

Recent Updates in Rheumatology

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MAY 4, 2019



ALASKA NATIVE
TRIBAL HEALTH
CONSORTIUM

Disclosures

I have no financial relationships to disclose.

Objectives

1. Identify recent developments in the diagnosis and management of rheumatic diseases.
2. Recognize newly described diseases in rheumatology.
3. Apply information from recently published rheumatology studies to improve the care of patients with rheumatic diseases.

Case 1

A 60 year old man presents with new-onset inflammatory polyarthritis. He is found to have a positive rheumatoid factor and ANA with negative anti-CCP antibody. He has a sister with rheumatoid arthritis.

Past medical history is notable for non-small cell lung cancer. He has responded well to treatment with nivolumab (anti-PD1), which he has been taking for 5 months.

He has been started on prednisone 10 mg daily without much improvement in his joint symptoms.

What is the most likely diagnosis?

Immune-Related Adverse Events with Checkpoint Inhibitors

Immune checkpoint blockade increasing used in cancer treatment and highly effective

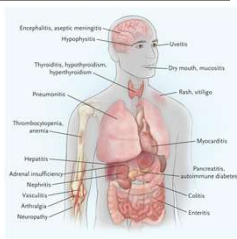
Target downregulators of immunity

- CTLA-4, PD-1, PD-L1

Immune-related adverse events increasingly recognized in many organ systems

No prospective trials to guide management

Glucocorticoids often used as first-line treatment



MA Postow et al. N Engl J Med 2018;378:158-168.

Arthritis Associated with Checkpoint Inhibitors

Two case series recently published of arthritis (n=10) and arthritis and other rheumatic diseases (n=43; 34 with arthritis) in setting of checkpoint inhibitors

Both found mean age in 60s and ~50% female

Some had preceding symptoms or family history but most did not

Polyarthritis or oligoarthritis most common

ANA positive at low titer in 6/8 tested in one series; elevated ESR or CRP in other series; only 2 cases of 44 with anti-CCP antibodies

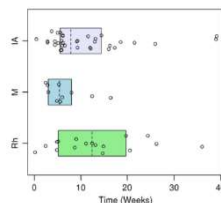
Other organ systems involved in 50-70%

Time from onset of therapy to joint symptoms was 4-6 months

Treatment with prednisone in most cases

- Some also treated with DMARDs
- Mean dose 30 mg in one series and <20 mg in other series

Mean arthritis symptom duration 9 months after stopping immunotherapy in one series and treatment duration 4 months in other



Smith MH, Bass AR. Arthritis Care Res 2019;71: 362.
Richter MD, et al. Arthritis Rheumatol 2019;71:468.

Use of Checkpoint Inhibitors in Patients with Pre-Existing Autoimmune Disease

Systematic review of [published case reports](#) identified 123 patients in 49 publications

Most common diseases were psoriasis/PsA or RA

46% had active disease at time of starting checkpoint inhibitor

43% were on treatment for their autoimmune disease

Exacerbation of autoimmune disease or de novo irAE occurred in 75%

- Exacerbation of preexisting disease more common
- Events less common if on immunosuppressive therapy at baseline

3 patients died of adverse events

Abdel-Wahab N, et al. *Ann Intern Med* 2018. doi:10.7326/M17-2073

Use of Checkpoint Inhibitors in Patients with Pre-Existing Autoimmune Disease

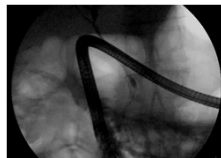
Table 3. CPI-Related Adverse Events Reported in the Literature According to the Disease Activity of the Preexisting Autoimmune Disease and the CPI Therapy Used

Variable	Patients, n	Adverse Event, n (%)		
		Any	Exacerbation of Autoimmune Disease	De Novo irAE
Status of autoimmune disease at start of CPI therapy†				
Active	49	33 (67)	23 (47)	16 (33)
Inactive or stable	57	42 (75)	30 (53)	14 (25)
Receiving any therapy for autoimmune disease at start of CPI therapy†				
Yes	44	26 (59)	17 (39)	10 (23)
No	57	47 (83)	33 (58)	20 (35)
Receiving immunosuppressive therapy for autoimmune disease at start of CPI therapy				
Yes	27	18 (67)	13 (48)	5 (19)
No	74	55 (74)	37 (50)	25 (34)
CPI used				
Ipilimumab	55	36 (66)	20 (36)	23 (42)
Anti-PD-1 or anti-PD-L1 agent	45	52 (82)	40 (82)	17 (24)
Combination of ipilimumab and nivolumab	3	3 (100)	1 (33)	2 (67)

