RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

RHAPP NATIONAL CONFERENCE

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Year in Review

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Faculty Disclosures

Speakers Bureau: Abbvie, Sanofi

Objectives

- Review new and clinically relevant articles from the past year
- Consider practice changes due to new information

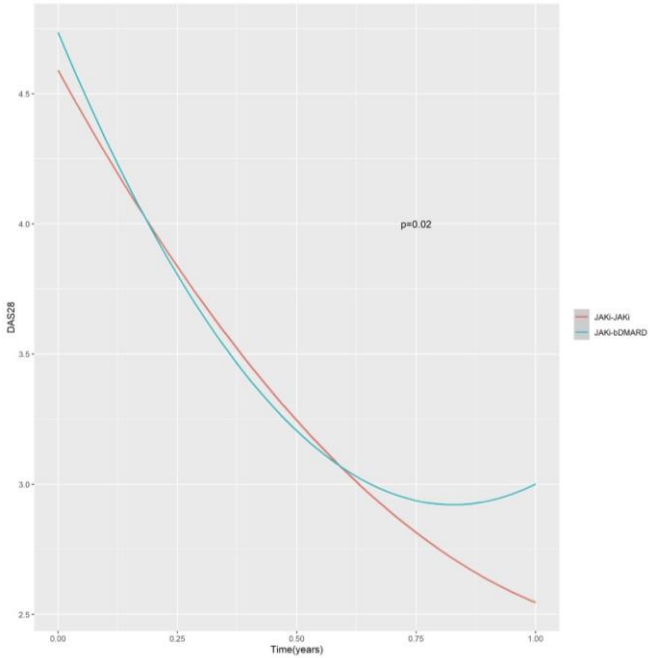
Rheumatoid Arthritis

- Cycling or switching biologics?
- Steroid use and side effects?
- JAK safety?
- Can we withdraw therapy?
- Depression Risk?
- Can we prevent RA?

Cycle or Switch?

- Cohort study included prospectively collected data on 708 RA patients who failed 1st JAK and were then treated with either a 2nd JAK (cycling) or a biologic DMARD (switching)
- Compared the effectiveness of both treatment strategies on drug retention and disease activity, measured by DAS-28 for 1 year after they started their second treatment.
- Results: 154 cycled and 554 switched. Patients cycling JAK inhibitors tended to be older, had longer RA, had already received more biological DMARDs, and had more prolonged exposure to the first JAK inhibitor than those who switched to a biologic
  - Similar drug survival after 2 years of follow-up
  - Over time, test results of patients' disease activity improved similarly in the cycling and switching groups, showing improvement after a year

Figure 2. Age- and gender-adjusted DAS28

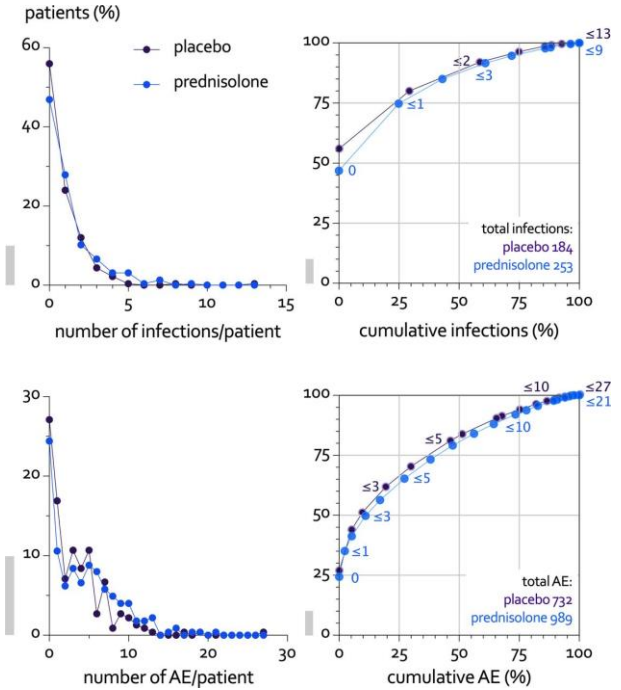


Steroid Safety-GLORIA Trial

- Background Low-dose glucocorticoid (GC) therapy is widely used in rheumatoid arthritis (RA) but the balance of benefit and harm is still unclear.
- Methods: double-blind randomized trial compared 2 years of prednisolone, 5 mg/day, to placebo in patients aged 65+ with active RA. Benefit outcomes included disease activity (DAS28, coprimary) and joint damage (Sharp/van der Heijde, secondary) and pt's with ≥1 adverse event (AE) of special interest.

