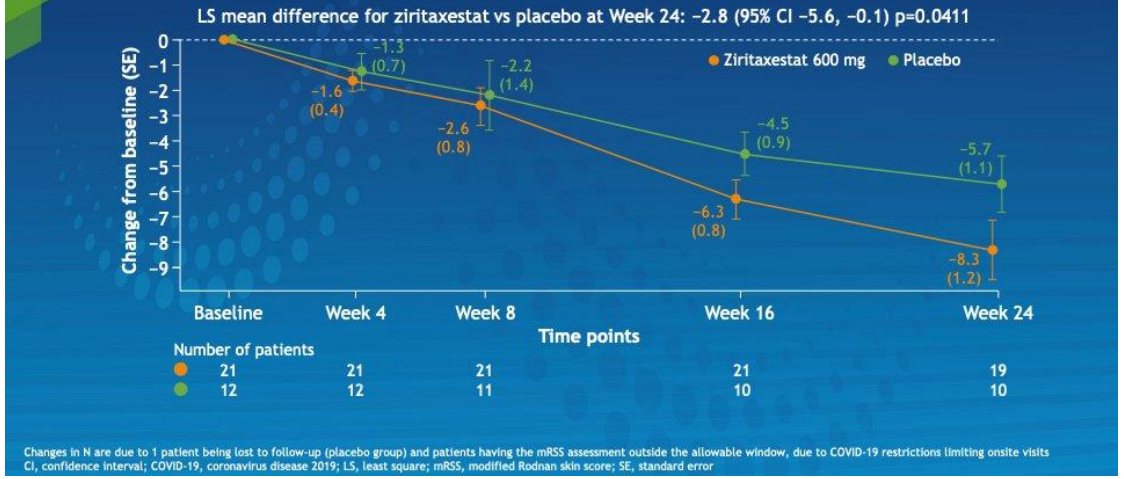
ACR Convergence Where Rheumatology Meets

- Patients with dcSSc were randomized (2:1) to oral ziritaxestat 600 mg QD or matching placebo for 24 weeks
- Protocol-defined immunosuppressive background therapies could continue if doses were stable for ≥3 months prior to randomization
- Primary endpoint: change from baseline in modified Rodnan skin score at 24 weeks
- Secondary endpoints: TEAEs, SAEs and tolerability
- Other endpoints: FVC, HAQ-DI and ACR CRISS score, LPA levels
- Statistical analysis: a mixed-effects model for repeated measures was used
  - LS mean (95% CI) was calculated for the primary endpoint
  - Descriptive statistics for other endpoints
  - Covariates included baseline mRSS and country

ACR, American College of Rheumatology; CI, confidence interval; CRISS, Combined Response Index for Systemic Sclerosis; dcSSc, diffuse cutaneous systemic sclerosis; EULAR, European League Against Rheumatism; FVC, forced vital capacity; HAQ-DI, Health Assessment Questionnaire Disability Index; LPA, lysophosphatidic acid; LS, least square; mRSS, modified Rodnan skin score; OLE, open-label extension; QD, once daily; SAE, serious adverse event; SSc, systemic sclerosis; TEAE, treatment-emergent adverse event

CHANGE FROM BASELINE IN mRSS

ACR Convergence Where Rheumatology Meets



Changes in N are due to 1 patient being lost to follow-up (placebo group) and patients having the mRSS assessment outside the allowable window, due to COVID-19 restrictions limiting onsite visits
CI, confidence interval; COVID-19, coronavirus disease 2019; LS, least square; mRSS, modified Rodnan skin score; SE, standard error

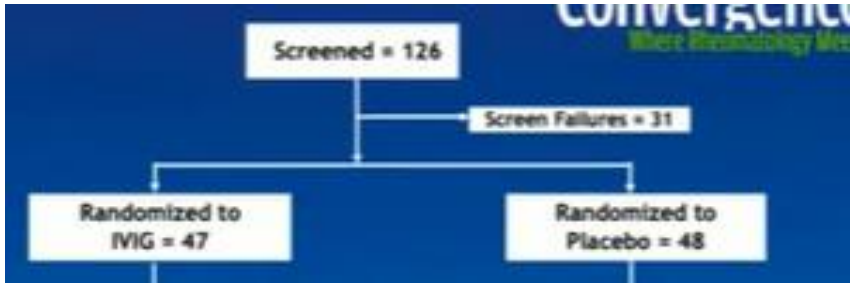
Efficacy and Safety of IVIG (Octagam 10%) in patients with active dermatomyositis.

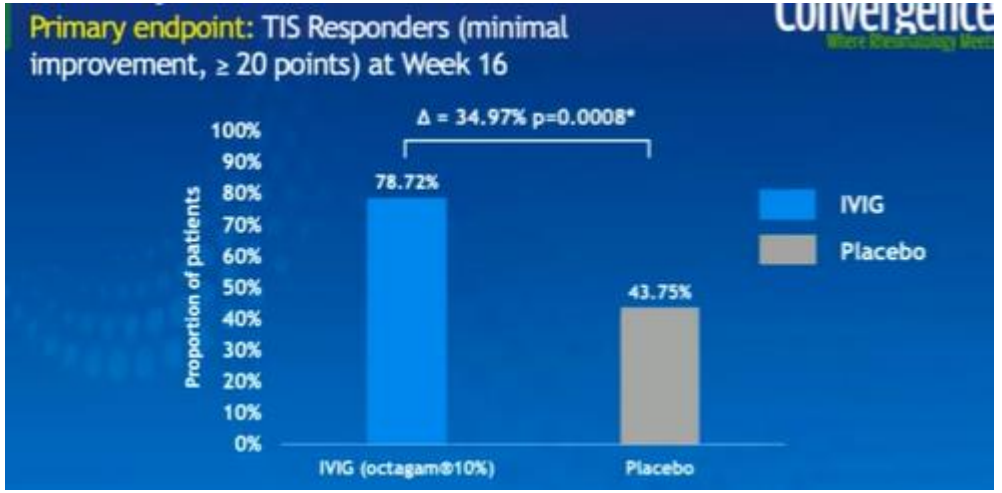
A Randomized, Double-Blind, Placebo-Controlled Phase III Trial (ProDERM Study)

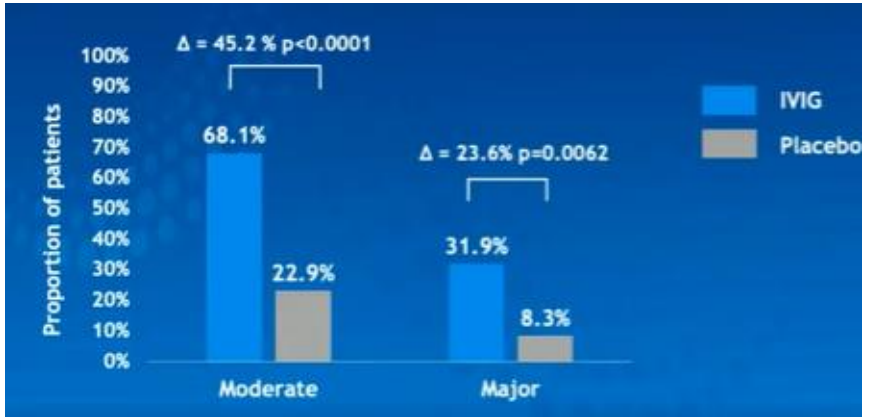
Aggarwal R, Charles-Schoeman C, Schessl J, Bata-Csorgo Z, Dimachkie MM, Griger Z, Moiseev S, Oddis CV, Schiopu E, Vencovsky J, Beckmann I, Clodi E, Levine T, & the ProDERM investigators

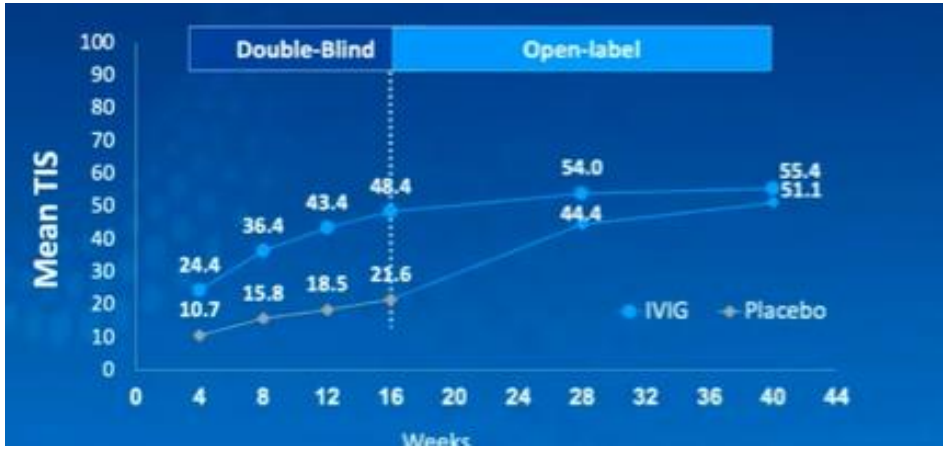
Prospective, parallel-group, double-blind, randomized, placebo-controlled, multicenter Phase 3 study.

- **Primary endpoint:** Proportion of responders at week 16 (end of the placebo-controlled, double-blind First Period).
- **Responder:** Subject with ≥20 points on the Total Improvement Score (TIS) of 2016 ACR/EULAR Myositis Response Criteria.





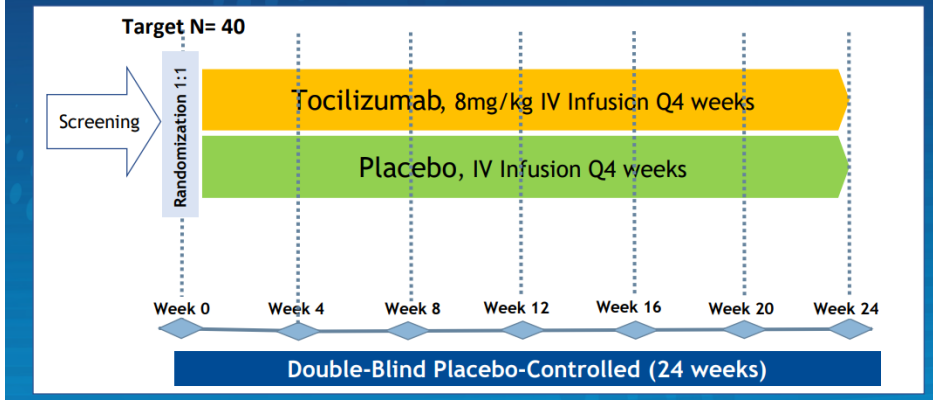


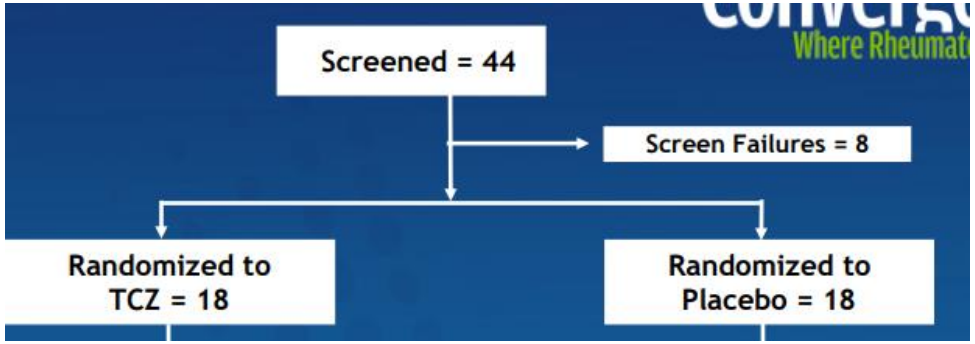


Tocilizumab in Myositis (TIM) Study: Results of a Phase IIb Double-Blind Randomized Controlled Trial

Rohit Aggarwal, Howard Rockette, Swamy Venturupalli, Galina Marder, Mazen Dimachkie, David Gazeley, Floranne Ernste, Leslie Crofford, Siamak Moghadam-Kia, Diane Koontz, Lei Zhu, Chester V. Oddis

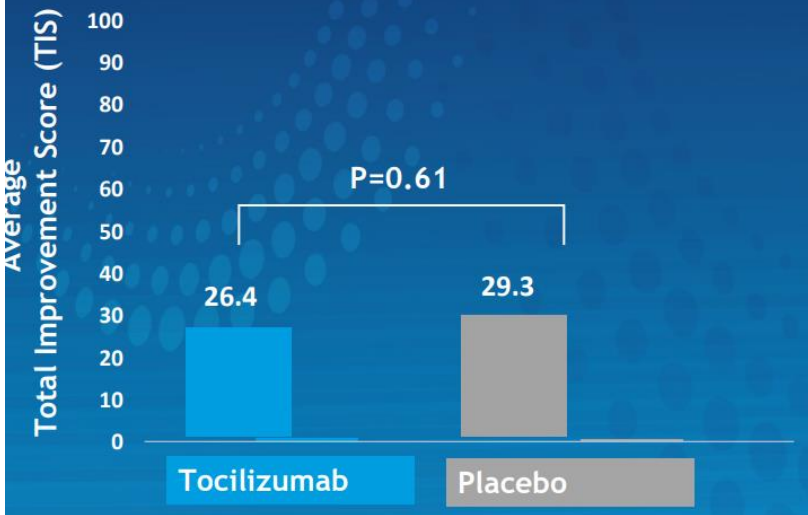
Double-blind, Randomized, Placebo-controlled, multicenter Phase 2b study.