Case 2

61 year old man is referred for possible systemic disease with multiple features over the past 9 years:

- Dacryoadenitis of right lacrimal gland 9 years ago
- Chronic sinusitis, nasal polyps, and cough-variant asthma with relatively unremarkable evaluation by allergist in the past.
- Submandibular gland mass 2 years ago
- Recently diagnosed with cholangitis after presenting with weight loss, elevated LFTs, and biliary strictures on ERCP. There was also a question of possible mass in the head of the pancreas.
- Several physicians have suspected GPA (Wegener's) or sarcoidosis in the past.



What is the most likely unifying diagnosis for this patient?

IgG4 Related Disease History

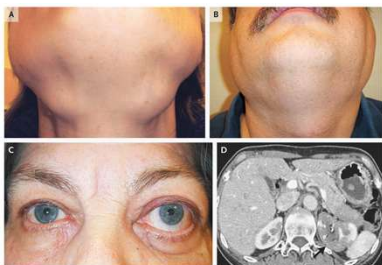
Autoimmune pancreatitis linked to elevated serum IgG4 levels in 2001
 IgG4 positive plasma cells found in pancreatic tissue in autoimmune pancreatitis
 Recognized as systemic condition in 2003 and more widely known ~2012
 Described in almost every organ system
 Histopathologic features are characteristic
 Nomenclature has evolved

- At least 10 other names exist

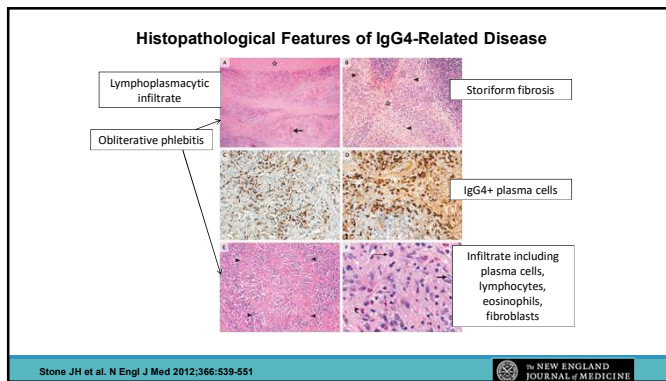
Clinical Manifestations of IgG4 RD

Type 1 autoimmune pancreatitis	Riedel's thyroiditis
IgG4-related cholangitis	Interstitial pneumonitis or inflammatory pseudotumors of lung
Salivary or lacrimal gland disease	Tubulointerstitial nephritis
Inflammatory orbital pseudotumor	Hypophysitis
Retroperitoneal fibrosis	Pachymeningitis
Aortitis and periaortitis	

Clinical and Radiologic Features of Selected Manifestations of IgG4-Related Disease.



Stone JH et al. N Engl J Med 2012;366:539-551.



What's New in IgG4 Related Disease?

ACR-EULAR Classification Criteria presented in 2018

Inclusion:

- At least one of these 10 organs involved: pancreas, bile ducts, orbits, lacrimal glands, major salivary glands, retroperitoneum, kidney, aorta, pachymeninges, and thyroid gland.

Exclusion:

- 21 exclusions categorized as clinical, laboratory, radiographic, and pathologic

Points:

- Must have at least 19 to classify as IgG4 RD

IgG4-related disease inclusion domains and point assignments

Domain	Points
IgG4 level	0
Abnormal and less than 2x upper limit of normal	3.7
2x to 5x UCL	6.1
Abnormal > 5x UCL	10.8
Histopathology and immunostaining	0
Classic lymphoplasmacytic infiltrate	3.7
DL plus obliterative phlebitis	6.1
DL plus storiform fibrosis	10.8
Lacrimal and/or major salivary gland enlargement	5.9
Two or more sets of glands involved	10.8
Chest and Renal aorta	3.8
Pericardiovascular and aortic thickening	3.8
Pericardial band-like soft tissue in the thorax	3.8
Pachymeningeal and Diffuse perineuritis (case of tubularization)	8.0
Diffuse perineuritis and capsule-like ring with decreased enhancement	10.5
Pericardial and biliary tree involvement	10.7
Kidney	5.8
Hypocomplementemia	5.8
Renal pathologic thickening in soft tissue or both	8.1
Retroperitoneum	4.2
Diffuse thickening of the abdominal aortic wall	7.8
Concentric or eccentric soft tissue around the abdominal aorta or their variants	7.8

