RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

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Year in Review 2023

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Disclosures

- Audrey Gibson, PA-C:
  - Speakers Bureau: Abbvie, Sanofi, Janssen
- Jessica Farrell, PharmD:
  - Speaker: Abbvie, Pfizer
  - Consultant: Boehringer Ingelheim

Objectives

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

Sputum RA-Associated Autoantibodies Independently Associate With Future Development of Classified RA in an At-Risk Cohort of Individuals With Systemic Anti-CCP Positivity

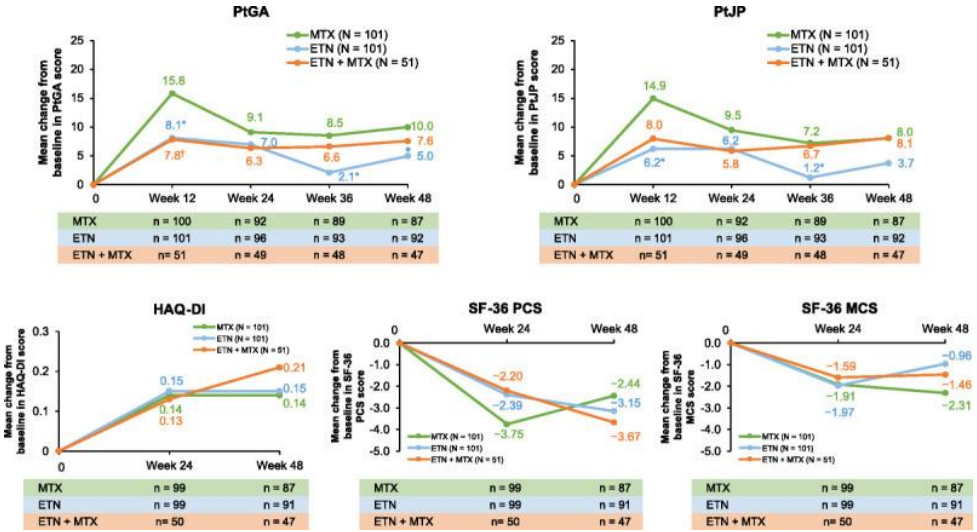
- **ABSTRACT NUMBER: 0533;** Wilson. Et al ACR 2022
- **Methods:** We evaluated 66 participants: 1) serum anti-CCP-IgG positive, 2) without IA on physical examination and 3) had a hypertonic saline-induced sputum sample available. Subjects were followed up to 5 years to determine incident
- **Results:** Thirteen (33%) of 39 DC participants and 8/27 (30%) VC participants developed RA. Prevalence of any sputum antibody (anti-CCP-IgG, anti-CCP-IgA or RF-IgM) was higher in subjects who developed RA compared to those who did not (67% vs. 20%, $p< 0.001$). The strongest single sputum antibody associated with developing RA was sputum anti-CCP-IgA (43% vs. 9%, $p=0.002$). Overall, sputum antibody positivity was 67% sensitive and 80% specific for future RA.
- **Conclusion:** Sputum anti-CCP-IgA, anti-CCP-IgG or RF-IgM positivity was independently associated with a 4-fold risk of developing classified RA in serum anti-CCP-IgG positive at-risk individuals. Overall, sensitivity for who will develop RA increased from 32% (using baseline serum anti-CCP-IgG positivity alone) to 67% (using baseline serum anti-CCP-IgG positivity plus sputum antibody positivity).

SEAM-RA Study

- Study of Etanercept and Methotrexate in Combination or as Monotherapy in Subjects With Rheumatoid Arthritis
- Phase 3, multicenter, randomized withdrawal, double-blind controlled study in patients with RA taking methotrexate plus etanercept and in remission (SDAI≤3.3). Pt's Global Assessment of Disease Activity, Patient's Assessment of Joint Pain, HAQ–Disability Index, and 36-Item Short-Form Health Survey were evaluated for 48 weeks following methotrexate or etanercept withdrawal.

SEAM-RA

- Of 253 patients, 121 experienced disease worsening and 132 did not.
- PtGA and Patient's Assessment of Joint Pain values deteriorated less in those on etanercept monotherapy compared with methotrexate monotherapy.
- Conclusions: Etanercept monotherapy showed benefit over methotrexate in maintaining PRO scores.