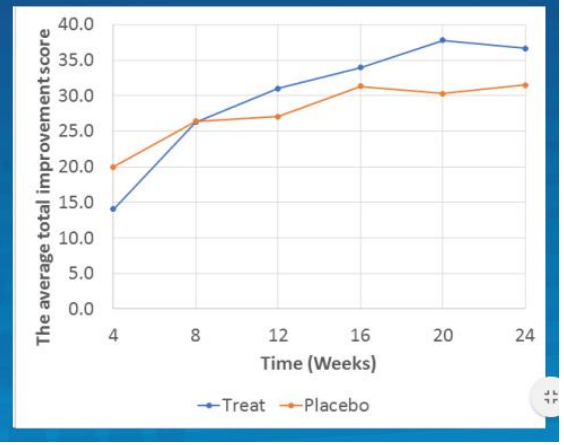


Tocilizumab treatment did not meet the primary or secondary efficacy outcomes in refractory DM and PM in a 24-week phase IIb study

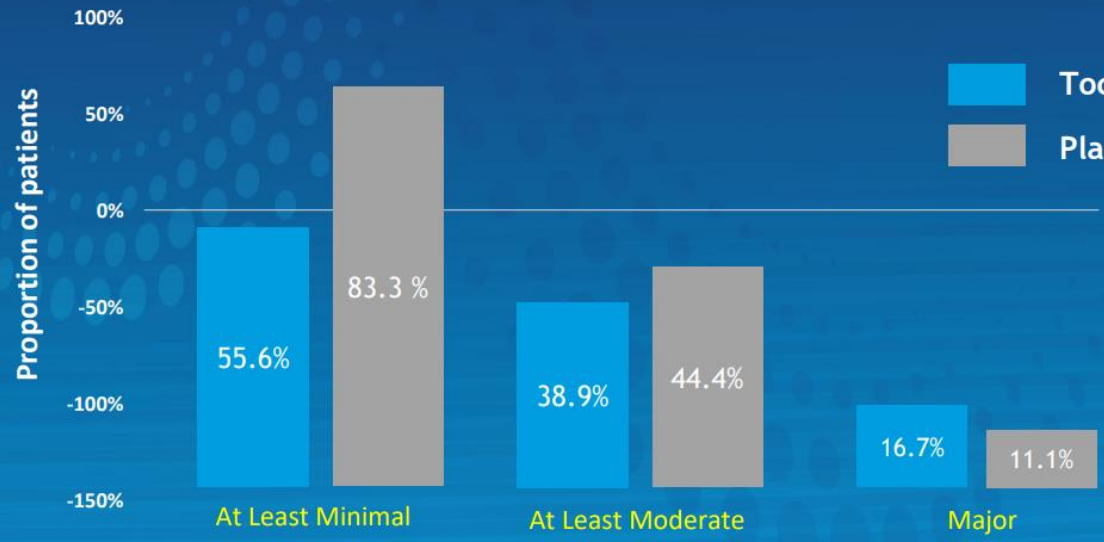
Primary endpoint: Average TIS at week 4-24 by GEE model including treatment groups, diagnosis and visit



TIS over time



Secondary endpoint: Proportion of responders with minimal, moderate or major improvement at week 24 was not significantly different (p=0.22)



Abstr#0452 Cleveland Clinic study on Shingrix safety

1. Rationale

IMID patients / IMID treatments = higher risk of zoster
Recombinant Zoster Vaccine: available, high efficacy, new adjuvant
Adjuvant → **Theoretical risk of flares after vaccine**

Are rheumatology patients at **higher risk of flares** after RZV?

2.Study

Retrospective single-center study (Rheumatology, CCF, USA)
Inclusion: ≥1 RZV dose between Feb. 2018 and May 2020
Data extracted from Electronic Medical Records

- **Flares in the 12-week period after each dose? Risk factors?**
- **Adverse events? Zoster outbreak?**

3. Results

n=622 rheumatology patients
n=359 IMID patients

67% female
Median age 67 yo
77% received 2 doses
8.7% adverse events
Median f/u = 36 weeks

Which IMID/treatment? Flared after RZV?

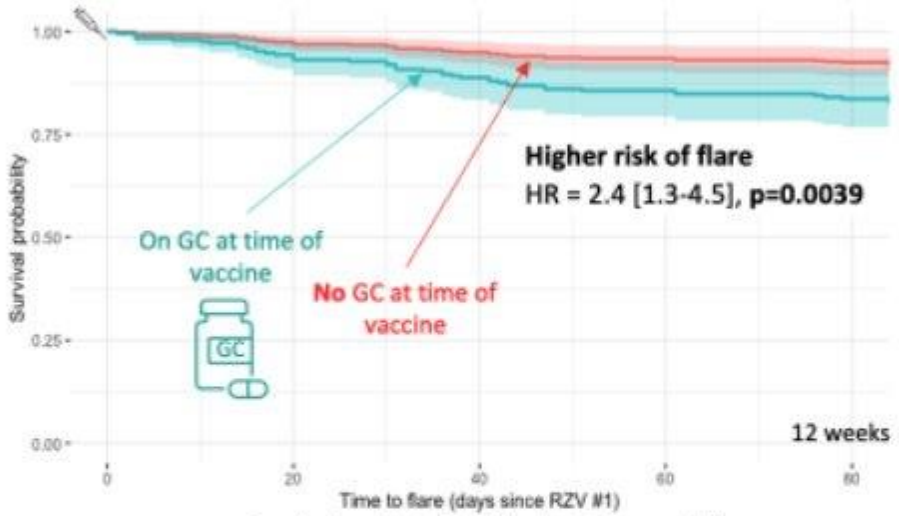
Description

IMID subgroups	Total from IMID (n=359)	On GC n=125 (35%)	≥1 Flare n=59 (16%)
RA	88 (25%)	37 (42%)	21 (24%)
Vasculitis	50 (14%)	23 (46%)	5 (10%)
PMR	29 (8%)	21 (72%)	5 (17%)
Gout	28 (8%)	3 (11%)	5 (18%)
SLE	24 (7%)	10 (42%)	4 (17%)

Flares: n=59
A change in IS treatment was needed in 25%

Logistic regression

Risk factor	No flare (n=300)	Flare (n=59)	Univariate p-value	Multivariate OR [IC95]	p-value
RA	67 (22%)	21 (36%)	**0.030**	1.57 [0.8-3]	0.173
GC	31%	53%	**0.002**	2.31 [1.3-4]	**0.004**
Jak-i	4%	10%	**0.032**	2.09 [0.6-6]	0.203



Survival analysis (multivariate Cox-model)

Key messages

- ✓ RZV appears safe in IMID patients
- ✓ GC at time of vaccine = higher risk of flare
- ✓ Patient + Provider discussion
- ✓ Informed consent
- ✓ Benefits / Risks Balance

GC

Reduced risk of serious pneumococcal infection up to 10 years after immunization with 7-valent conjugated pneumococcal vaccine in patients with inflammatory arthritis

Johanna Nagel, Göran Jönsson, Jan-Åke Nilsson, Chanchai Manuswin, Martin Englund, Tore Saxne, Pierre Geborek, Meliha C Kapetanovic

Pneumococcal vaccination is an easy win in inflamm arthritis.
In Lund, despite >50% on MTX and >70% on bDMARDs in the vaccinated patients group, pneumonia/serious pneumococcal infx halved.

ABST0456

Methods

Vaccinated arthritis patients (595)

Identifyed at the Dpt of Rheumatology Lund, Malmö :

- Diagnosis, regular follow-up
- Treatmentgroups
- Reumatoid Arthritis/RA (342) MTX, MTX+ bDMARD, bDMARD mono
- Spondyloarthritis/SpA (253) bDMARD mono, MTX+bDMARD, NSAID mono
- 1 injection of PCV7 i.m (Mai -08-Feb -12)

Non-vaccinated references (2379)

Identifyied in the Skåne Health care register:

- ICD-code: Arthritis diagnosis
- Age (+/- 5 years)
- Sex
- Geographical area

Table. Relative risk (RR) and ratio of relative risk (RRR) of all serious pneumococcal infections

	Vaccinated patients (n=595)	Non-vaccinated references (n=2379)
Events of serious infection, before vaccination, n	48	103
Events of serious infection after vaccination, n	85	307
Relative Risk (RR, after/before) (95% CI)	1.72 (1.12-1.63)	3.09 (2.33-4.10)

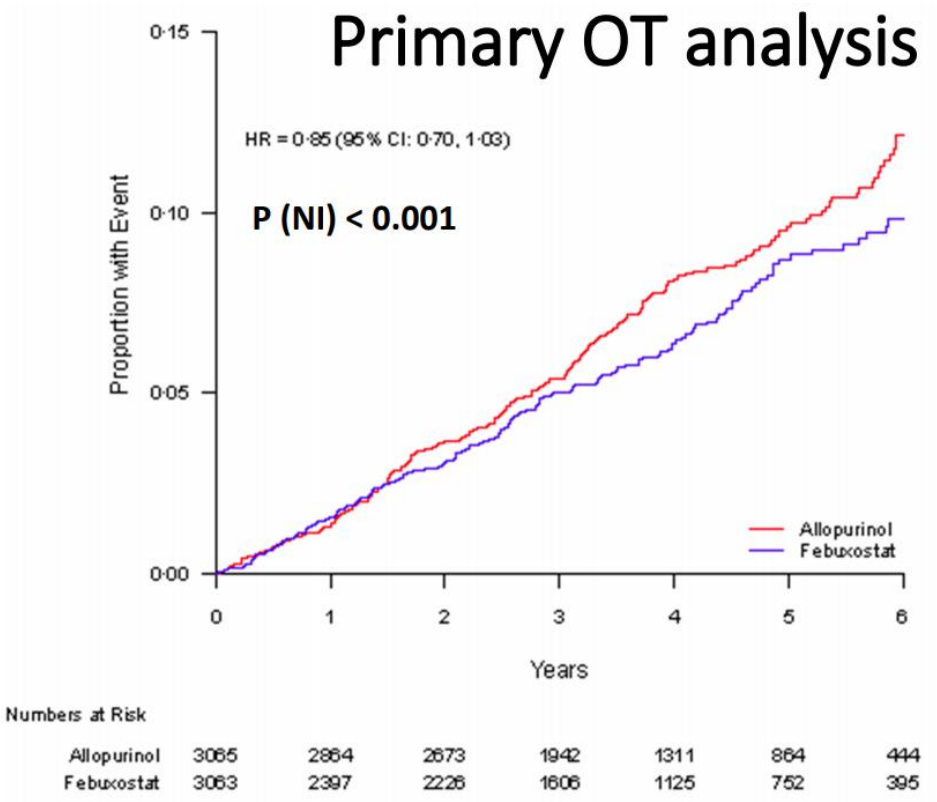
RRR of serious pneumococcal infection, vaccinated /non-vaccinated (95% CI): 0.54 (0.33-0.89) = 46% relative risk reduction

Long-term cardiovascular safety of febuxostat compared with allopurinol in patients with gout (FAST): a multicentre, prospective, randomised, open-label, non-inferiority trial

ACR Convergence Meeting
9th November 2020
Thomas MacDonald, Isla Mackenzie, Ian Ford and George Nuki
on behalf of the FAST Study Group
University of Dundee, Dundee, UK

- A prospective, randomised, open-label, blinded endpoint (PROBE) non-inferiority trial of febuxostat versus allopurinol in patients with gout recruited from primary and secondary care in the UK, Denmark, and Sweden.
- 6128 patients (mean age 71, 85·3% male, 33·4% prior CV disease) were randomized to receive allopurinol (n=3065) or febuxostat (n=3063) and followed up to 31 December 2019

Primary OT analysis



Summary

- **Febuxostat 80-120mg was non-inferior to allopurinol 100-900mg with respect to adverse cardiovascular events in patients aged over 60 years with gout and at least one additional cardiovascular risk factor.**
- **In contrast to previous studies there was no evidence of increased mortality with febuxostat**
- **Regulators should review febuxostat licensing restrictions**