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IgG4 Related Disease Treatment

International Consensus Statement published in 2015

- Glucocorticoids are used for induction of remission
- Few studies to support conventional immunosuppressive agents
 - Retrospective case reports suggest possible benefit of methotrexate, azathioprine, mycophenolate mofetil
- B-cell depletion therapy has more evidence but not available in all countries for IgG4 RD

B cell depletion therapy

- Rituximab effective in open label trial
- Clinical trials ongoing for obexelimab (XmAb5871, non-depleting anti-CD19) in IgG4 RD and SLE

INTERNATIONAL CONSENSUS STATEMENT ON THE MANAGEMENT AND TREATMENT OF IgG4-RELATED DISEASE

SPECIAL ARTICLE

International Consensus Guidance Statement on the Management and Treatment of IgG4-Related Disease

A. Kikuchi^{1,2}, Z. S. Wilson³, J. L. Cervera⁴, T. Akizuki⁵, A. Arino⁶, M. N. Gershwin⁷, S. T. Chan⁸, T. Ishii-Tani⁹, L. Fardipour¹⁰, D. Gao¹¹, P. A. Han¹², T. Kawanishi¹³, S. Kato¹⁴, M. Kawanishi¹⁵, M. K. Kim¹⁶, V. Kozlov¹⁷, R. Kozlov¹⁸, M. M. Kozlov¹⁹, R. L. Luthi²⁰, V. Mavroukaki²¹, S. Mavroukaki²², S. Nishimura²³, T. Nishimura²⁴, H. Nishimura²⁵, A. Okada²⁶, J. B. Park²⁷, T. Saito²⁸, S. Shimizu²⁹, A. Shimizu³⁰, T. Shimizu³¹, H. Takahashi³², M. Takahashi³³, A. Tanaka³⁴, M. Taniuchi³⁵, G. J. Willems³⁶, J. P. Willems³⁷, M. Yamasaki³⁸, W. Zhang³⁹, T. Chiba⁴⁰ and J. H. Stone⁴¹

Case 3

A 53 year old man with rheumatoid arthritis and severe degenerative changes of the right knee is being considered for elective total knee arthroplasty. You are asked to provide pre-operative risk assessment and recommendations for medication management. He is currently taking methotrexate 17.5 mg PO weekly, folic acid 1 mg daily, and infliximab 400 mg IV every 8 weeks.

Questions:

1. Which medications need to be held in the perioperative period?
2. For those that need to be stopped, when should they be stopped and when can they be restarted after surgery?

ACR-AAHKS Guidelines

Arthritis Care & Research
Vol. 30, No. 66, March 2017, pp 98-107
DOI: 10.1093/arthritis/rkx001
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SPECIAL ARTICLE

**2017 American College of Rheumatology/
American Association of Hip and Knee Surgeons
Guideline for the Perioperative Management of
Antirheumatic Medication in Patients With
Rheumatic Diseases Undergoing Elective Total Hip
or Total Knee Arthroplasty**

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ACR-AAHKS Guidelines: DMARDs to CONTINUE through surgery

DMARD	Dosing Interval	Continue/Withhold
Methotrexate	Weekly	Continue
Sulfasalazine	Once or twice daily	Continue
Hydroxychloroquine	Once or twice daily	Continue
Leflunomide	Daily	Continue
Doxycycline	Daily	Continue

ACR-AAHKS Guidelines: STOP Biologic Agents

DMARD	Dosing Interval	Schedule Surgery	Stop prior to surgery at interval as noted
Adalimumab	Weekly or every 2 weeks	Week 2 or 3	Resume at minimum 14 days after surgery in the absence of wound healing problems, surgical site infection, or systemic infection.
Etanercept	Weekly	Week 2	
Infliximab	Every 4, 6, or 8 weeks	Week 5, 7, or 9	
Certolizumab	Every 2 or 4 weeks	Week 3 or 5	
Golimumab	Every 4 weeks (SQ) or 8 weeks (IV)	Weeks 5 or 9	
Abatacept	Monthly IV or weekly SQ	Week 5 or Week 2	Also stop: <ul style="list-style-type: none"> Anakinra Secukinumab Ustekinumab Belimumab
Rituximab	2 doses every 4-6 months	Month 7	
Tocilizumab	Weekly SQ or every 4 weeks IV	Week 2 or Week 5	
Tofacitinib	Daily or twice daily	7 days after last dose	