GLORIA Trial

- Results: n= 451 patients with established RA and mean 2.1 comorbidities, age 72, disease duration 11 years and DAS28 4.5. 79% were on disease-modifying treatment, including 14% on biologics.
- Dz activity was 0.37 points lower on prednisolone; joint damage progression was 1.7 points lower. 60% versus 49% of patients experienced harm outcome, adjusted relative risk 1.24 with the largest contrast in (mostly non-severe) infections
- Conclusion: Add-on low-dose prednisolone has beneficial long-term effects in senior patients with established RA, with a trade-off of 24% increase in patients with mostly non-severe AE



JAK Safety

- Phase 3B/4 ORAL surveillance trial to determine whether tofactinib use was associated with an increased risk of cardiovascular events and malignancies.
- Noninferiority of tofacitinib was not met for MACE or malignancy. In combined analysis of both doses of tofacitinib, hazard ratios were 1.33 (95% confidence interval [CI] 0.91–1.94) and 1.48 (95% CI 1.04–2.09) respectively, compared with TNFα inhibitors. This most recent update from the study was the first to show a potential increased risk of cancer in patients taking jaks
- In September 2021, the FDA updated its earlier Boxed Warning to reflect an increased risk of MACE, malignancy, thrombosis and mortality for tofacitinib as well as for the baricitinib and upadacitinib.

Drug Withdrawal

- ARTIC REWIND trial, which examined decreased therapeutic dosages in RA patients in remission.
  - Compared RA patients in remission kept on stable doses of csDMARDs with those whose doses were cut in half. Patients whose csDMARDs were tapered to half dose experienced a statistically significant increased number of flares during the 12 months of the study.
  - Measures: The primary end point was the proportion of patients with a disease flare between baseline and the 12-month follow-up
  - Results: n=156. Flare occurred in 19 patients (25%) in the half-dose csDMARD group vs. 5 (6%) in the stable-dose csDMARD group
- 2021 ACR guideline for the management of RA, which conditionally recommend continuing the same dose of csDMARD in RA patients in remission

Depression

- EULAR June 2022; Pedersen and colleagues analyzed DANBIO registry data
- Objective: To examine mortality rates associated with depression — defined as the first filling of antidepressants in patients with RA, who were diagnosed with incident RA between Jan. 1, 2008, and Sept. 30, 2018.
- Researchers defined depression as an initial filling of a prescription for antidepressants, while death dates were collected from the Danish Civil Registration System
- N=11,071 patients with RA were followed for 56,993 person-years. 10% filled prescriptions for antidepressants
- Patients with seropositive RA had higher mortality rates (HR = 3.45; 95% CI, 2.66 – 4.47) than seronegative RA diagnoses (HR = 3.08; 95% CI, 2.17-4.37).
- Conclusions:
  - The adjusted risk for mortality increased by 6-fold in patients younger than age 55
  - Patients with incident RA aged 55 to 70 years demonstrated a 3-fold increased risk for mortality (HRR 3.30; 95% CI, 2.27-4.80), followed closely by those over age 70 years (HRR 2.94; 95% CI, 2.26-3.83).

RA Prevention – Abstract Number: 0455

- Abatacept Reverses Subclinical Arthritis in Patients with High-risk to Develop Rheumatoid Arthritis -results from the Randomized, Placebo-controlled ARIAA Study in RA-at Risk Patients
- Abatacept vs placebo reverses subclinical arthritis in patients with ACPA and MRI signs of inflammation,
- Methods: RA-at risk individuals that ACPA + and show MRI signs of inflammation. 6 months treatment phase with either abatacept SQ 125 mg weekly or placebo and 12 months follow up with no treatment.
- Results: n=139 patients; 100 patients were randomized to receive either abatacept or placebo.
  - 61% of the patients in the abatacept group improved in at least one of the MRI parameters (synovitis, tenosynovitis, and osteitis) vs only 31% in the placebo group (p=0.0043).
  - Arthritis developed in 17 patients in the placebo group (34.7%) but only 4 patients (8.2%) in the abatacept group (p= 0.0025).
- Conclusion: These data show that abatacept significantly improves subclinical arthritis in patients at high risk to develop RA. In addition, the data also support the concept that early intervention may prevent or at least delay the development of RA.