ABSTRACT NUMBER: 1466

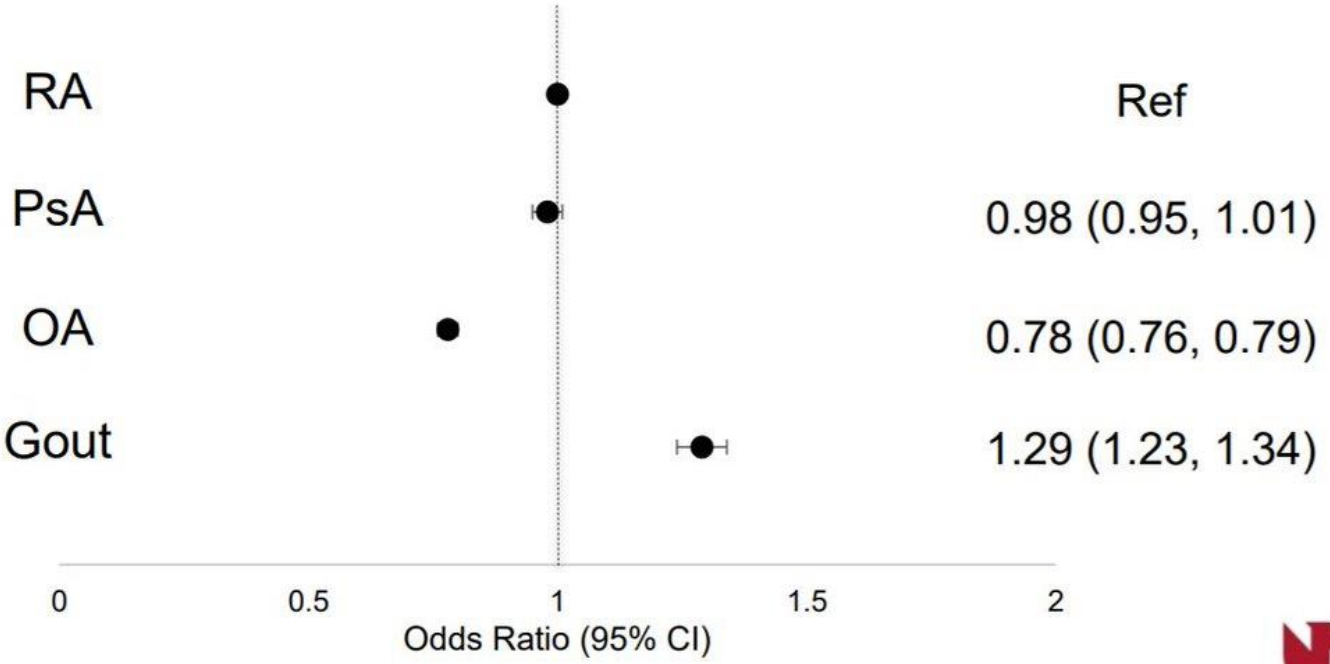
Multimorbidity in Rheumatoid Arthritis, Psoriatic Arthritis, Gout, and Osteoarthritis Within the Rheumatology Informatics System for Effectiveness (RISE) Registry

Bryant England[1], Huifeng Yun[2], Lang Chen[3], Kaleb Michaud[1], Ted Mikuls[1] and Jeffrey R Curtis[2], [1]University of Nebraska Medical Center, Omaha, NE, [2]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, [3]University of Alabama at Birmingham, Birmingham, AL

Cross-sectional study

356,820 patients

Prevalence of Multimorbidity Across Rheumatic & Musculoskeletal Diseases



Models adjusted for age, sex, race, U.S. region, insurance status, number of visits, and size of rheumatology practice

ABSTRACT NUMBER: 0688

The Discontinuation of Allopurinol in the Inpatient Settin and the Risk of Gout Flare: A Community-Hospital Experience

Artem Minalyan[1], Waqas Ullah[2], Shristi Khanal[3], Bikash Basyal[4] and Qian Zhang[3],
[1]Department of Medicine/Abington Hospital - Jefferson Health, Jenkintown, PA,

Dr Minalyan and colleagues report rates of gout flare following hospital admission of patients prescribed allopurinol.
Gout flare 14 times more likely if allopurinol stopped or omitted.

	Gout flare +	Gout flare -	Total
Allop. continued	8	363	371
Allop. discontinued	7	23	30
Total	15	386	401

OR* 13.8, 95% CI 4.6 - 41.4, p <=0.0001)

* Odds ratio (OR) was calculated using the two-tailed Fisher exact probability test

Reported reasons for allopurinol discontinuation (30 patients):

NPO was recommended in 8 patients

AKI in 6 patients

Unclear or not listed in 16 patients

ABSTRACT NUMBER: 0533

Characterization of Older Male Patients with a Fragility Fracture

Setareh A Williams[1], Shanette G Daigle[2], Richard Weiss[1], Yamei Wang[1], Tarun Arora[2] and **Jeffrey R Curtis**[3], [1]Radius Health, Inc., Waltham, MA, Waltham, MA, [2]University of Alabama at Birmingham, Birmingham, AL, Birmingham, AL, [3]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

k dao
@KDAO2011

Screen older men for osteoporosis! >90% men w/fracture had no DXA w/in 2 yrs of event!

Characteristerics of 9876 male Medicare pts w/fragility fx:
👉 61% were >75 y.o
👉90% white
👉<6% had BMD w/in 2 years of fx
👉 spine>hip>ankle fx

Abstr#0533 #ACR20 @rheumnow @RADoctor

ABSTRACT NUMBER: 0538

Autoimmune Disease Outcomes of Women with Breast Implants: A Population-Based Study

Madeline Peterson[1], Thomas O'Byrne[1], John Davis[1], Vanessa Kronzer[1], Lynne Peterson[1], Michael Weisman[2] and Cynthia Crowson[3], [1]Mayo Clinic, Rochester, MN,

No increase in the modern era for the risk of #autoimmunedisease in #women with #breastimplants

Table 2. Risk of autoimmune disease in implant patients by reason for breast implant

Reason for breast implant	Number of events*		Cumulative incidence at 10 years (95% CI)**		Hazard ratio (95% CI)***	p-value
	Implant cases	*Comparators*	*Implant cases*	*Comparators*		
Any reason	74	222	11.0 (8.5, 14.1)	11.3 (9.8, 13.0)	0.98 (0.75, 1.27)	0.86
Cosmetic	41	121	10.2 (7.2, 14.3)	9.8 (8.0, 11.9)	0.96 (0.68, 1.37)	0.84
Cancer	25	76	12.5 (7.9, 20.0)	13.9 (11.0, 17.6)	1.04 (0.66, 1.63)	0.88
Prophylactic	7	23	13.6 (6.7, 27.5)	15.0 (9.8, 23.0)	0.85 (0.36, 2.00)	0.72

*The number of events is the number of patients who develop any autoimmune disease

A population-based study from #MayoClinicRheumatology

Gems from scientific sessions – state-of-the-art lectures

THE GREAT DEBATE

Janus Kinase Inhibitors Should Be Used Before Biologics After Methotrexate Failure in RA

Vibeke Strand, MD, MACR, FACP
Biopharmaceutical Consultant
Adjunct Clinical Professor, Division of Immunology/Rheumatology
Stanford University, Palo Alto CA

#ACR20

JAKi's in RA: Overall Clinical Efficacy

ACR Convergence
Where Rheumatology Meets

- All JAKi's studied to date in RA are effective: 3 approved
- Early onset of benefit, including ALL PROs:
  - Within 1 – 2 weeks
  - Maximal at 3 months
  - Regardless of population
- JAKi's v bDMARDs in MTX-IR patients:
  - Baricitinib 4mg+MTX > ADA+MTX
  - Upadacitinib 15mg+MTX > ADA+MTX
  - Tofacitinib 5mg+MTX and Filgotinib 100mg/200mg+MTX non-inferior to ADA+MTX

In Conclusion:

ACR Convergence
Where Rheumatology Meets

- The JAK Inhibitor class is an exciting development for rheumatology and a broad variety of autoimmune diseases, and in RA they should be used early!
- Based on phase 3 RCTs, responses are better in progressively earlier disease duration, less treatment experienced patients
- Well established efficacy in RA; H2H comparisons w/ one TNFi indicate equivalent/better efficac
- Convenience
- Short half-life; AEs can often resolve over short time-frame
- Risks identified: need for vaccination and careful history, attention to risk factors for VTEs, ATEs; surveillance for SIEs and malignancies

Jak inhibitors should **NOT** be use before anti-TNF therapies in RA

Michael E. Weinblatt, M.D.
John and Eileen Riedman Professor of Medicine, Harvard Medical School
Bruce and Joan Mickey Chair in Rheumatology
Brigham and Women's Hospital

BRIGHAM AND WOMEN'S HOSPITAL
HARVARD MEDICAL SCHOOL TEACHING AFFILIATE

Serious infections with a Jak vs bDmards Lancet Rheum 2020;2 e84

- Multi-database cohort study- 8 exclusive groups of RA pts initiating Tofa or bDmards using Medicare and Optum and Market Scan. Primary outcome was admission to hospital for serious infection
- 130718 pts were studied– HR for serious infection
- Tofa vs Etanercept 1.41, vs Abatacept 1.2, vs Toci 1.17,vs Ada 1.06 and lower than Inflix 0.81.
- Tofa was associated with a 2 fold higher risk of Zoster

JAKs vs Anti-TNF Issues

- Colonic Perforations– Yes with Jaks not with anti-tnf
- Reproductive– OK with anti-tnf including breast feeding—not ok with jaks
- Lab monitoring- Yes with Jaks not with anti-tnf
- Dosing – daily with Jaks– weekly to every several months with anti-tnf
- DVT/PE?
- 22 years of clinical use and over 30 years of clinical data with anti-tnf
- Biosimilar Anti-tnf major cost savings!

IN SUMMARY

- 1. Equal efficacy between compounds
- 2. Dose flexibilities with the anti-tnf
- 3. Higher rates of zoster with Jakinibs
- 4 Uncertainty regarding risk of VTE/PE
- 5. Requirement for lab monitoring with Jakinibs
- 6 Issues with pregnancy and lactation with Jakinibs
- 7.Over 22 years of clinical use of anti-TNF
- 8. Cost of jakinibs vs biosim anti-tnf
- 9. The choice is obvious!!

ACR Review Course

Seronegatives and Psoriatics: Navigating therapy

Christopher Ritchlin, MD, MPH. MACR
Professor and Chief
Allergy, Immunology & Rheumatology Division
University of Rochester Medical Center
Rochester, New York

Therapy of IBD-Associated Arthritis

Therapy	Crohn's Disease	Ulcerative Colitis	Peripheral arthritis	Axial arthritis	Reference
NSAIDS	No	No	+	+	1
Corticosteroids	++	++	++	No	1
Sulfasalazine	Colitis	No	+	No	2,3
MTX	+	No	++	No	4,5
TNFi	++/-ETN	++/-ETN	++	++	6
IL-23i	+?	+?	++	No	7,8
IL-17i	No	No	++	++	9
Jak-Stat	++/Tofa -	++Tofa+	++	+?	10,11,12

1. Olivieri I. Autoimmune Rev. 2014
2. Haibel H. ARD, 2007
3. Van der Heijde D. ARD 2011
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12. Vermeire S. Lancet 2017

Pregnancy in Rheumatic Disease

Megan E.B. Clowse, MD, MPH
Associate Professor of Medicine
Division of Rheumatology and Immunology
Duke University School of Medicine

Inflammatory Arthritis

Control disease with pregnancy-compatible meds

1. **IA may improve during pregnancy, but not as much as you think.**
   - ***Pregnancy is good… TNF-inhibitors are better***

2. **Active IA increases preterm birth**
   - ***Control arthritis with pregnancy-compatible meds***

3. **RA flares post-partum… if you let it**
   - ***Most medications are compatible with breastfeeding***

Megan Clowse at ACR review course. Use HCQ 400mg daily for all pregnant women with Ro antibodies regardless of diagnosis or body weight. #ACR20

Μετάφραση Tweet

12:35 μ.μ. · 11 Νοε 2020 · Twitter Web App

Start ASA 81 mg/day in all SLE patients at the end of the first trimester (or earlier with APA's) to decrease risk of pre-eclampsia

Dr. M Clowse #ACRReview #ACR20 @rheumnow

Μετάφραση Tweet

Switching from MMF to AZA for pregnancy

Caution: there is a real risk for flare

1. **Get disease quiet and stable on MMF for >6months**
2. **Transition from MMF to AZA –** Options:
    a. Quickly decrease MMF and increase AZA
    b. Slowly decrease MMF and increase AZA
    c. Sudden switch (stop MMF, start AZA)
3. **Observe for <u>3-9months</u> for stability on AZA**
    - Push AZA dose, as tolerated
    - Add tacrolimus, if needed

Medications for Inflammatory Arthritis

Pregnancy Compatible	Caution	Teratogenic
Hydroxychloroquine **Sulfasalazine** **Azathioprine** **TNF-inhibitors** • Certolizumab: continue • Others: consider holding last 1-2 months to limit transfer **Prednisone** *(use sparingly)*	**Biologics beyond TNF-inhibitors** **Leflunomide** (washout with cholestyramine) **New small molecules** (tofacitinib, apremilast, etc.) **NSAIDs**	**Methotrexate**

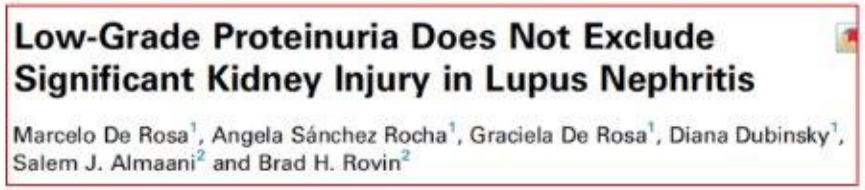
Lactation

Women do NOT need to choose between themselves or their baby.