ACR-AAHKS Guidelines and SLE

Medication	Severe SLE	Not Severe SLE	Severe SLE: Current treated for severe organ manifestations (induction or maintenance): <ul style="list-style-type: none"> Lupus nephritis CNS lupus Severe hematologic manifestations Pneumonitis Others in Table 1 of guidelines
Mycophenolate mofetil	Continue	Withhold*	
Azathioprine	Continue	Withhold*	
Cyclosporine	Continue	Withhold*	
Tacrolimus	Continue	Withhold*	

* Discontinue one week prior to surgery.

Case 3

A 53 year old man with rheumatoid arthritis and severe degenerative changes of the right knee is being considered for elective total knee arthroplasty. You are asked to provide pre-operative risk assessment and recommendations for medication management. He is currently taking methotrexate 17.5 mg PO weekly, folic acid 1 mg daily, and infliximab 400 mg IV every 8 weeks.

Questions:

- Which medications need to be held in the perioperative period? **Infliximab**
- For those that need to be stopped, when should they be stopped and when can they be restarted after surgery? **Schedule surgery 9 weeks after last infusion**

Case 4

There is a mumps outbreak in Anchorage. Your patient, a 43 year old woman with rheumatoid arthritis, has been identified as part of a high risk group. She received the two doses of MMR previously recommended for her, but she has been offered a 3rd dose to provide her additional medication.

Which of the following medications would be a contraindication for MMR vaccination?

1. Methotrexate 15 mg PO weekly
2. Prednisone 5 mg PO daily
3. Hydroxychloroquine
4. Adalimumab

Vaccines and Biologics

Live vaccines are contraindicated for patients on biologic agents and JAK inhibitors.

In adults, this includes:

- MMR
- Flumist
- Zostavax (no longer recommended)
- Varicella (for those born in 1980 or later)

Zoster and Rheumatic Diseases

Increased incidence of zoster in RA, SLE, and other autoimmune diseases

Risk highest in SLE

Risk as high or higher than general population age 60 and over in RA starting at age 40 and SLE at all ages

Suggests zoster vaccination would be beneficial at younger ages

Table 2: Incidence rate of herpes zoster per 1000 person years by 10 year age group and autoimmune disease or comparator cohort

Age group	Cohorts							
	Healthy ^a IR	SLE IR	SLE IR	RA IR	RA IR	RA IR	RA IR	RA IR
20-29	2.7	7.8	11.6	6.6	N/A	0.9	N/A	0.9
30-39	3.3	7.3	11.1	6.2	9.8	0.7	8.1	0.3
40-49	3.9	6.5	10.4	10.0	8.8	0.4	7.1	0.1
50-59	5.8	8.2	11.7	10.4	13.2	0.7	8.3	0.9
60-69	8.1	10.4	14.6	14.1	18.0	1.3	14.3	0.3
70-79	10.6	13.1	18.0	18.0	26.3	2.0	20.3	0.3
80-89	13.1	15.6	20.0	20.0	30.0	2.5	25.0	0.3

IR = Incidence rate per 1000 person years
^a Healthy cohort: no autoimmune disease, inflammatory conditions or diabetes
 IR = Incidence rate per 1000 person years
 Compared to healthy older people aged 60-69 (IR=10.0), rates were classified as significantly higher (dark red shading), comparable (light yellow shading) and other (i.e. inconclusive or lower, not shaded)
 Based upon the IRs of 822 reported in the Shingrix Preventive Study for the healthy general population age 60-69 of 10.0 per 1000 PYs and comparing to the IR for patients age 70-79 years old of 6.7 per 1000 PYs in another randomized study, we selected a non-inferiority margin of 0.42 (incidence rate ratio of 6.7/10.0 = 0.67)

RA = Rheumatoid arthritis, SLE = Systemic lupus erythematosus, IR = Incidence rate per 1000 person years
 Healthy: IR = 2.7, SLE = 7.8, RA = 6.6, RA = 0.9, RA = 0.9, RA = 0.9, RA = 0.9, RA = 0.9

Zoster Vaccination in Rheumatic Diseases

Preferred vaccine for zoster in adults is recombinant zoster vaccine (Shingrix)

ACIP gives no recommendation for use in immunocompromised patients

NOT a live vaccine

Concern:

- Vaccine contains a potent adjuvant
- It is not yet known if it could cause exacerbations of autoimmune disease

patients:

50+
years old

doses:

2-6 months
apart

Who should get Shingrix

While Shingrix is not contraindicated in immunocompromised people, it is not recommended by the Advisory Committee on Immunization Practices (ACIP) at this time. ACIP will review evidence for Shingrix in immunocompromised people as it becomes available.