RA Prevention – EULAR 2022 Poster 0531

- ABATACEPT DELAYS THE DEVELOPMENT OF RA– CLINICAL RESULTS AFTER 18 MONTHS FROM THE RANDOMIZED, PLACEBO-CONTROLLED ARIAA STUDY IN RA-AT RISK PATIENTS
- 18 month extension of ARIAA
- Results: 1 year after cessation of treatment (18 months after inclusion) the number of patients progressing to RA was lower in the abatacept group (35%) than in the placebo group (57%; p=0.0421).

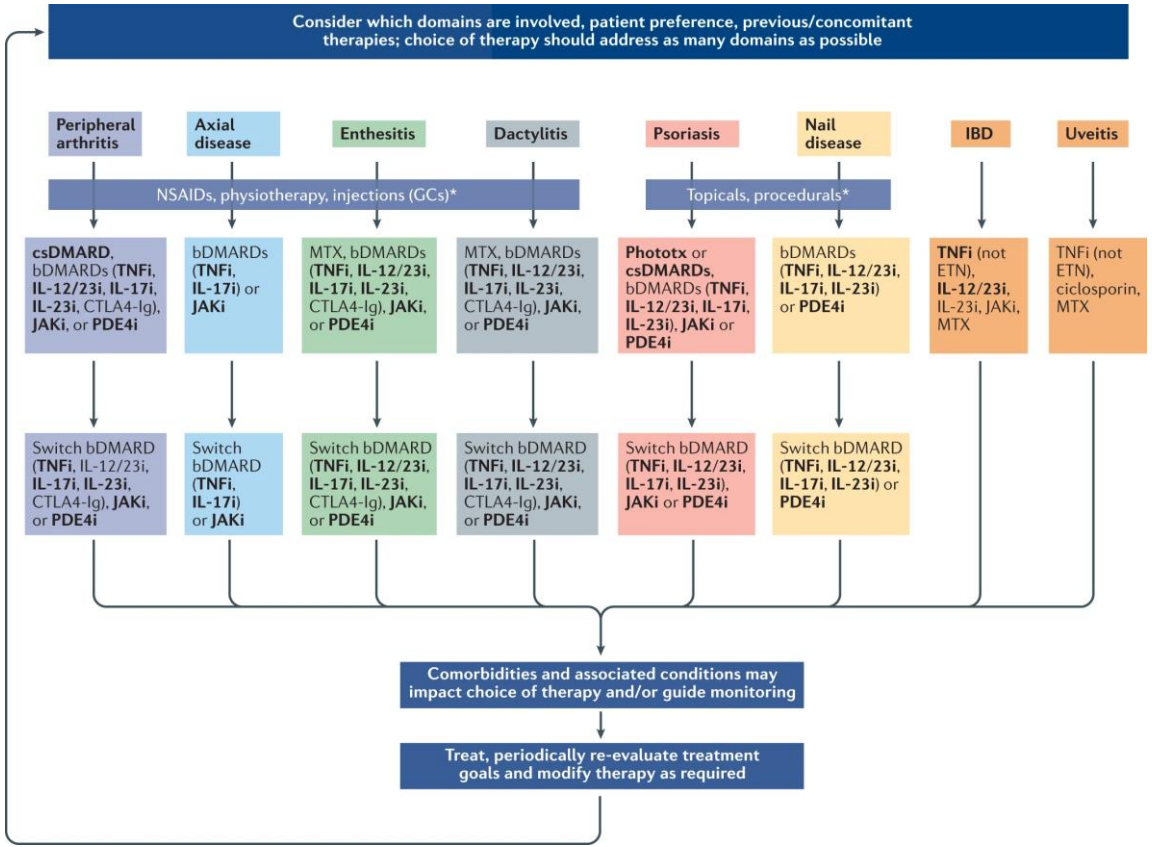
PsA – Prevention

- Can we prevent PsA in PsO pts?
  - Retrospective, non-randomized, using EMR data from University Hospital of Verona in Italy
  - Methods: 464 adults dx with mod-to-severe chronic plaque psoriasis – but not initially PsA. eligible to receive treatment with phototherapy or bDMARD.
    - Group 1: 234 people with psoriasis who had been prescribed at >5 years of bDMARD treatment.
    - Group 2: 230 people who had received at least three courses of phototherapy.
    - Compared how many people went on to develop psoriatic arthritis over 5 years in each of the groups.
  - Results: Pts treated with bDMARDs had a lower risk of developing PsA vs treated with phototherapy.
    - 8% of people in the bDMARD group developed psoriatic arthritis, vs 14% of people in the phototherapy group. Limitations: factors that were associated with a higher risk of developing PsA. These included being older, having nail psoriasis, and having had psoriasis >10 years

PsA – GRAPPA Updates

- The initial guidelines, developed in 2009, were updated in 2015
- 2021 treatment recommendations for psoriatic arthritis (PsA) use a domain-based approach, but, considering that most patients present with disease in multiple domains, this treatment schema combines the recommendations for each domain to guide therapeutic decisions.
- Disease activity should be assessed in each of the domains and consideration given to comorbidities, previous therapies and patient preference.
- Standard ‘step-up’ approaches, as well as expedited treatment routes, are indicated.
- Treatment efficacy and tolerability should be re-evaluated periodically and treatment adjusted as appropriate.
- The order of the products in the boxes is sorted by mechanism of action and does not reflect guidance on relative efficacy or suggested usage.

GRAPPA