Lactation Compatible	Caution	Worrisome *(but little data)*
Hydroxychloroquine **Sulfasalazine** **Azathioprine** **Colchicine** **NSAIDs *(prefer ibuprofen)*** **TNF-inhibitors** **Prednisone *(≤20mg)*** **Biologics beyond TNF-inhibitors**	**Methotrexate** **Prednisone *(>20mg)***	**Leflunomide** **Mycophenolate** **Cyclophosphamide** **New small molecules**

Diagnosis requires renal biopsy

- At baseline
- At flare
- ? In remission
- What is remission – beyond the scope of this talk but refer to recent papers from Brad Rovin and collaborators



Kidney Int Rep 2020

- **Not all kidney disease in an SLE patient is LN**
  - **5% of SLE patients may have other glomerular diseases and lupus podocytopathy may co-exist with LN in 1.3% of cases**
  - **Anti-phospholipid antibody syndrome nephropathy with or without LN (up to 24% of LN cases)**
  - **Interstitial Nephritis (fairly rare in absence of GN)**

- **Not all kidney disease in LN needs to be treated aggressively with immunosuppression**
  - **Class II LN**
  - **Chronic changes with little active inflammation**

Philip Seo, Johns Hopkins

Update in Vasculitis

- Tocilizumab may enable prednisone tapers < 6 months for GCA
- Plasma exchange is generally not effective for AAV and should be considered only in patients presenting with renal failure
- Even severe AAV may be effectively treated with much less glucocorticoids than are currently standard
- Avocapan may allow glucocorticoid-free remission induction
- Mepolizumab, and other anti-IL-5 agents are effective primarily for the sinopulmonary manifestations of EGPA

Mepolizumab: Pros and Cons

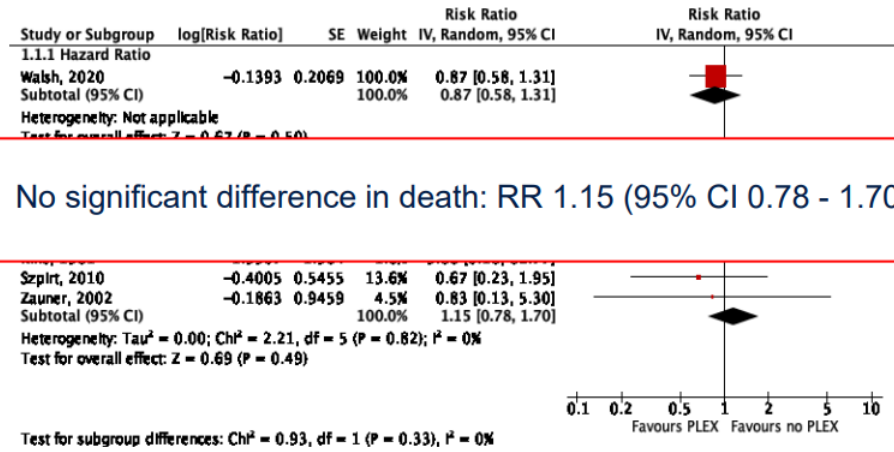
- Mepolizumab reduces glucocorticoid dependence among patients with EGPA, ***but***
- 300 mg = 3 subcutaneous injections, every month
  - 100 mg may be adequate for some patients
- The majority of patients will still require some dose of steroids
- Clinically more effective for asthma than for sinusitis
- The majority of patients in MIRRA did *not* have vasculitic symptoms
  - Most patients also could be diagnosed w/ ***chronic eosinophilic pneumonia***
  - Efficacy of mepolizumab for EGPA-associated glomerulonephritis unclear
  - Reports of patients developing cardiomyopathy and neuropathy while treated with mepolizumab

UCSF School of Medicine

State of the Art: Treatment of ANCA-Associated Vasculitis in 2020

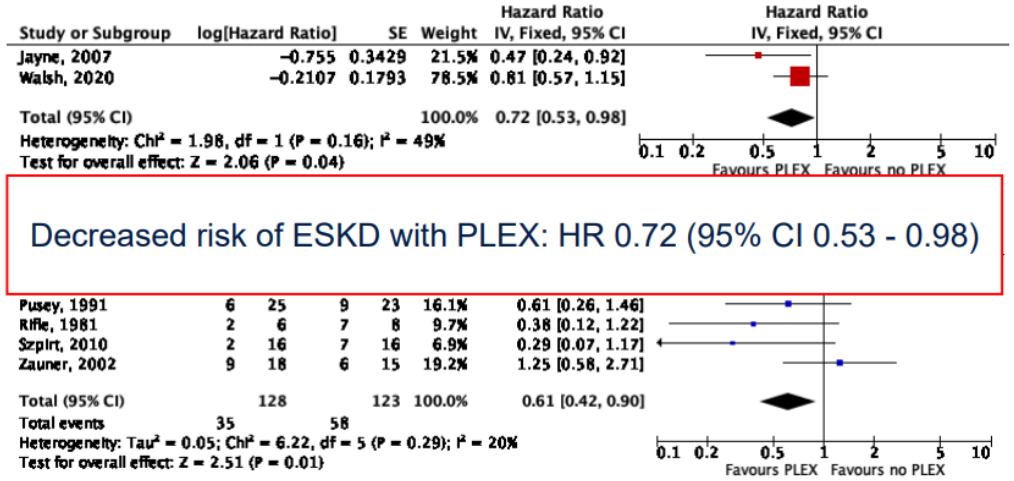
Sharon A. Chung, MD MAS
Associate Professor of Clinical Medicine, UCSF Division of Rheumatology
Director, UCSF Vasculitis Clinic
Associate Director, Clinical and Translational Medicine, Immune Tolerance Network

Meta-analysis: Death (PLEX)



No significant difference in death: RR 1.15 (95% CI 0.78 - 1.70)

Meta-analysis: ESKD (PLEX)



Decreased risk of ESKD with PLEX: HR 0.72 (95% CI 0.53 - 0.98)

Consider PLEX for patients at highest risk of ESKD (e.g., Cr ≥ 3.4 mg/dL [300 umol/L])

 Springer JM et al., ACR Open Rheumatol (under review)

UCSF

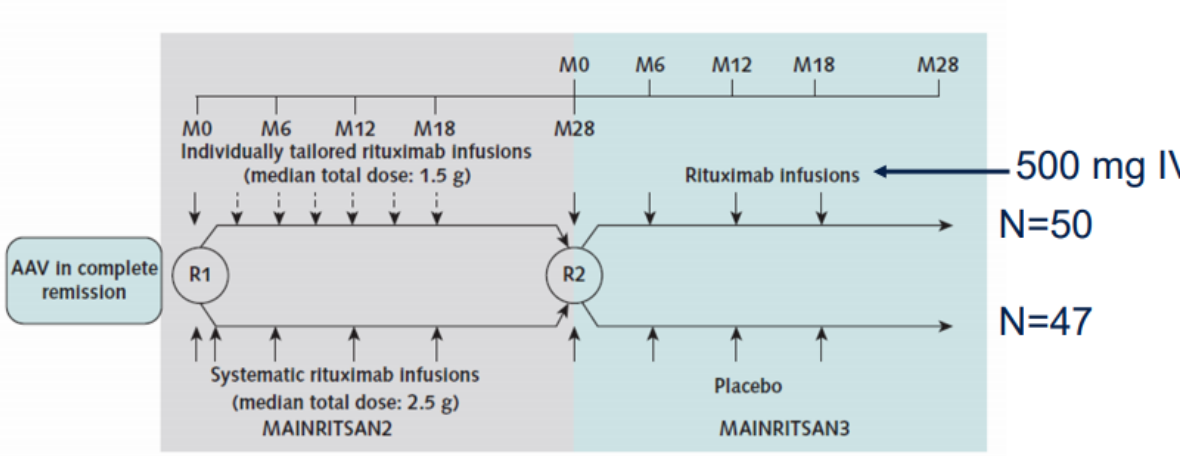
UCSF School of Medicine

State of the Art:
Treatment of ANCA-Associated Vasculitis in 2020

Sharon A. Chung, MD MAS
Associate Professor of Clinical Medicine, UCSF Division of Rheumatology
Director, UCSF Vasculitis Clinic
Associate Director, Clinical and Translational Medicine, Immune Tolerance Network

How long should remission maintenance therapy continue?

- MAINRITSAN3: randomized, double-blinded, placebo-controlle



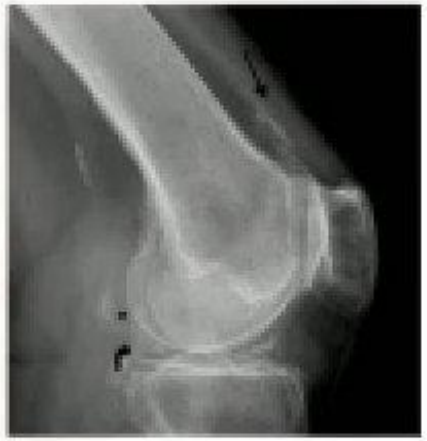
MAINRITSAN3

	Continued RTX	Placebo	P
Relapse-free survival (month 28), % (95% CI)	96 (91-100)	74 (63-88)	0.008
Major relapse–free survival (month 28), % (95% CI)	100 (93- 100)	87 (78- 97)	0.009
Infectious SAEs	12%	9%	

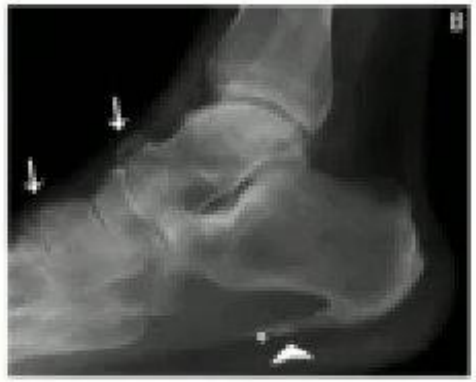
- Consider prolonged RTX for pts at high risk for relapses (e.g., PR3-ANCA+ or prior relapse)

Charles, P et al., Ann Intern Med 2020

UCSF



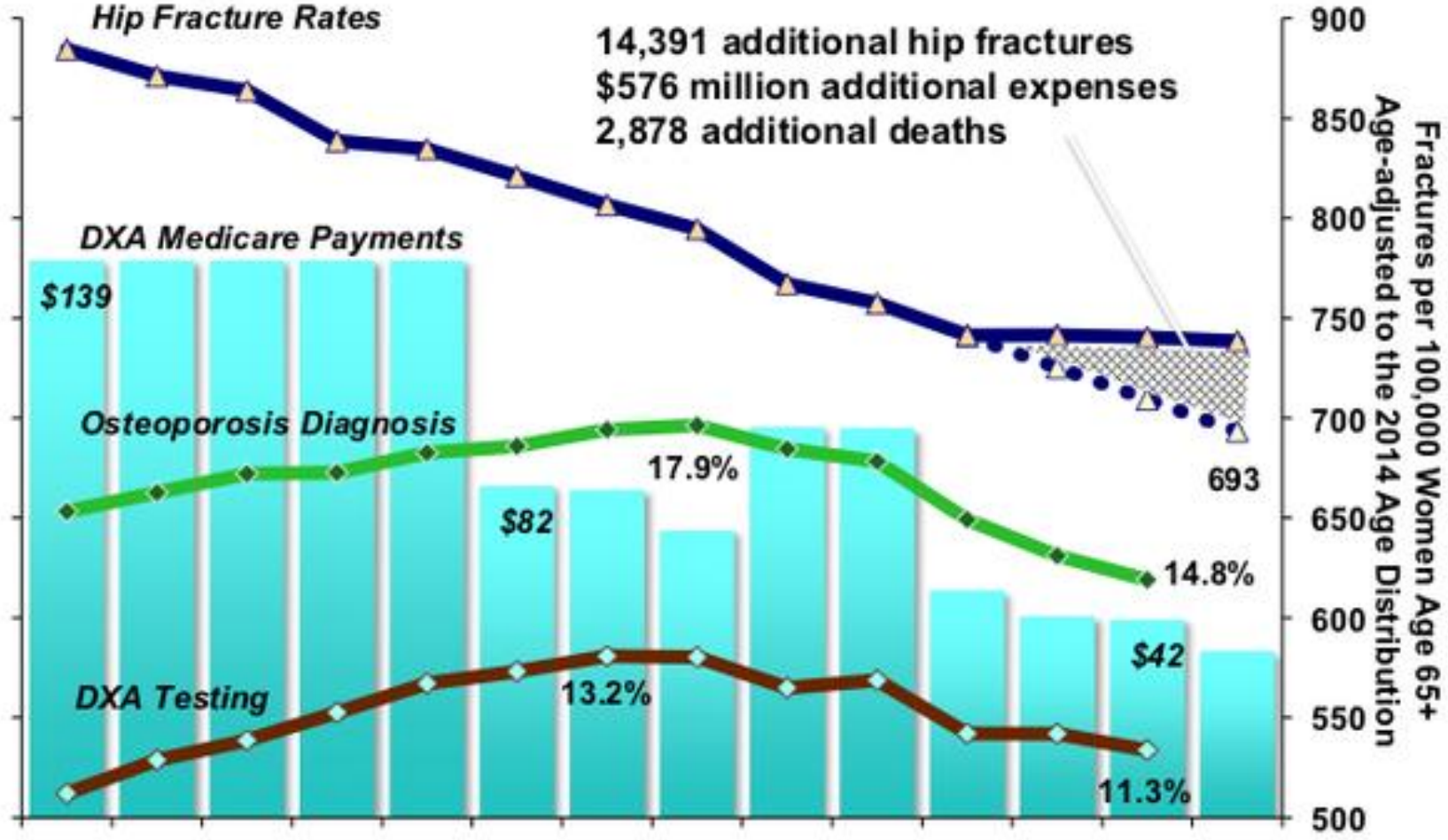
TENDON CALCIFICATIONS ARE IMPORTANT CLUES TO CPPD



ACR Convergence
Where Rheumatology Meets

ACR Convergence
Where Rheumatology Meets
ALL VIRTUAL

US Hip Fracture Trends 2002-2015



Drug Holidays in Osteoporosis: Evidence and Practice

Karen E. Hansen, MD, MS
Professor of Medicine
Rheumatology Division

8 questions I ask, when contemplating a BP drug holiday

QUESTION	ANSWER
Would I treat her now, based on her FRAX score?	
Did she adhere to therapy?	
Did she sustain spine or hip fracture before or during therapy?	
Did her bone mineral density increase, stabilize, or decrease during therapy?	
Does she still have a hip T-score ≤-2.5?	
How often does she fall?	
Does she have an ongoing risk factor for bone loss? (prednisone, cancer, weight loss)	
What does my patient think?	