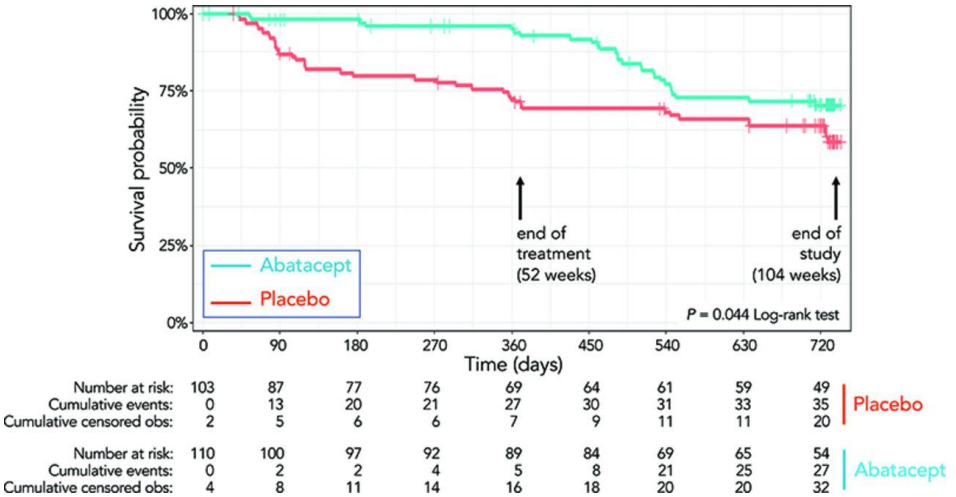


APIPPRA Study: Pre-Clinical RA

- OPO130: ABA in individuals at risk of developing RA
- Phase IIB RCT, double blind, placebo-controlled trail
- +RF, +ACPA, individuals with arthralgia
- 52 wk SQ ABA vs PCO, and followed for an 52 wks after stopping treatment
- Primary endpoint: time to develop synovitis >3 joints or RA
- Secondary endpoints: multiple disease activity assessments, the time to commencing DMARDs and/or corticosteroids, X-ray and ultrasound scores, as well as safety data.

APIPPRA Study: Pre-Clinical RA

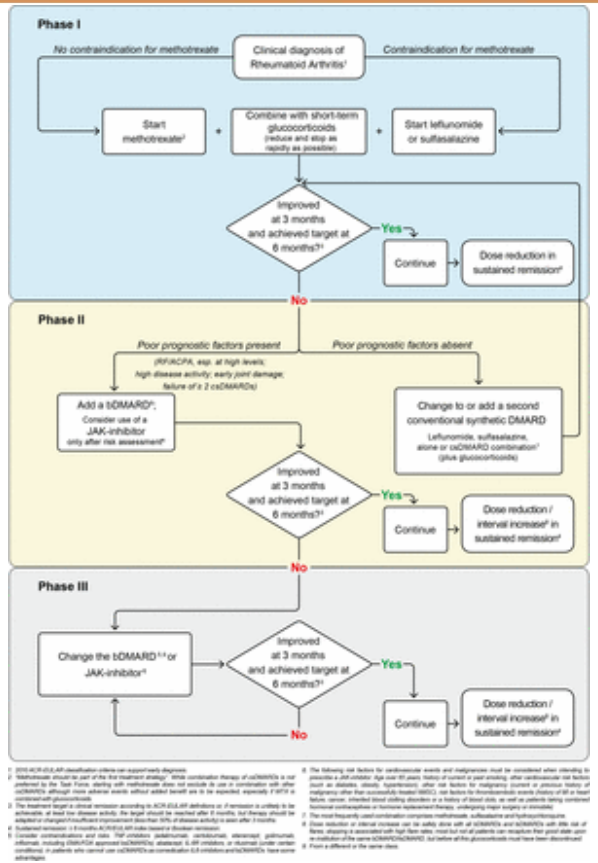
- Dec 2014-Jan 2019, 280 individuals were evaluated, 213 were randomized, 103 to placebo and 110 to abatacept.
- After stopping treatment at 52 weeks there were 30 events (29%) in the placebo arm and 7 (6%) in the abatacept arm. By the end of the study there were 38 (37%) and 27 (25%) events, respectively, resulting in differences in mean arthritis-free survival time between arms of 99.2 days (95% CI 37.5 – 160.9; *p*-value=0.002), in favour of abatacept.
- The cumulative proportion of arthritis-free participants at 52 weeks was 0.692 (SE 0.047) in the placebo arm and 0.928 (SE 0.026) for the abatacept arm, and 0.585 (SE 0.054) for placebo and 0.704 (SE 0.048) for abatacept at 104 weeks.
- *Post hoc* analysis revealed that individuals with an extended autoantibody profile at baseline were more likely to remain arthritis-free following abatacept therapy.
- Conclusions: T cell co-stimulation modulation with abatacept for 52 weeks showed a reduction in the development of RA over two years. There were no new safety signals.