Consider which domains are involved, patient preference, previous/concomitant therapies; choice of therapy should address as many domains as possible
Peripheral arthritis
Axial disease
Enthesitis
Dactylitis
Psoriasis
Nail disease
IBD
Uveitis
NSAIDs, physiotherapy, injections (GCs)*
Topicals, procedurals*
csDMARD, bDMARDs (TNFi, IL-12/23i, IL-17i, IL-23i, CTLA4-Ig), JAKi, or PDE4i
bDMARDs (TNFi, IL-17i) or JAKi
MTX, bDMARDs (TNFi, IL-12/23i, IL-17i, IL-23i, CTLA4-Ig), JAKi, or PDE4i
MTX, bDMARDs (TNFi, IL-12/23i, IL-17i, IL-23i, CTLA4-Ig), JAKi, or PDE4i
Phototx or csDMARDs, bDMARDs (TNFi, IL-12/23i, IL-17i, IL-23i), JAKi or PDE4i
bDMARDs (TNFi, IL-12/23i, IL-17i, IL-23i) or PDE4i
TNFi (not ETN), IL-12/23i, IL-23i, JAKi, MTX
TNFi (not ETN), ciclosporin, MTX
Switch bDMARD (TNFi, IL-12/23i, IL-17i, IL-23i, CTLA4-Ig), JAKi, or PDE4i
Switch bDMARD (TNFi, IL-17i) or JAKi
Switch bDMARD (TNFi, IL-12/23i, IL-17i, IL-23i, CTLA4-Ig), JAKi, or PDE4i
Switch bDMARD (TNFi, IL-12/23i, IL-17i, IL-23i, CTLA4-Ig), JAKi, or PDE4i
Switch bDMARD (TNFi, IL-12/23i, IL-17i, IL-23i), JAKi or PDE4i
Switch bDMARD (TNFi, IL-12/23i, IL-17i, IL-23i) or PDE4i
Comorbidities and associated conditions may impact choice of therapy and/or guide monitoring
Treat, periodically re-evaluate treatment goals and modify therapy as required

Dual Biologic Therapy

- Dual Biologic or Small Molecule Therapy for Treatment of Inflammatory Bowel Disease: A Systematic Review and Meta-analysis
- Systematic review and meta-analysis to summarize emerging data on the safety and effectiveness of dual biologic therapy in combination or with tofacitinib in patients with refractory IBD
- 30 studies reporting 288 trials of dual biologic or small molecule therapy in 279 patients (76% Crohn's disease).
- The most common combinations TNF-α & anti-integrins (48%), ustekinumab & anti-integrins (19%); 61% of patients had previously failed at least one of the two therapies used in combination.
- Over a median follow-up of 32 weeks, pooled rates of adverse and serious adverse events were 31% and 6.5%; pooled rates of clinical and endoscopic remission were 59% and 34%, respectively. Rates of success were higher in patients on dual.
- Conclusions: Dual biologic or small molecule therapy may be a possible option in highly selected, refractory IBD patients at specialized centers. More data is needed.