CDC Fact Sheet: <https://www.cdc.gov/shingles/fact-sheets/shingles-factsheet-hcp.html>

Influenza vaccination in RA

Increased risk of influenza in RA

Vaccination is indicated but responses may be blunted by medications

Recent studies have found:

- Influenza vaccination in patients with autoimmune rheumatic diseases reduced the risk of hospitalization for pneumonia, hospitalization for COPD exacerbation, all-cause mortality and death due to pneumonia in that flu season (aHR(95%CI) 0.59(0.51-0.69), 0.59(0.44-0.80), 0.52(0.47-0.59), 0.47(0.35-0.63) respectively). (2018 ACR Abstract #940)
- High dose influenza vaccine in RA patients increased the immune response to vaccination compared to standard dose vaccine (based on antibody titer increases). (2018 ACR Abstract #837)
- Holding methotrexate for 2 weeks prior to influenza vaccination increased likelihood of immunologic response (also based on antibody titers). (2017 ACR Abstract #827)

Case 4

There is a mumps outbreak in Anchorage. Your patient, a 43 year old woman with rheumatoid arthritis, has been identified as part of a high risk group. She received the two doses of MMR previously recommended for her, but she has been offered a 3rd dose to provide her additional medication.

Which of the following medications would be a contraindication for MMR vaccination?

1. Methotrexate 15 mg PO weekly
2. Prednisone 5 mg PO daily
3. Hydroxychloroquine
4. Adalimumab

Case 5

41 year old man presents with 2 months of increasing pain and swelling of his left knee, right ankle, and several joints in the hands and feet. He had never noticed it much but his wife tells you he has dandruff.

On exam, you find several areas of plaque psoriasis on his scalp and on his abdomen. He has DIP joint swelling, knee and ankle swelling, and a swollen 2nd toe on the left foot.

Labs are notable for elevated ESR and negative CCP and RF. X-rays show no joint damage.

What treatment do you recommend?



ACR/NPF 2018 Guideline for Psoriatic Arthritis Treatment

Non-pharmacologic therapies	• PT, OT, smoking cessation, weight loss, massage therapy, exercise
Symptomatic treatments	• NSAIDs, glucocorticoids, local glucocorticoid injections
Oral small molecules (OSM)	• Methotrexate, sulfasalazine, cyclosporine, leflunomide, apremilas
TNFi	• Etanercept, infliximab, adalimumab, golimumab, certolizumab pegol
IL12/23i	• ustekinumab
IL17i	• Secukinumab, ixekizumab, brodalumab
JAK inhibitor	• tofacitinib

Singh JA, et al. Arthritis Rheumatol 2018; DOI 10.1002/art.40726

Recommendations for initial treatment of PsA in treatment-naïve patients

Recommendation	Level of evidence
1. Treat with TNF inhibitor over an OSM (conditional, consider OSM if not severe or contraindication to biologic)	Low
2. Treat with a TNF inhibitor over an anti-IL-17 (conditional, consider anti-IL-17 if contraindications to TNFi or severe psoriasis)	Very low
3. Treat with a TNF inhibitor over an IL-12/23 biologic (conditional, consider if severe psoriasis, wants less frequent injections, or has contraindications to TNFi)	Very low
4. Treat with an OSM over an IL-17 biologic (conditional, consider if severe psoriasis or PsA)	Very low
5. Treat with an OSM over an IL-12/23 biologic (conditional, consider if has IBD or severe psoriasis)	Very low
6. Treat with MTX over NSAIDs	Very low
7. Treat with an IL-17 over an IL-12/23 biologic	Very low

SEAM Trial

ACR 2018 Abstract #LB11: Etanercept and Methotrexate As Monotherapy or in Combination in Patients with Psoriatic Arthritis: A Phase 3, Double-Blind, Randomized Controlled Study