Bisphosphonate Drug Holidays

- Consider if low risk of fracture after 5 years of alendronate, or 3 years of zoledronate
- Use caution if:
  - High fracture risk
  - Prior compression or hip fracture, esp. during therapy
  - Hip T-score ≤-2.5
  - Other factors: glucocorticoid therapy, weight loss, cancer therapy or frequent falls
- If patient remains at high fracture risk, continue or switch Rx
- Final Comments:
  - No safety data for >10 years of alendronate
  - **Monitor bone density and ask about fractures**
  - Consider resuming therapy if FRAX rises above Rx threshold, 3% decline in hip BMD, or new fracture

Hypophosphatasia

- YOU are seeing this!!
  - Rheumatology
  - Metabolic Bone

Diagnosis of Hypophosphatasia

- Vigilant for low ALP
- Recurring poorly healing fractures
  - Metatarsal, femoral shaft
  - Other fractures with osteomalacia appearance
- Calcifying diseases
  - CPPD, Pseudogout
  - DISH, exostoses
  - Calcific tendonopathies, periarthritis
- Once diagnosed
  - Avoid using of potent antiresorptive
    - This is NOT osteoporosis, it is abnormal mineralization
    - Use in carriers w/o disease manifestations with low bone mass?

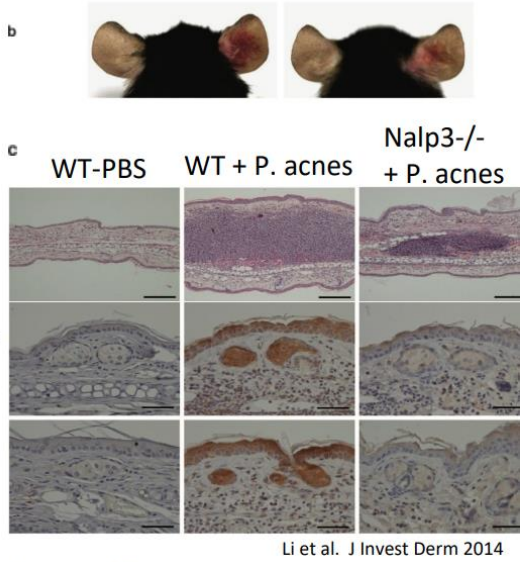
CRMO and SAPHO in Adults

Polly J. Ferguson, MD
Marjorie K. Lamb Professor

Infectious Trigger?

- *Cutibacterium acnes* (i.e., the bacteria formerly known as *Propionibacterium acnes)*
  - anaerobic gram-positive bacilli
  - 6 phylogenetic groups
- Positive bone cultures
  - Review of 14 studies = [n = 98] found 48% positive *C. acnes*
  - (62% if open bx/14% if needle)
    - (Zimmerman and Curtis, 2019)
  - Ped CRMO = rare

C. acnes activates NLRP3 inflammasome



Li et al. J Invest Derm 2014

- Human sebocytes + *P. acnes*

⇒ activation of caspase-1

⇒ secretion of IL-1β

⇒ knocking down NLRP3 abolished IL-1β

- Nlrp3-deficient mice + P. acnes = less severe disease
- Role of *C. acnes* in SAPHO remains unclear
- n = 1 SAPHO; PBMC + LPS/ATP had ↑ IL-1β production

(Colina et al. 2010)

- Review 66 cases SAPHO treated with biologics

AGENT (cytokine blocked)	# subjects	Bone & joint % + response	SKIN % + response
TNF	45	93.3	72.4
IL-1	7	85.7	Limited info
IL-23 (ustekinumab)	5	60	50
IL-17	8	37.5	57.1
IL-6	1		
JAK inhibitor, PDE4 inhibitors*	Case reports		

Daoussis et al. Semin Arthr Rheum, 48:618, 2019

The Adult with Undifferentiated Autoinflammatory Disease

Dan Kastner, MD, PhD
Intramural Research Program

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

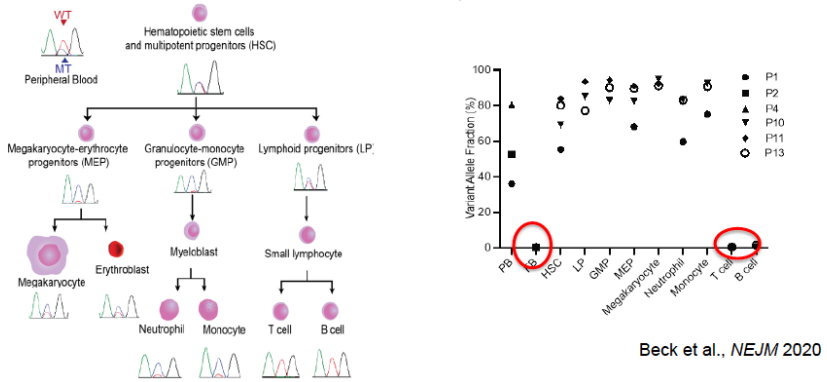
Somatic Mutations in *UBA1* and Severe Adult-Onset Autoinflammatory Disease

D.B. Beck, M.A. Ferrada, K.A. Sikora, A.K. Ombrello, J.C. Collins, W. Pei, N. Balanda, D.L. Ross, D. Ospina Cardona, Z. Wu, B. Patel, K. Manthiram, E.M. Groarke, F. Gutierrez-Rodrigues, P. Hoffmann, S. Rosenzweig, S. Nakabo, L.W. Dillon, C.S. Hourigan, W.L. Tsai, S. Gupta, C. Carmona-Rivera, A.J. Asmar, L. Xu, H. Oda, W. Goodspeed, K.S. Barron, M. Nehrebecky, A. Jones, R.S. Laird, N. Deuitch, D. Rowczenio, E. Rominger, K.V. Wells, C.-C.R. Lee, W. Wang, M. Trick, J. Mullikin, G. Wigerblad, S. Brooks, S. Dell'Orso, Z. Deng, J.J. Chae, A. Dulau-Florea, M.C.V. Malicdan, D. Novacic, R.A. Colbert, M.J. Kaplan, M. Gadina, S. Savic, H.J. Lachmann, M. Abu-Asab, B.D. Solomon, K. Retterer, W.A. Gahl, S.M. Burgess, I. Aksentijevich, N.S. Young, K.R. Calvo, A. Werner, D.L. Kastner, and P.C. Grayson

Meets Diagnostic or Classification Criteria for:

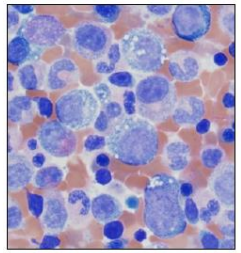
Relapsing polychondritis	**15 (60%)**
Sweet syndrome	**8 (32%)**
Myelodysplastic syndrome	**6 (24%)**
Multiple myeloma (MGUS)	**5 (20%)**
Polyarteritis nodosa	**3 (12%)**
Giant cell arteritis	**1 (4%)**

Identification of Myeloid-Restricted Somatic *UBA1 M*utations

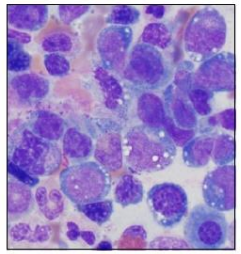


Beck et al., *NEJM* 2020

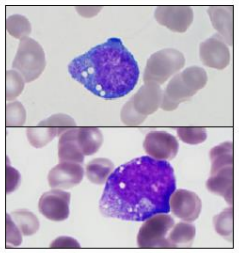
Bone Marrow-Resident Myeloid Cells in *UBA1* Patients Exhibit Striking Vacuoles



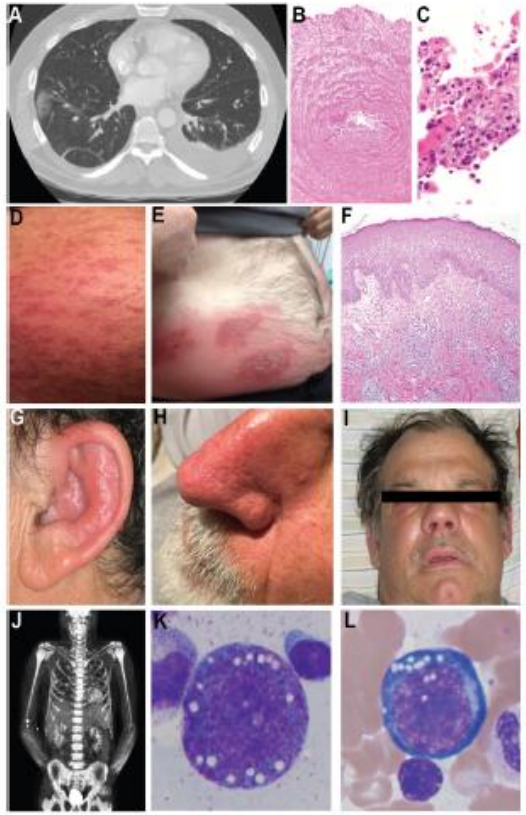
P1- 54 y/o male
Bone Marrow



P2- 61 y/o male
Bone Marrow



P3- 74 y/o male
Bone Marrow



V acuoles

E 1 ubiquitin-activating enzyme

X - linked

A utoinflammatory

S omatic

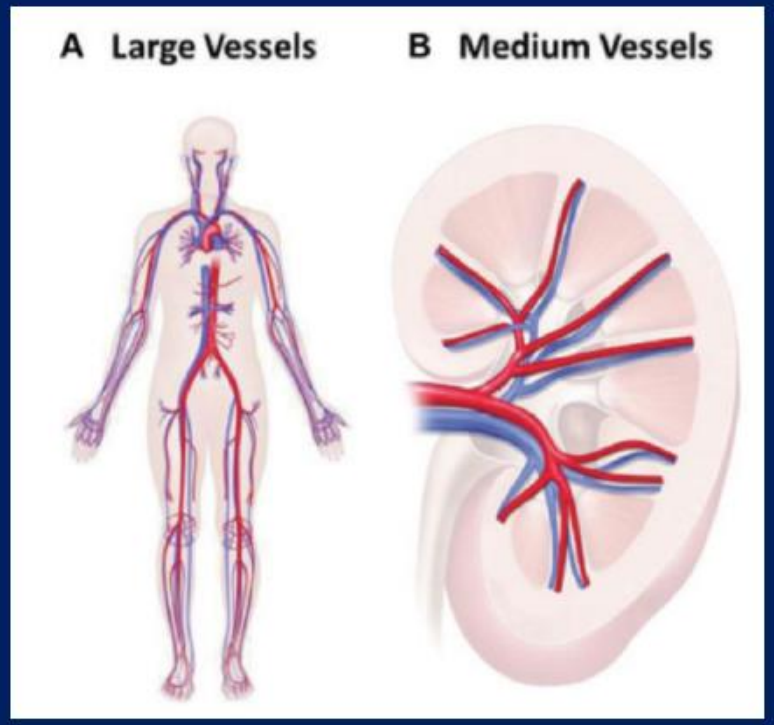
It rhymes with TEXAS!!

Beck et al., *NEJM* 2020

A Clinician's
Pearls & Myths
In Rheumatology

John H. Stone, M.D., M.P.H.
Professor of Medicine, Harvard Medical School
The Edward A. Fox Chair in Medicine
Massachusetts General Hospital

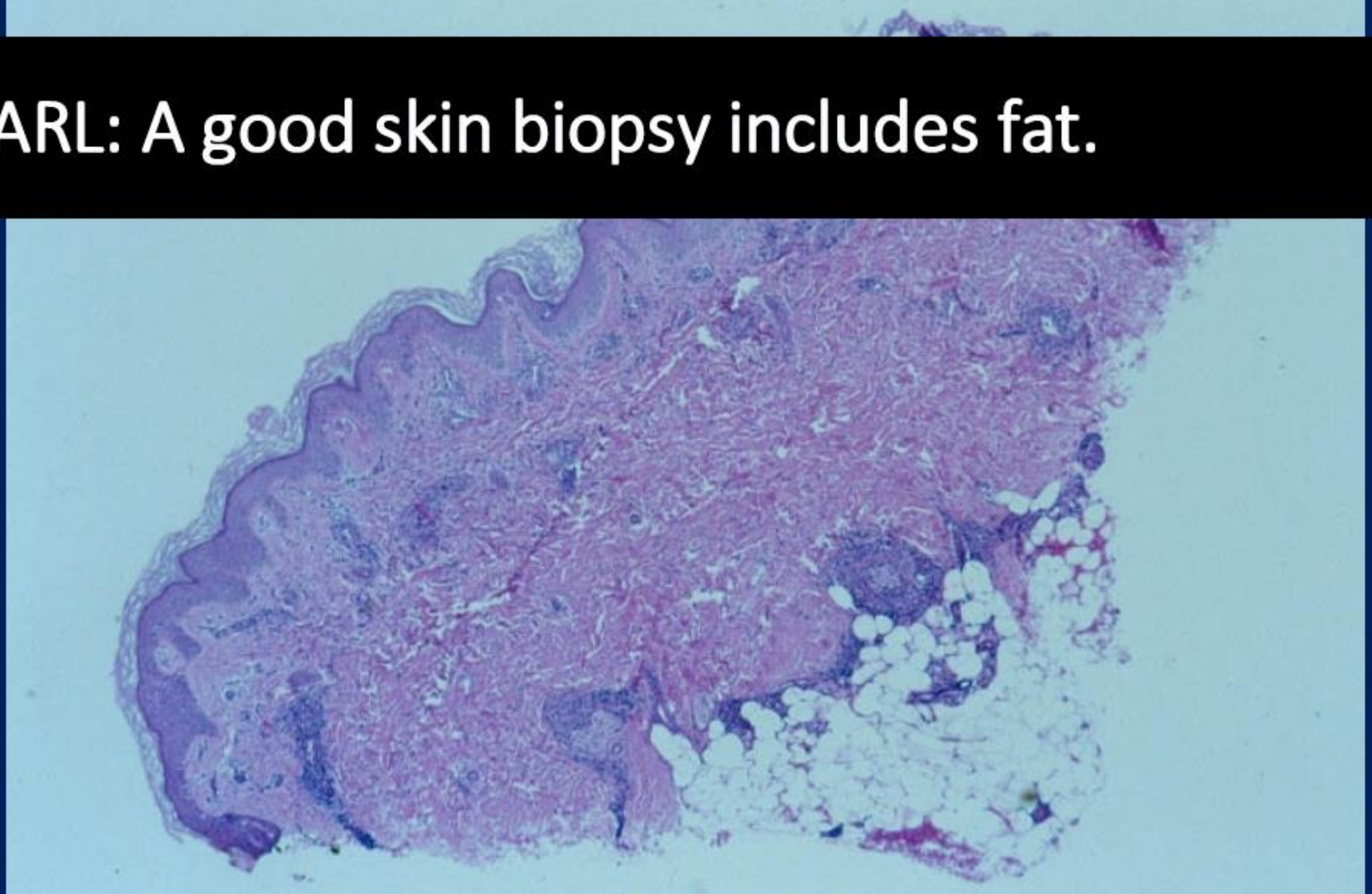
Pearl: A large artery becomes a medium-sized artery when it penetrates a viscus.