Duel BiologicTherapy

Guselkumab and Golimumab in Participants With Moderately to Severely Active Ulcerative Colitis (VEGA)

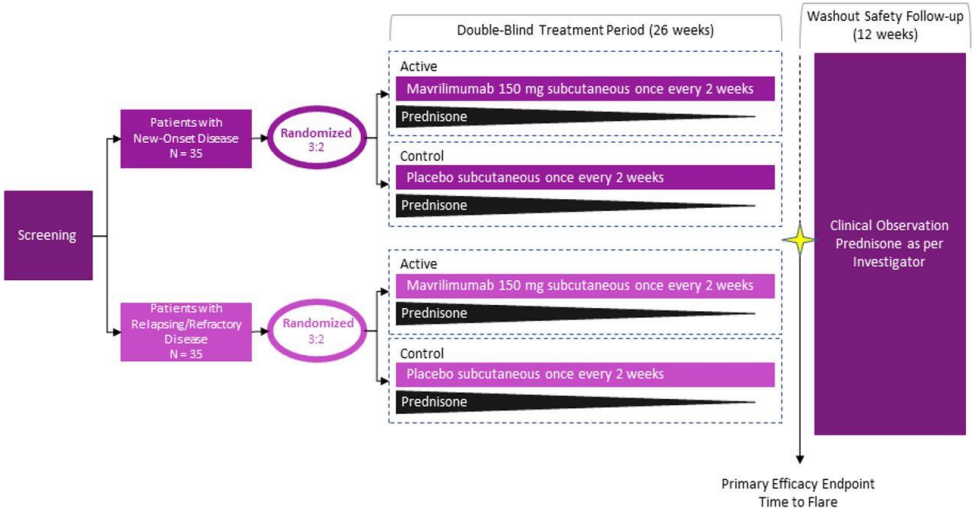
- Phase 2 study: n=214, mod to severe UC, failed conventional therapy
- GUS+GOL/ GUS+PBO/ GOL+PBO
- 1st: clinical response wk12, 2nd: remission
- Results: VEGA Phase 2a proof-of-concept study shows 83.1% of patients who received combination therapy achieved the primary endpoint of clinical response and 36.6% of patients achieved clinical remission at week 12
- The VEGA study represents a first-of-its-kind biologic combination assessment of IL-23p19 subunit antagonist TNFα antagonist in UC
- Safety events were similar among treatment groups.
  - AEs occurred in 40.8%, 43.7%, and 52.8% respectively.
  - Serious AE occurred in 1.4 %, 2.8%, and 1.4%, respectively.
  - Infections were reported in 14.1 % in each of the combo and guselkumab groups and in 22.2 % of the golimumab group
  - No deaths, malignancies, or TB cases were reported through week 12 of the study.
  - One patient receiving combination therapy experienced concurrent serious infections of influenza and sepsis.

PsA Duel Therapy

- Guselkumab and Golimumab Combination Therapy in Active PsA (AFFINITY)
  - Double-blind Phase from Weeks 0 to 24 which includes the active treatment phase and the primary efficacy visit (Week 24), and Safety Follow-up Phase from Week 24 to Week 36. Key safety assessments will include adverse events (AEs).The total duration of the study is up to 42 weeks.
  - Actual Study Start Date: October 25, 2021
  - Estimated Primary Completion Date: December 16, 2022
  - Estimated Study Completion Date: February 17, 2023
  - Inclusion: Dx of PsA for (>=) 6 months, at least 3 SJC and at least 3 TJC; and hs-CRP >3mg/dL
    - Have at least 1 of the following PsA subsets: DIP joint involvement, polyarticular arthritis with absence of rheumatoid nodules, arthritis mutilans, asymmetric peripheral arthritis, or spondylitis with peripheral arthritis
    - Have active plaque psoriasis, with at least one psoriatic plaque of >=2 cm diameter or nail changes consistent with psoriasis
    - Have an inadequate response (IR) to 1 anti-TNF-alpha therapy,
  - Outcomes:
    - 1st:Primary Outcome Measures : % who Achieve MDA at Week 24
    - Secondary Outcome Measures : % of pts ACR 50 at Week 24, % MDA at Week 16, % PASI 90 at Week 24, % PASI 100 at Week 24 Among the Participants with >=3% BSA Psoriatic involvement and an IGA Score of >=2 (Mild) at Baseline, % with an IGA-psoriasis Response of IGA Psoriasis Score of 0 or 1, Change from Baseline in HAQ-DI at Week, % With Resolution of Enthesitis at Week 24, % Resolution of Dactylitis at Week 24, Change from Baseline in Short Form Health Survey (SF-36) Physical Component Score (PCS) at Week Percentage of Participants With Adverse Events (AEs), Serious Adverse Events (SAEs), and Reasonably Related