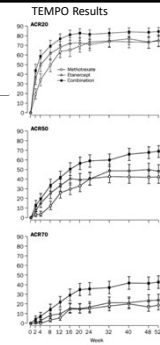
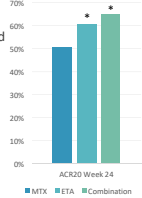
Similar design to TEMPO trial in RA

Different primary endpoints

Interpretation has been that combination therapy with etanercept and methotrexate is no more effective than etanercept alone

No placebo

SEAM Primary Endpoint



Klareskog L, et al. Lancet 2004;363:675 and ACR 2018 Abstract #L11

Case 6

48 year old woman referred for question of rheumatoid arthritis

5 years ago she noticed her joints looking crooked and big

Not much pain and no morning stiffness

Affects DIP and PIP joints

She saw an orthopedic surgeon who told her he didn't know what she had, so she was referred to Rheumatology

What is her diagnosis?



Inflammatory (Erosive) Osteoarthritis

More aggressive form of OA associated with inflammation, erosions, and joint space loss

Affects DIP and PIP joints

Classic radiographic findings of "gull-wing" pattern

Mixed results in previous studies of treatment with steroids or DMARDs

RCT of etanercept vs. placebo for inflammatory hand OA published in 2018

- No difference in primary endpoint, pain by VAS at week 24
- Possible beneficial effects on radiographic changes in actively inflamed joints



Ann Rheum Dis 2018;77:1757-1764.

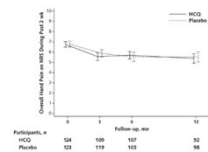
Recent Studies in Hand Osteoarthritis

Hydroxychloroquine ineffective in hand osteoarthritis

2018 EULAR recommendations for management of hand OA, section on medications:

- Topical treatment preferred over systemic
- Limit duration of oral analgesics
- Intra-articular injection of glucocorticoids should not generally be used in hand OA but may be considered if painful IP joints
- Do not treat with conventional or biologic DMARDs
- Chondroitin sulfate may be used (one trial supporting this in hand OA)

Hydroxychloroquine Effectiveness in Reducing Symptoms of Hand Osteoarthritis: A Randomized Trial
 Scott D, Knapik M, Pineda A, et al. *Ann Intern Med*. 2018;169(5):291-299. DOI: 10.7326/M17-2812



Case 7

54 year old woman with RA seropositive for CCP and RF presents for follow-up. She has been on methotrexate, sulfasalazine and hydroxychloroquine for one year and has high disease activity. X-rays show new erosive changes at several MCP joints and the wrists. You feel that she would benefit from a TNF inhibitor. She had cervical cancer 4 years ago, treated with hysterectomy and radiation. She has heard about cancer risk and TNF inhibitors and does not want to start one.

Is she at increased risk of cancer recurrence if she takes a TNF inhibitor?

Cancer Recurrence with TNF Inhibitors

TNF- α is involved in tumor cell destruction but its role in cancer is variable

Studies of incident cancer with TNF inhibitors are generally reassuring

TNF inhibitors often been avoided in patients with a history of cancer due to concerns they might increase risk of recurrence

Population-based cohort study of patients with RA and a history of cancer in Sweden

- Compared cancer recurrence in those treated with TNF inhibitors vs. no biologics
- Using national register data

Conclusion:

- TNF inhibitors not associated with increased cancer recurrence
- Does not completely rule out increased risk based on upper limits of confidence intervals

Raaschou P, et al. *Ann Intern Med*. 2018;169(5):291-299. DOI: 10.7326/M17-2812

New Benefits and Risks of DMARDs

RA confers an increased risk of cardiovascular events and mortality

- Meta-analysis found decreased excess risk since 2000
- Studies have identified decreased CV risk with TNF inhibitors

New JAK inhibitor approved

- Baricitinib and tofacitinib now available
- Risk of zoster is higher in tofacitinib than other DMARDs
 - Increased further if glucocorticoids included
 - Also increased in baricitinib
- Risk of VTE may be increased with JAK inhibitors

ACR 2018 Abstract #2364; Winthrop K, et al. Arthritis Rheumatol 2017;69:1960.

Case 8

63 year old woman with diffuse systemic sclerosis (scleroderma) diagnosed about 10 years ago presents for follow-up. She has interstitial lung disease (ILD) with UIP pattern. Early in her disease she was treated with cyclophosphamide and steroids and has been maintained on mycophenolate mofetil. Her skin disease has been stable, but recent 6 minute walk test demonstrated an oxygen requirement on exertion.