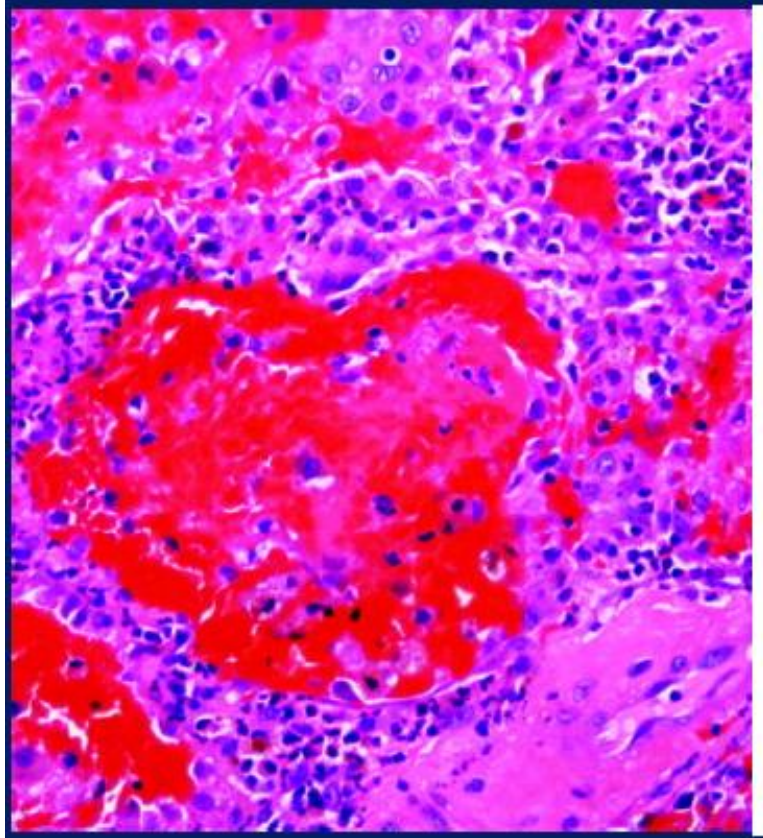
Renal artery involvement:
- Takayasu's arteritis
- Fibromuscular dysplasia

Segmental or lobar artery involvement (within the kidney):
- Polyarteritis nodosa

PEARL: A good skin biopsy includes fat.



PEARL: Remember to order antiphospholipid antibodies in patients with alveolar hemorrhage.



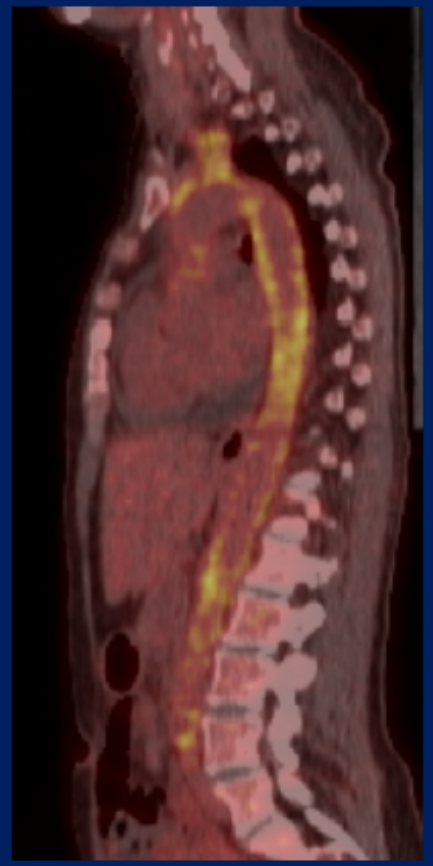
Seminars in Arthritis and Rheumatism
Volume 35, Issue 3, December 2005, Pages 154-165

Antiphospholipid Antibodies as a Cause of Pulmonary Capillaritis and Diffuse Alveolar Hemorrhage: A Case Series and Literature Review

Kevin D. Deane MD *, Sterling G. West MD †

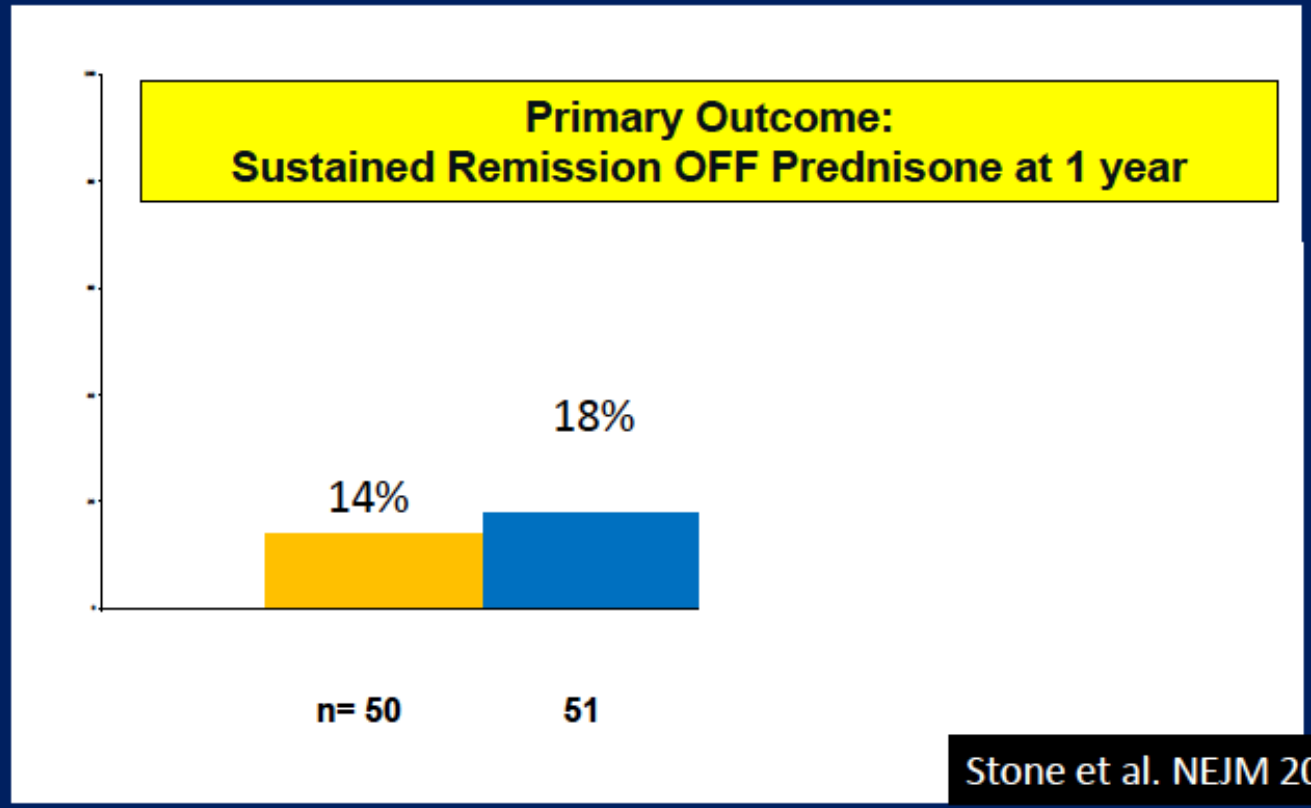
MYTH:
Temporal artery biopsy is the gold standard in diagnosis.

1. Skip lesions
2. Temporal arteries not involved
3. Inadequate biopsy length
4. Involved side not biopsied
5. Correct part of the artery not biopsied
6. Pathological interpretation wrong



The HISTORY is the rheumatologist's scalpel.

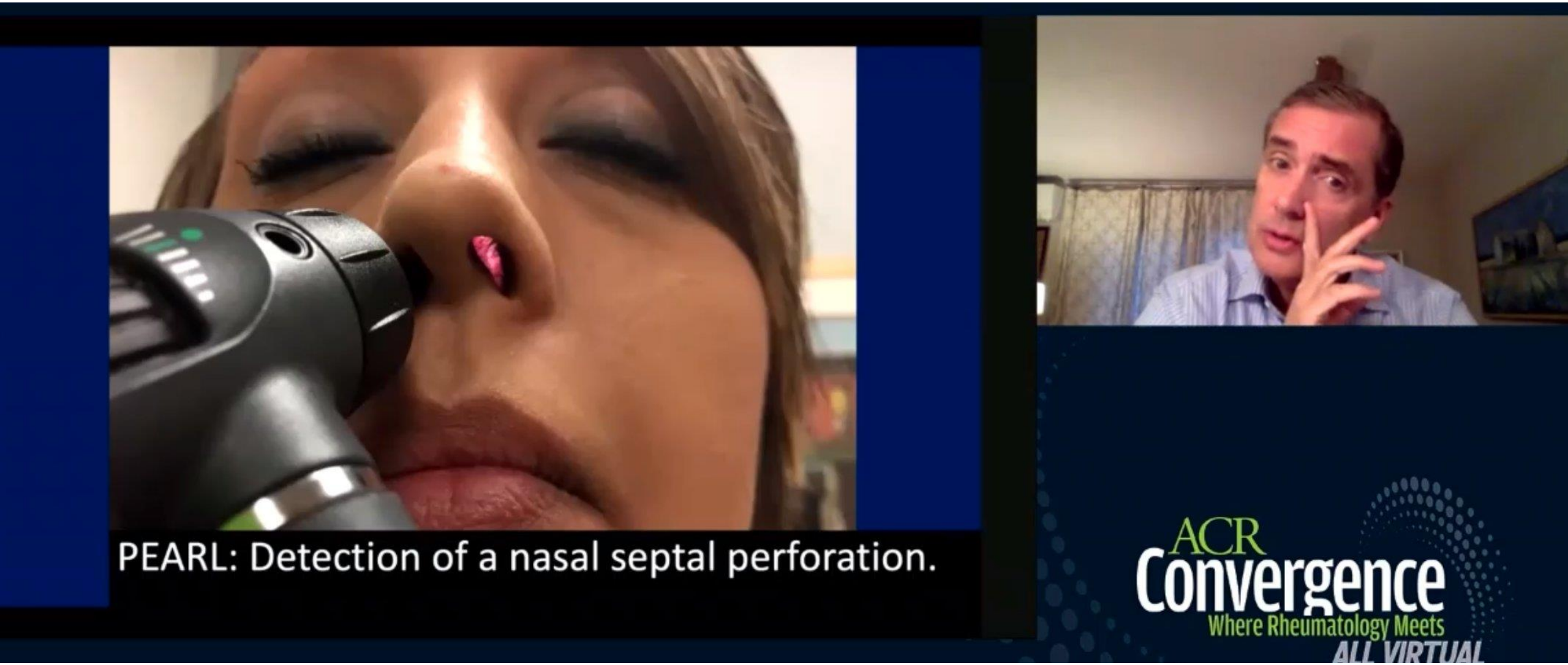
MYTH:
Save tocilizumab for GCA patients who fail prednisone. (Prednisone works most of the time).