GCA-Mavrilimumab

- Mavrilimumab for GCA
  - Fully human monoclonal antibody against GM-CSFR
  - Phase 2, both new and relapsing pts
  - 3:2 ratio to mavrilimumab 150 mg or placebo injected SQ every 2 weeks. Both groups received a 26-week prednisone taper.
  - The primary outcome was time to adjudicated flare by week 26. A prespecified secondary efficacy outcome was sustained remission at week 26. Safety was also assessed.



GCA-Mavrilimumab

- 42 mavrilimumab recipients, flare occurred in 19% (n=8). Of 28 placebo recipients, flare occurred in 46% (n=13).
- Median time to flare was 25.1 weeks in the placebo group, but the median was not reached in the mavrilimumab group (HR 0.38; 95% CI 0.15 to 0.92; p=0.026).
- Sustained remission at week 26 was 83% for mavrilimumab and 50% for placebo recipients (p=0.0038).
- Adverse events occurred in 78.6% (n=33) of mavrilimumab vs. 89.3% (n=25) of placebo recipients.
- No deaths or vision loss occurred in either group.

Systemic Sclerosis Associated ILD

- March 4, 2021 FDA approved SQ and intravenous tocilizumab to slow the rate of declining pulmonary function in adults with SSc-associated ILD
- Methods: Participants underwent baseline and serial spirometry along with high-resolution chest computed tomography at baseline and at week 48. Quantitative interstitial lung disease (QILD) and fibrosis scores were assessed by computer software. We classified QILD into the following categories of lung involvement: mild (>5-10%), moderate (>10-20%), and severe (>20%).
- Results: 210 participants recruited for the trial, 136 patients (65%) had ILD. 77% had moderate-to-severe involvement (defined as >10% lung involvement). TCZ arm preservation of FVC% over 48 weeks vs placebo (-6.3%).
- Conclusions: TCZ in early SSc-associated ILD with progressive skin disease stabilized FVC% over 48 weeks, independent of the extent of radiographically evident QILD.

Systemic Sclerosis Associated ILD

- Long-Term Safety and Efficacy of Tocilizumab in Early Systemic Sclerosis-Interstitial Lung Disease: Open-Label Extension of a Phase 3 Randomized Controlled Trial
- Objectives: long-term safety and efficacy of tocilizumab.
- Methods: Adults with diffuse cutaneous SSc for <60 months and elevated acute-phase reactants, including those with ILD, received weekly placebo or TCZ 162 mg SQ in the 48-week, double-blind period and then open-label TCZ from Weeks 48 to 96
- Main Results: 82% of 107 patients in the placebo-tocilizumab group and 85 of 105 patients in the continuous-tocilizumab group completed 96 weeks. Hr-CT revealed ILD in 61%.
  - Mean (95% confidence interval [CI]) change in modified Rodnan skin score from baseline to week 96 was -8.4 (-10.0 to -6.8) for placebo-tocilizumab and -9.6 (-10.9 to -8.4) for continuous-tocilizumab.
  - Mean (95% CI) change in FVC from baseline to week 96 was -3.3 (-5.1 to -1.5) for placebo-tocilizumab and -0.5 (-2.4 to 1.3) for continuous-tocilizumab among completers
  - Rates per 100 patient-years of serious adverse events from Weeks 48 to 96 were 14.8 for placebo-tocilizumab and 15.8 for continuous-tocilizumab.
- Conclusions: TCZ preserved lung function, slowing decline in FVC, in patients with SSc, including those with ILD. Long-term safety was consistent with the known safety profile of tocilizumab.