LB0001 Head-to-Head Comparison of TLL-018 and Tofacitinib in Patients With Active Rheumatoid Arthritis

- TLL-018 is a highly selective dual JAK1/TYK2
- 101 patients with moderate-to-severe active RA who had inadequate response or were intolerant to methotrexate were randomized (1:1:1:1 ratio) to receive twice-daily oral TLL-018 10mg, 20mg, 30mg or tofacitinib 5mg.
- The Primary endpoint is the proportion of patients achieving ACR50 at Week 12.
- Secondary endpoints: DAS28-CRP <2.6, ACR20, ACR70 at all scheduled time points, ACR50 at scheduled time points exclude week 12, CDAI and other parameters at 12 week. Safety was assessed via adverse event (AE) and laboratory examinations.
- ACR50 response rates of 65.4% and 72.0% for the two highest doses of TLL-018 were significantly greater than the 41.7% seen for tofacitinib.
- TLL-018 20mg and 30mg were statistically superior to tofacitinib ($p<0.05$). Proportions of patients achieving clinical remission (DAS28-CRP<2.6) at week 12 were 39.1%, 34.8%, 54.5% and 17.4% at week 12 for the 10, 20, 30mg TLL-018 and tofacitinib, respectively.
- The TLL-018 trial didn't reveal notably higher rates of infections in comparison with tofacitinib, but it was a small study (101 patients distributed among four arms)

EULAR Recommendations for the Management of RA



- Initially, MTX plus GCs is recommended and on insufficient response to this therapy within 3–6 months, treatment should be based on stratification according to risk factors
- With poor prognostic factors (presence of autoantibodies, high disease activity, early erosions or failure of two csDMARDs, any bDMARD should be added to the csDMARD; after careful consideration of risks of MACEs, malignancies and/or thromboembolic events tsDMARDs may also be considered in this phase.
- If the first bDMARD (or tsDMARD) fails, any other bDMARD (from another or the same class) or tsDMARD (considering risks) is recommended.
- With sustained remission, DMARDs may be tapered but should not be stopped.

PsA-GRAPPA Guidelines Updates

- Safety considerations, particularly regarding the use of JAK inhibitors, are of utmost importance in the 2023 update to EULAR guidelines.
- Selection of therapy should now take into account the complete clinical presentation, explicitly considering non-musculoskeletal manifestations.
- Manifestation-oriented approach, integrating a growing range of available drugs in a stepwise manner to optimize the balance between safety and efficacy and achieve the highest quality of care.

GRAPPA Guidelines Updates

- Safety Considerations With JAK Inhibitors
- Introduced a 7th principle: "The choice of treatment should consider safety considerations regarding individual modes of action to optimize the benefit-risk profile."
- Example: in the context of peripheral arthritis, JAK inhibitors may now be considered if there is an inadequate response to at least one csDMARD and at least one bDMARD.

GRAPPA Guidelines Updates

- Consider Nonmusculoskeletal Manifestations in Treatment Decisions
- In the case of inflammatory bowel disease, EULAR advises the use of anti-TNF agents, IL-12/23 or IL-23 inhibitors, or a JAK inhibitor.
- Skin involvement should prompt the use of IL-17A or IL-17A/F or IL-23 or IL-12/23 inhibitors
- Uveitis should be treated with tumor necrosis factor (TNF) inhibitors.