She heard about stem cell treatment as an option for scleroderma and wonders if she is a candidate. What do you recommend?

SCOT Trial in Systemic Sclerosis

Many medications have been studied but few are effective

RCT data supports cyclophosphamide in SSc-related ILD and possibly mycophenolate mofetil

SCOT trial enrolled patients with severe diffuse systemic sclerosis, with lung or renal disease but not pulmonary hypertension

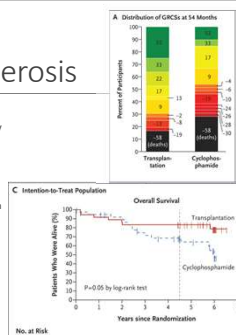
Interventions compared:

- Myeloablation with total-body irradiation followed by reconstitution with a CD34+ selected autograft versus cyclophosphamide

Enrollment at 26 sites over 6 years, with 75 patients total

- Original design was for 226 participants with primary outcome of event-free survival
- Redesignated for 114 participants, stopped at 75

Primary outcome at 4.5 years was a composite score



Sullivan KM, et al. N Engl J Med 2018; 378:35-47 DOI: 10.1056/NEJMoa1703327

Other Trials in Systemic Sclerosis

Tocilizumab in systemic sclerosis

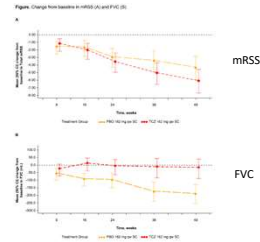
- Phase 3 trial
- Primary endpoint not achieved (mRSS)
- Possibly some benefit with respect to lung disease (FVC)

Pirfenidone in SSc-associated ILD

- Phase 3 trial ongoing

Nintedanib in SSc-associated ILD

- Phase 3 trial enrollment complete
- Submitted to FDA for approval



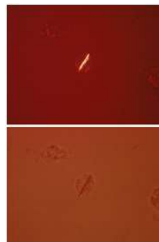
ACR 2018 Abstract #898

Case 9

64 year old man with CKD and HTN, on lisinopril and HCTZ, presents with severe pain, redness, and warmth of his R knee. In the past he had several similar episodes in the big toe. Arthrocentesis of the knee reveals WBC 32,000, 98% PMNs, with negative gram stain and intracellular needle-shaped negatively birefringent crystals. Serum uric acid is 10.8 mg/dL.

He knows about gout and has heard of allopurinol for long-term management, but knows that there are newer medications and would prefer something new.

What do you recommend?



Allopurinol vs. febuxostat as urate-lowering therapy in gout

In acute gout, focus is on treating inflammatory response

In chronic gouty arthritis, urate lowering therapy is the cornerstone

Xanthine oxidase inhibitors first line

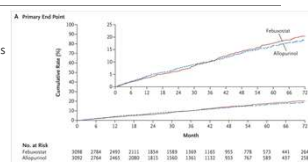
- Inhibit uric acid production
- Allopurinol and febuxostat

Increased risk of CVD in gout

Previous trials suggested higher CVD risk with febuxostat than allopurinol

FDA required an additional trial (CARES)

- Primary endpoint: first occurrence of CV death, nonfatal MI, nonfatal stroke, or urgent revascularization for unstable angina



Non-inferior for primary endpoint, but higher CV mortality and all cause mortality with febuxostat

White WB, et al. N Engl J Med 2018; 378:1200-1210 DOI: 10.1056/NEJMoa1710895

Initiating Urate-Lowering Therapy

Risk of inducing acute gout attack

Prophylaxis:

- Best evidence for colchicine 0.6 mg qd-bid
- NSAIDs also possible
- Use for ~ 6 mo. or until tophi gone

Target serum uric acid < 6.0 mg/dl

Coming soon..

ACR Reproductive Health Guidelines

Biosimilars in the US

New DMARDs

- More JAK inhibitors
- More biologics and more indications for existing biologics

Final Quiz: New Names for Old Diseases

Churg Strauss → EGPA (eosinophilic granulomatosis with polyangiitis)

Wegener's granulomatosis → GPA (granulomatosis with polyangiitis)

Reiter's syndrome → Reactive arthritis

For more information



American College of Rheumatology
www.rheumatology.org
Patient and Caregiver Resources
PDF for Medications and Diseases

Arthritis Foundation
www.arthritis.org

Creaky Joints
www.creakyjoints.org