Vasculitis – Avacopan

- FDA approved the drug in October 2021, with some controversy
- ADVOCATE trial, which examined the oral C5a inhibitor avacopan as an add-on therapy for ANCA-associated vasculitis. Compared prednisone (tapered to 0 by week 21) with avacopan in patients receiving standard treatment with either CYC (followed by AZA) or rituximab.
- Results: Avacopan was noninferior to prednisone for remission at 26 weeks and superior to prednisone for sustained remission at 52 weeks. The two groups showed no significant difference in serious adverse events.

Gout

- July 8, 2022: FDA Approves pegloticase Co-Administered With Methotrexate, Expanding the Labeling to Help More People with Uncontrolled Gout Achieve a Complete Response to Therapy
  - The MIRROR trial included 152 participants with gout, with 100 randomized to receive both pegloticase and methotrexate, and 52 randomized to receive pegloticase and placebo.
  - Patient response to the coadministered injection was more than 30% greater vs patient response to pegloticase injection with placebo.
  - 71% of patients who received both pegloticase and MTX achieved the primary endpoint, defined as serum urate levels below 6 mg/dL for at least 80% of the time during month 6, compared with 39% of patients in the control group.
  - Pegloticase injection coadministered with methotrexate was linked to notable reductions in infusion reactions. 4% of patients who received both treatments experienced infusion rxns vs 31% of patients who received only pegloticase.

COVID Updates

- Study confirmed known risk factors for poor outcomes from COVID-19, such as male sex and increasing age. It also found an increased risk of death from COVID-19 in patients taking glucocorticoid doses higher than 10 mg daily, in those with moderate or high rheumatic disease activity and in those taking certain immunosuppressants, such as rituximab.
- One study by Deepak et al. found that most patients with chronic inflammatory disease treated with immunosuppressives do develop detectable antibodies. However, the number of antibodies they produce is lower than in immunocompetent controls, especially in patients on prednisone and B-cell depleting therapies.
- Evolving ACR, CDC and FDA guidelines continue to reflect new information.

COVID Updates

- COVID-19 vaccine safety in pts with rheumatologic diseases (April 2022)
- There are limited data regarding the risk of flare of existing rheumatic disease following COVID-19 vaccination.
- In a large cohort including over 4600 patients with inflammatory systemic rheumatic diseases who received one or more doses of any COVID-19 vaccine,
  - Approximately 4% of patients experienced a disease flare at a mean of six days following vaccination
  - The majority of flares were mild to moderate in severity, with approximately 1/3 of the flares resulting in medication changes.
- The majority of patients tolerated their vaccination well with rare reports flare and very rare reports of serious AEs. These findings should provide reassurance and promote confidence in SARS-CoV-2 vaccine safety in I-RMD patients.