GRAPPA Guidelines Updates

- Systemic Glucocorticoids Removed
- The use of systemic glucocorticoids as adjunctive therapy is no longer recommended.
- NSAIDs and local glucocorticoids are now limited to specific patient populations, those affected by oligoarthritis without poor prognostic factors, entheseal disease, or predominant axial disease.
  - Use should be short-term, generally no longer than 4 weeks

GRAPPA Guidelines Updates

- No Specific Biologic Treatment Order Recommended for Peripheral Arthritis
- Regarding patients with peripheral arthritis, refrain from recommending any specific order of preference for the use of bDMARDs

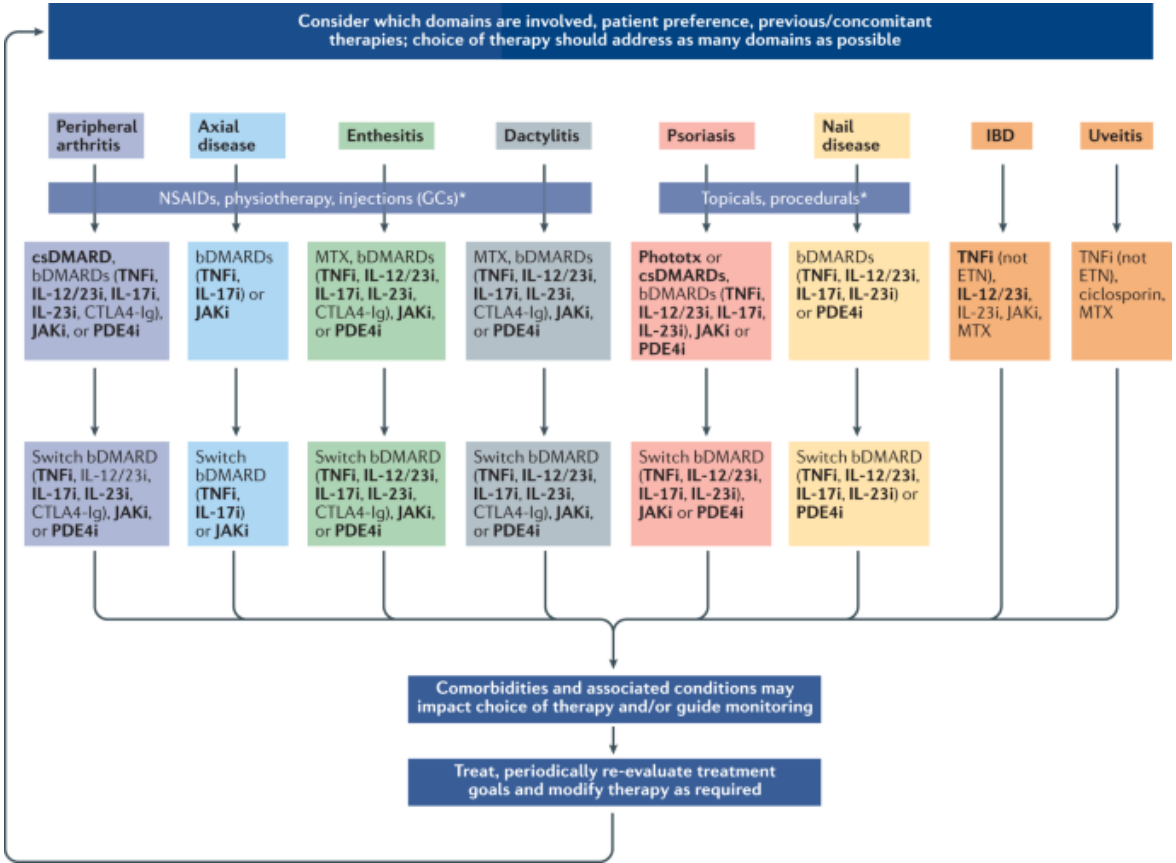
GRAPPA Guidelines Updates

- The recommendation for patients with mono- or oligoarthritis and poor prognostic factors now aligns with the previous recommendations for polyarthritis
- In cases of clinically relevant axial disease and an inadequate response to NSAIDs, therapy with an IL-17A inhibitor, a TNF inhibitor, an IL-17A/F inhibitor, or a JAK inhibitor may be considered.