Stone et al. NEJM 2017;37 (4):317-328

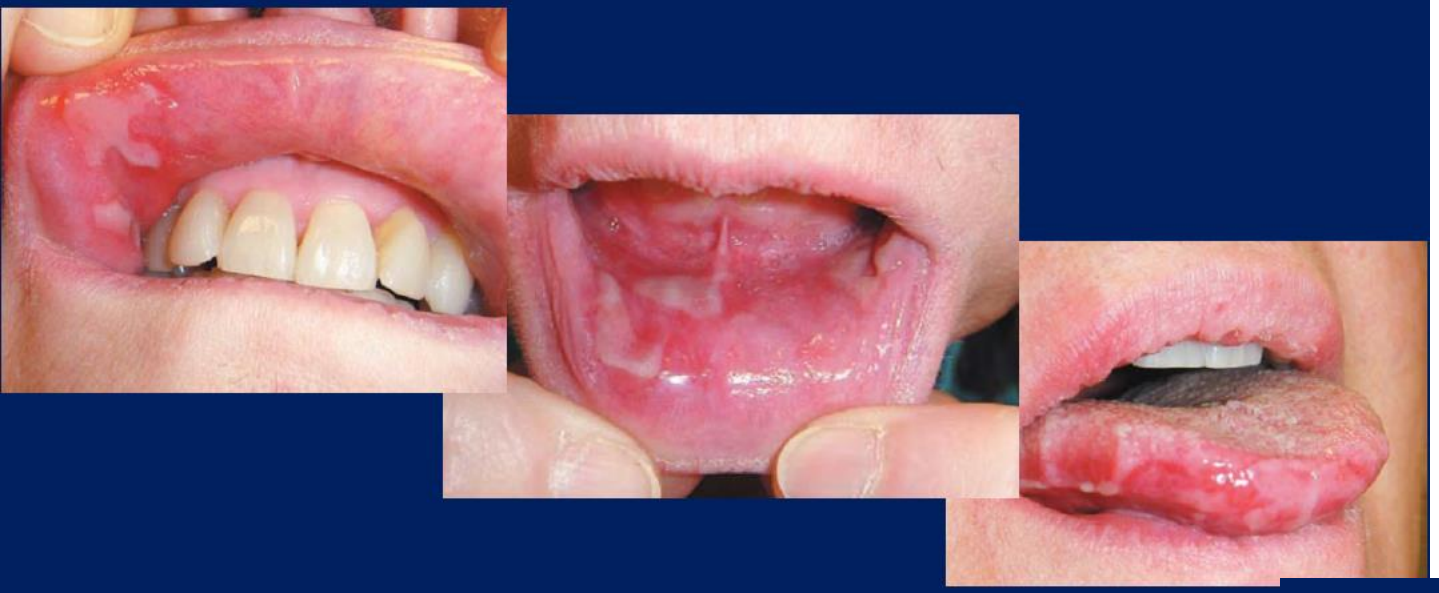
Consider this:

- Women are three times more likely to get GCA.
- Women are FIVE times more likely to fail treatment with prednisone alone.
- Women are 2.4 times likely to fail treatment with prednisone plus tocilizumab:
  - Even though women got MORE tocilizumab per kg than men.

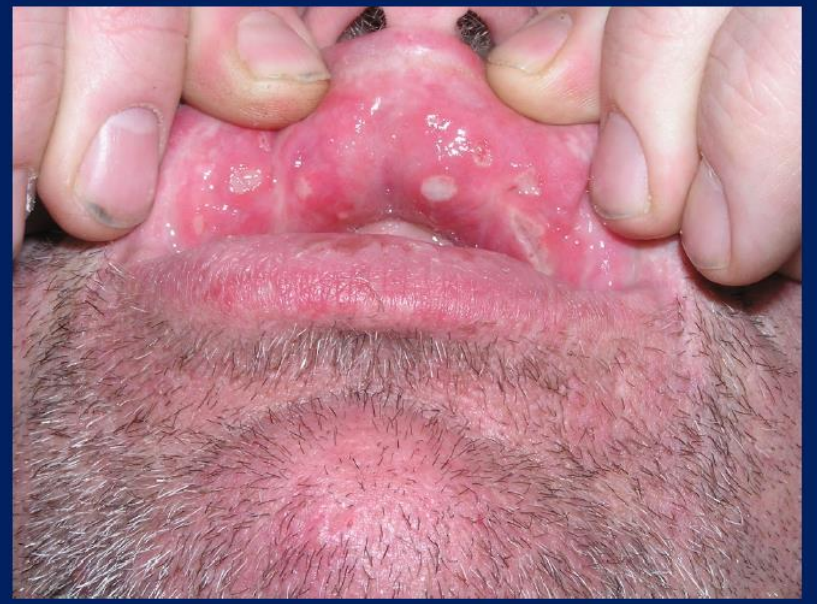


This is a great pearl from John Stone. Rapid bedside detection of nasal septal perforation in GPA. Shine light in on nostril, if you see it like this in the other then septum is perforated #ACR20 @rheumnow

MYTH: 28 yo woman with oral ulcers. Behcet's?



Behcet's Disease



ACR Convergence
Where Rheumatology Meets

Rheumatology Top Secrets & Pearls

Rheum Hacks: A Clinician's Tricks of the Trade

Jason R. Kolfenbach
Associate Professor of Medicine & Ophthalmology
University of Colorado School of Medicine
Director, Rheumatology Fellowship Program

#ACR20

Pearls #9-10 (Critical digital ischemia)

ACR Convergence
Where Rheumatology Meets

Pearl #9: Fight the urge to cut. Autoamputation is often best.

If concern for infection or intractable pain, then consider the OR.

Pearl #10: If isolated digital ischemia to the 4th & 5th digits, especially unilateral, consider proximal ulnar artery disease

-proximal vessel disease in wrist uncommon but can occur

-Allen's test; formal angiogram; consider re-vascularization if confirmed[1]

1) J Rheumatol. 2002;29(1):102

Pearls #15-17 (Pulmonary)

ACR Convergence
Where Rheumatology Meets

Pearl #15: Not all SSc-ILD progresses

Baseline risk factors: low FVC (FVC<70%), extensive fibrosis (high-res CT w/ > 20-50% fibrosis), high mRSS, male gender, significant GI involvement[1-4]

Patients with *low mRSS, less extensive fibrosis, near normal FVC*[2]: ↓ *response to CYC* in SLS-I

Pearl #16: If PAH + vasodilator therapy → pulmonary edema, think of PVOD[5]

Pearl #17: Be cautious when considering PAH-specific therapy in patients w/ PH-ILD

-clinical response less than PAH; potential for decompensation due to VQ mismatch[6]

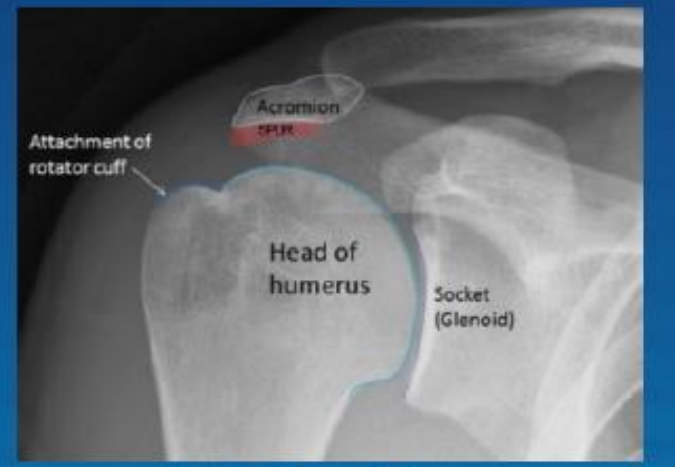
1) Khanna D. Arthritis & Rheum. 2011;63(10):3078-85.
2) Roth MD. Arthritis & Rheum. 2011;63(9):2797-2808.
3) Goh NSL. Am J Respir Crit Care. 2008;177:1248-1254.
4) Hoffmann-Vold AM. Ann Rheum Dis. 2020;Epub online
5) Montani D. Respiratory Medicine. 2010;104: S23-S32
6) Chauvelot L. Arthritis & Rheum. 2020;Sept online

Pearls #20 & 21

ACR Convergence
Where Rheumatology Meets

Pearl #20: Recurrent 'subacromial bursitis' is more often than not rotator cuff tendinopathy

- Address underlying problem with PT/rotator cuff exercises
- Rule out subacromial bone spur

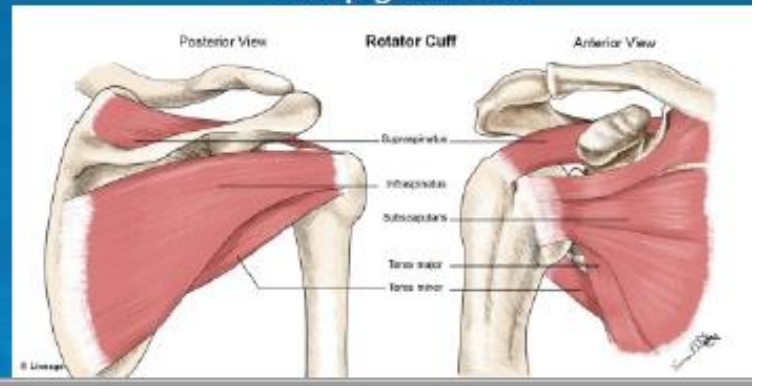


newcastleshoulderandelbow.com.au

Pearl #21: With knee pain, consider sources above & below

- IT band: lateral knee pain
- pes anserine bursae: inferomedial
- pes planus: contributes to patellofemoral disease (flat foot shifts patella laterally)

Fakepigskin.com

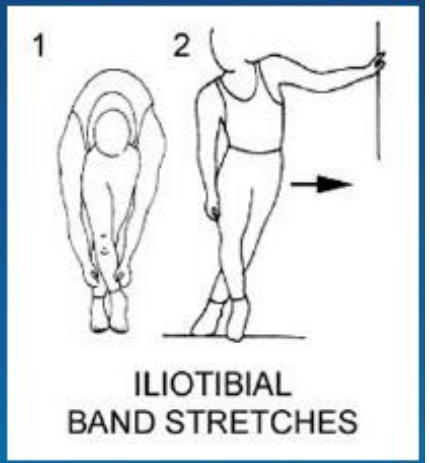


Pearl #22: Recurrent 'trochanteric bursitis'

Bursitis often 2° process: PT for IT band, gluteal m. tightness

If persistent pain, rule out:

- Leg-length discrepancy > 1in
- Hallux rigidus
- Gluteus medius/minimus tear
- Too short of a needle on prior inj. (consider spinal needle)



www.knee-pain-explained.com
osteopathy.colganosteo.com/glutes-stretching-exercises

Pearl #23: BACK PAIN-identify the suspected lesion with history & exam first

ACR Convergence
Where Rheumatology Meets

A) MRI of thoracolumbar spine can be non-specific

- *DDD and disk bulges are commonly coincidental rather than causal*

Lumbar CT or MRI findings in Asymptomatic Individuals[1]			
	20yr olds	50yr olds	70yr olds
Disk degeneration	37%	80%	93%
Disk bulge	30%	60%	77%
Disk protrusion	29%	36%	40%

B) *MR edema at SI joint comes with a DDx, not a definitive Dx*

- Use/overuse, infection, insuff. fracture, OCI, malign.

Bone marrow edema in SI joints[2,3]		
Athletes	Gen pop.	Post partum
25-40%	20-25%	50%
NOTE: erosion and 'deep' bone marrow edema virtually absent in these 3 groups		

1) Jarvik JG. Am J Neuroradiol. 2015. 36(4):811-16.
2) De Winter. Arthritis Rheumatol. 2018. 70(7):1042-48
3) Weber U. Arthritis Rheumatol. 2018. 70(5):736

RA and Interstitial Lung Disease: Management Challenges

Joan M Bathon, MD
Professor of Medicine
Columbia University Irving Medical Center
New York, NY

NOVEMBER 5-9 #ACR20

3S010. How I Treat Difficult RA: Panel Session

THEATER MODE

John Richards, MBBS
Veterans Affairs Pittsburgh Healthcare System
Rheumatology Section Chief

Joan Bathon, Joan M Bathon MD
Columbia University
Chief, Division of Rheumatology

Josef Smolen
Medical University of Vienna
MD

Stanley Cohen, MD
Metroplex Clinical Research Center
MD

6:00 PM - 7:00 PM EET on Saturday, November 7
Add to Calendar

Treatment Questions

- Did MTX or leflunomide cause or worsen his ILD? unlikely
- Is there a DMARD that will treat both his ILD and his arthritis? maybe
- Would nintedanib or perfenidone be more efficacious than a DMARD for managing RA-ILD? No direct comparison data
- Is it safe to combine nintenanib or perfenidone with a conventional DMARD and/or a targeted DMARD ? Probably
  - How early to initiate? How to identify rapid progressors?

Rheumatoid Arthritis and Liver Disease

Stanley Cohen MD
Clinical Professor of Internal Medicine, UTSouthwestern Medical School
Medical Director, Metroplex Clinical Research Center
Rheumatology Program Director, THR Presbyterian Hospital
Dallas, Texas

Risk stratification for HBV reactivation

ACR Convergence — Where Rheumatology Meets

Therapy	HBsAg positive	HBsAg negative Anti-HBc positive
Anti-CD20 Hematopoietic Stem cell Transplantation	Very high***	Moderate
High dose corticosteroids* Other cytokine inhibitors (e.g. anti-CD52)	High	Low
Combination cytotoxic chemotherapy** (without corticosteroids) Anti-TNF Anti-rejection therapy for solid organ transplant recipients	Moderate	Rare
Methotrexate Azathioprine	Low	Rare

*Doses of corticosteroids in excess of 20mg of prednisone (or equivalent) have been reported to have high risk of HBV reactivation
**Examples of combinations of cytotoxic therapy that have been associated with HBV reactivation include cisplatin-based chemotherapy for squamous cell carcinoma and CHOP for lymphoma.
***Although reported rates of HBV reactivation vary considerably, rough estimates of very high risk could be considered to be in excess of 20%, high in the 11-20% range, moderate somewhere between 1 and 10% and low less than 1%.