References

1. Dr. Manuel Pombo-Suarez et al. *Hospital Clinico Universitario Santiago De Compostela*. Spain. ACR 201.
2. Boers M, Hartman L, Opris-Belinski D For the GLORIA Trial consortium, et al. *Low dose, add-on prednisolone in patients with rheumatoid arthritis aged 65+: the pragmatic randomised, double-blind placebo-controlled GLORIA trialAnnals of the Rheumatic Diseases.* 2022;81:925-936.
3. Lillegraven S, Paulshus Sundlisæter N, Aga AB, Sexton J, Olsen IC, Fremstad H, Spada C, Madland TM, Høili CA, Bakland G, Lexberg Å, Hansen IJW, Hansen IM, Haukeland H, Ljoså MA, Moholt E, Uhlig T, Solomon DH, van der Heijde D, Kvien TK, Haavardsholm EA, et al. Effect of Half-Dose vs Stable-Dose Conventional Synthetic Disease-Modifying Antirheumatic Drugs on Disease Flares in Patients With Rheumatoid Arthritis in Remission: The ARCTIC REWIND Randomized Clinical Trial. *JAMA*. 2021 May 4;325(17):1755-1764. doi: 10.1001/jama.2021.4542. PMID: 33944875; PMCID: PMC8097499.
4. Reference: Pedersen JK, Risbo N, Pedersen A, et al. More than six-fold increased mortality risk in patients with incident rheumatoid arthritis and depression in a large cohort with 10-year follow-up. Presented at*: EULAR Congress*. 2022; June 1-4, 2022. Copenhagen, Denmark. Abstract OP0067.
5. Rech J, Ostergaard M, Tascilar K, Hagen M, Valor Mendez L, Kleyer A, Kroenke G, Simon D, Schoenau V, Hueber A, Kleinert S, Baraliakos X, Fleck M, Rubbert-Roth A, Behrens F, Kofler D, Feuchtenberger M, Zaenker M, Voll R, Glaser C, Feist E, Burmester G, Karberg K, Strunk J, Cañete J, Naredo E, Filkova M, Senolt L, Schett G, et al. Abatacept Reverses Subclinical Arthritis in Patients with High-risk to Develop Rheumatoid Arthritis -results from the Randomized, Placebo-controlled ARIAA Study in RA-at Risk Patients [abstract*]. Arthritis Rheumatol*. 2021; 73 (suppl 10).
6. Gisondi P, et al. Biological disease-modifying antirheumatic drugs may mitigate the risk of psoriatic arthritis in patients with chronic plaque psoriasis. *Ann Rheum Dis.* 2022;81:68–73. doi:10.1136/annrheumdis-2021-219961.
7. Laura C. Coates, Nadia Corp, Danielle A. van der Windt, Denis O'Sullivan, Enrique R. Soriano, and Arthur Kavanaugh, et al. *The Journal of Rheumatology*. March 2022, jrheum.211331; DOI: https://doi.org/10.3899/jrheum.211331.
8. Waseem Ahmed, MD et al. Breaking the Therapeutic Ceiling: Dual Biologic or Small Molecule Therapy for Refractory Inflammatory Bowel Disease, Crohn's & Colitis 360, Volume 4, Issue 1, January 2022, otac005, https://doi.org/10.1093/crocol/otac005.
9. John H. Stone, M.D., M.P.H., Katie Tuckwell, Ph.D. et al, Trial of Tocilizumab in Giant-Cell Arteritis. July 27, 2017. N Engl J Med 2017; 377:317-328. Cid MC, Unizony SH, Blockmans D For the KPL-301-C001 Investigators, et al. *Efficacy and safety of mavrilimumab in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial Annals of the Rheumatic Diseases*. 2022;81:653-661.
10. Roofeh D, Lin CJF, Goldin J, Kim GH, Furst DE, Denton CP, Huang S, Khanna D, et al. focuSSced Investigators. Tocilizumab Prevents Progression of Early Systemic Sclerosis-Associated Interstitial Lung Disease. *Arthritis Rheumatol.*. 2021 Jul;73(7):1301-1310.

References

11. Khanna D, Lin CJF, Furst DE, Wagner B, Zucchetto M, Raghu G, Martinez FJ, Goldin J, Siegel J, Denton CP, et al. Long-Term Safety and Efficacy of Tocilizumab in Early Systemic Sclerosis-Interstitial Lung Disease: Open-Label Extension of a Phase 3 Randomized Controlled Trial. *Am J Respir Crit Care Med*. 2022 Mar 15;205(6):674-684. doi: 10.1164/rccm.202103-0714OC. PMID: 34851799.

12. Jayne DRW, Merkel PA, Schall TJ, et al. Avacopan for the treatment of ANCA-associated vasculitis. *N Engl J Med*. 2021 Feb 18;384(7):599–609.

13. Strangfeld A, Schäfer M, Gianfrancesco MA, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: Results from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 2021 July;80(7):930–942.

14. Machado PM, Lawson-Tovey S, Strangfeld A, Mateus EF, Hyrich KL, Gossec L, Carmona L, Rodrigues A, Raffeiner B, Duarte C, Hachulla E, Veillard E, Strakova E, Burmester GR, YardımcıGK, Gomez-Puerta JA, Zepa J, Kearsley-Fleet L, Trefond L, Cunha M, Mosca M, Cornalba M, Soubrier M, Roux N, Brocq O, Durez P, Conway R, Goulenok T, Bijlsma JW, McInnes IB, et al. *Mariette X Ann Rheum Dis*. 2022;81(5):695. Epub 2021 Dec 31.

THANK YOU!