Relative Risk of Reaction HBV

ACR Convergence — Where Rheumatology Meets

HIGHEST → LOWEST

CHRONIC HBV INFECTION	INNACTIVE CARRIER	RESOLVED HBV	RESOLVED HBV
HBs Ag+ High HBV DNA	HBs Ag + Low HBV DNA	Anti-HBc alone	HBsAg neg anti-HBc + anti-HBs +

All patients with a past history of HBV are at some finite risk of reactivation regardless of presence or absence of serologic markers

Important things to take note of re: HBV reactivation (risk stratification and RR) when we consider therapies for our RA pts.

HOW I TREAT DIFFICULT RA: TREATMENT REFRACTORY RA

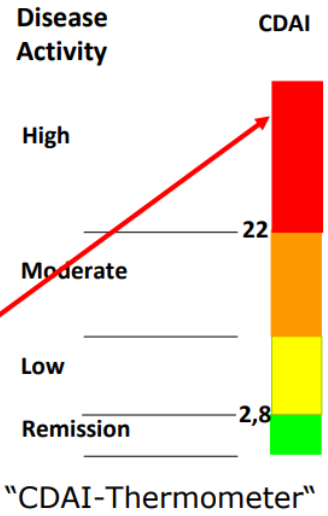
Josef S. Smolen
Division of Rheumatology, Department of Medicine 3,
Medical University of Vienna, Austria

MEDICAL UNIVERSITY OF VIENNA

TJC:	14
SJC:	10
Pt global:	7.7/10
Ev global:	6.2/10
CRP:	5 mg/dl

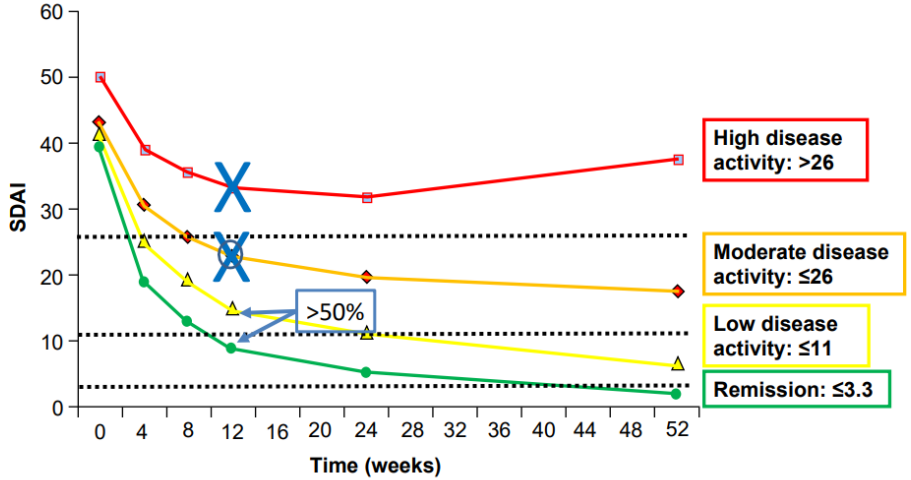
CDAI =
14 + 10 + 7.7 + 6.2 =35.9

SDAI = CDAI + 5.0 = 40.9



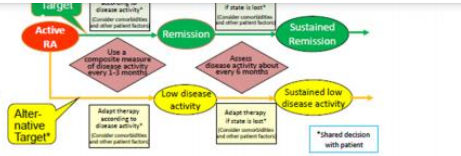
"CDAI-Thermometer"

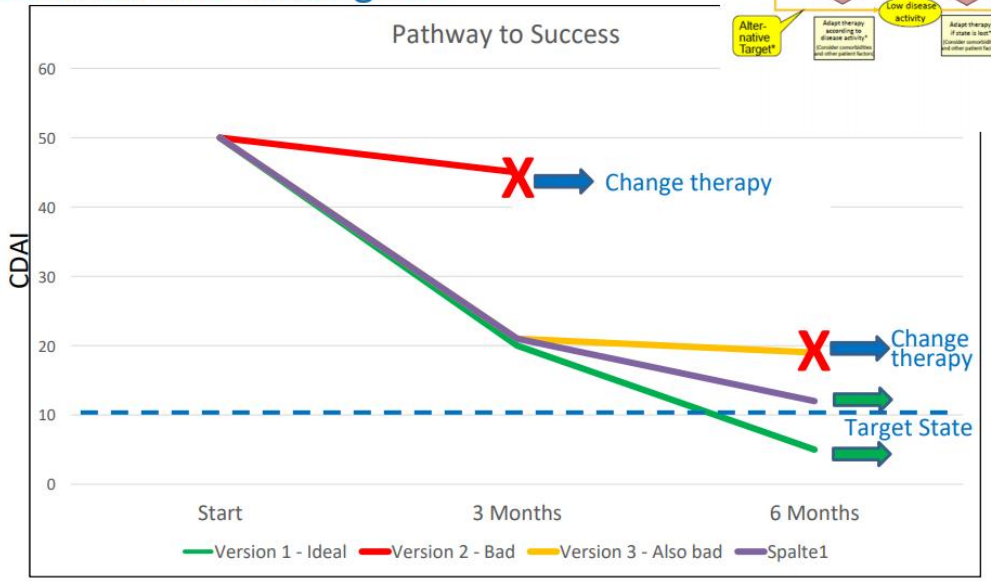
Response at 3 Months From Treatment Initiation Predicts Long-Term Response



Aletaha, et al. Arthritis Rheum 2007;56:3226–35

What Does T2T Mean? Adherence of Rheumatologists!





Back to 2F014. Evaluation and Treatment of Systemic Sclerosis-ILD in the New Decade

Systemic Sclerosis-ILD Treatment

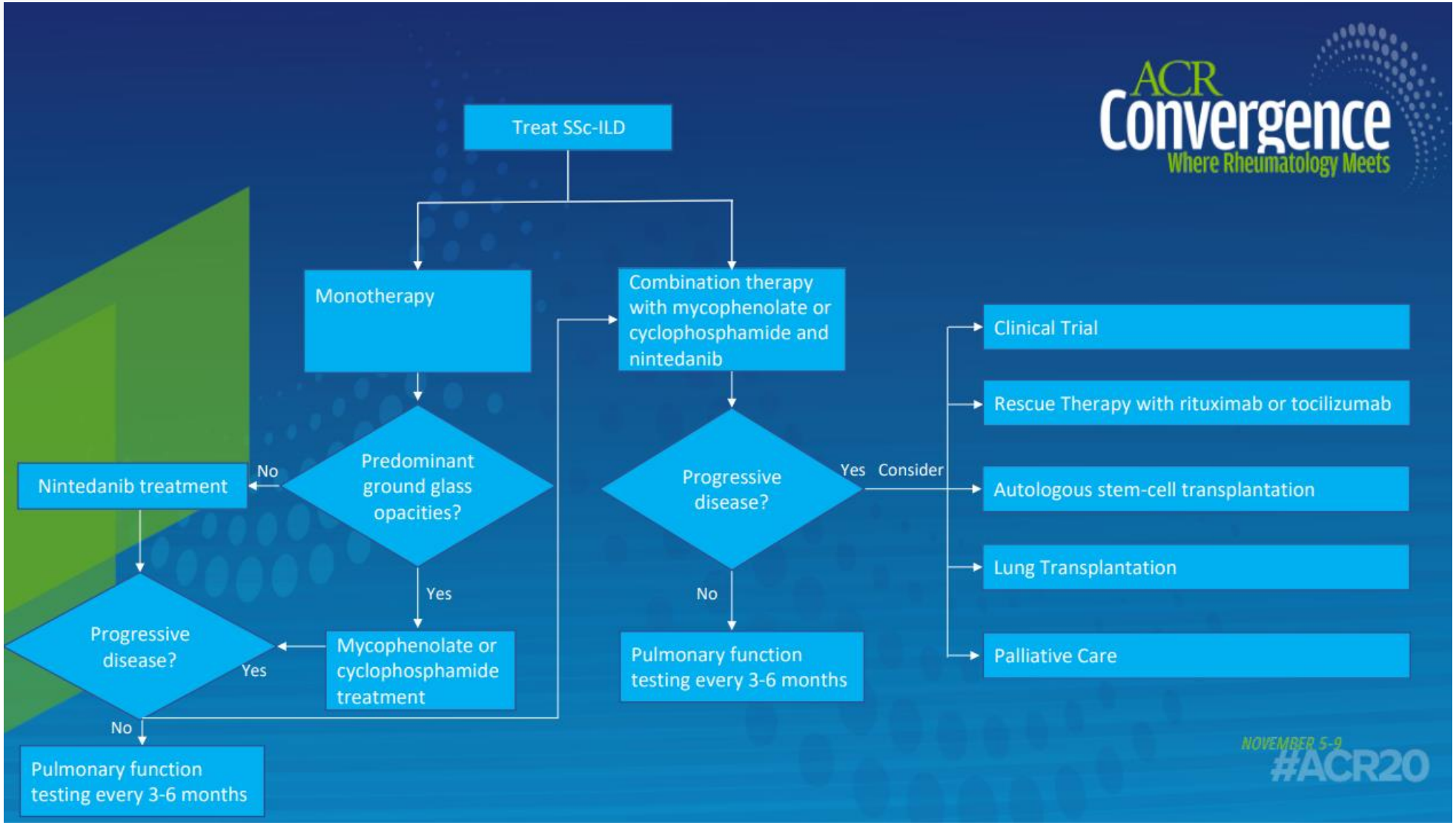
7:20 PM - 7:40 PM EET on Friday, November 6

Add to Calendar

SCIENTIFIC SESSION

Speakers

Richard Silver, MD
Medical University of South Carolina
Distinguished University Prof

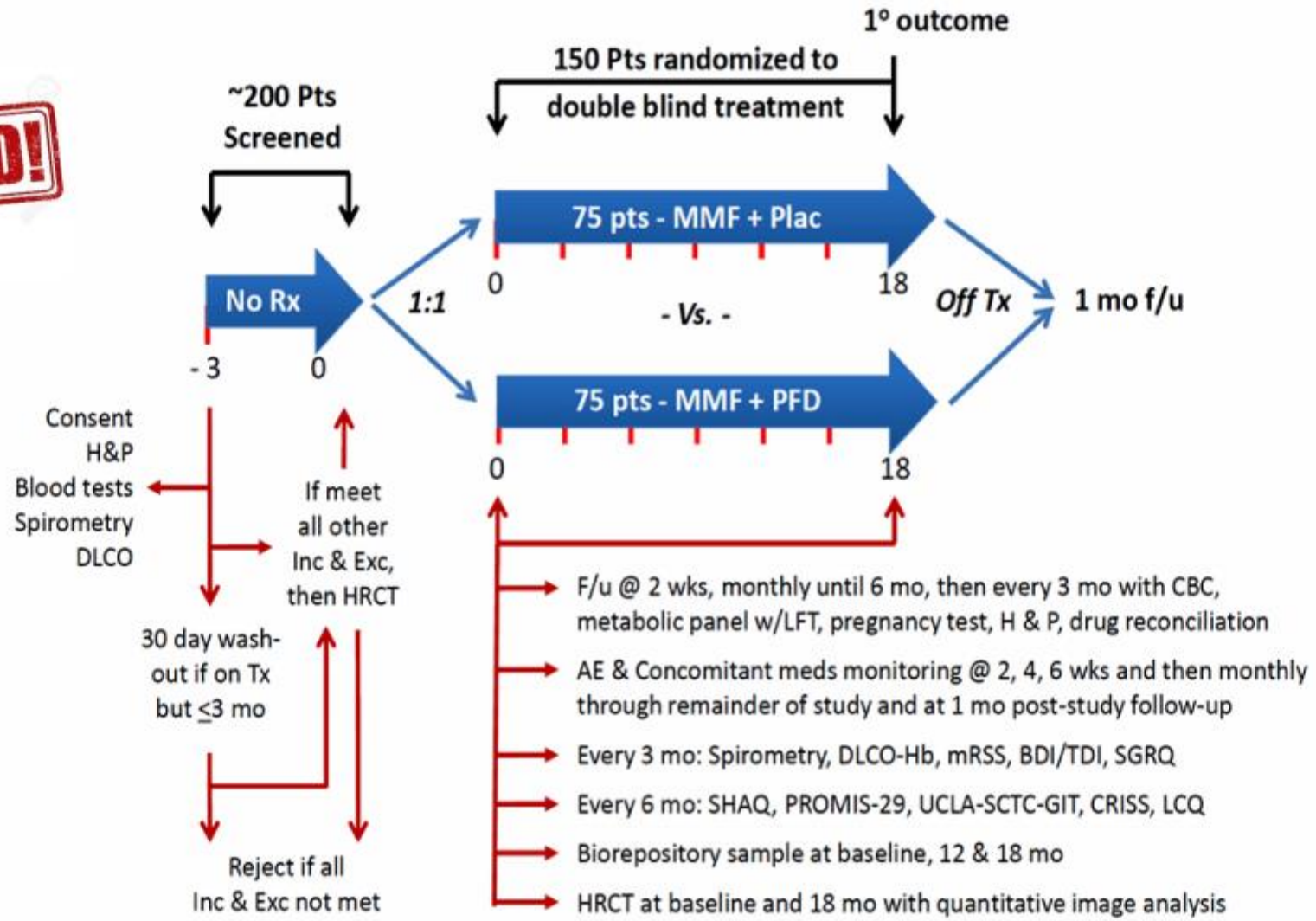


Scleroderma Lung Study III

ACR

Where Rheumatology Meets

STAY TUNED!




LOONEY TUNES
That's all Folks!