GRAPPA Guidelines Updates

- Which Disease Manifestation to Treat First?
- PsA is highly heterogeneous, and determining the predominant manifestation is sometimes challenging
  - Starting with peripheral arthritis, which can lead to structural damage. If peripheral arthritis is not present, attention should be directed towards axial disease

GRAPPA Guidelines Updates

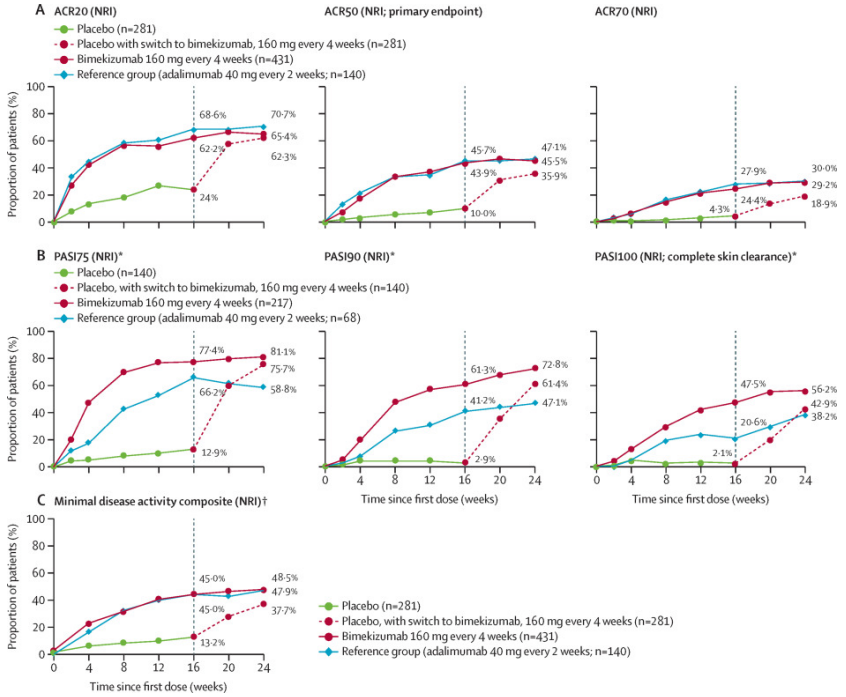


Bimekizumab – BE OPTIMAL

- Bimekizumab is a monoclonal antibody that inhibits interleukin (IL)-17A and IL-17F
- BE OPTIMAL was a 52-week, phase 3, multicenter, RCT, double-blind, placebo-controlled
- Adult-onset PsA in naive to biologic DMARDs. Randomization schedule to bimekizumab 160 mg every 4 weeks, placebo every 2 weeks, or the reference group (adalimumab 40 mg every 2 weeks), all administered SQ.
- At week 16, patients randomly assigned to placebo switched to bimekizumab 160 mg every 4 weeks.
- The primary endpoint was the proportion of patients reaching 50% or greater improvement in ACR50 at week 16

Bimekizumab – BE OPTIMAL

- 852 were randomly assigned to bimekizumab (n=431), placebo (n=281), and reference (adalimumab; n=140) groups.
- At week 16, significantly more patients receiving bimekizumab (189 [44%] of 431) reached ACR50 response vs placebo (28 [10%] of 281; adalimumab 64 [46%] of 140).
- All secondary endpoints were met.
- Treatment-emergent AEs week 16 were reported in 258 [60%] of 431 patients receiving bimekizumab, 139 [49%] of 281 patients receiving placebo, and 83 [59%] of 140 patients receiving adalimumab. No deaths occurred.
- **Conclusions:** Bimekizumab treatment had superior improvements in joint, skin, and radiographic efficacy outcomes at week 16 compared with placebo in patients with psoriatic arthritis who were naive to biologic DMARDs.
- The safety profile of bimekizumab, including the occurrence of fungal infections, was consistent with previous phase 3 studies in patients with plaque psoriasis, and with IL-17A inhibitors.

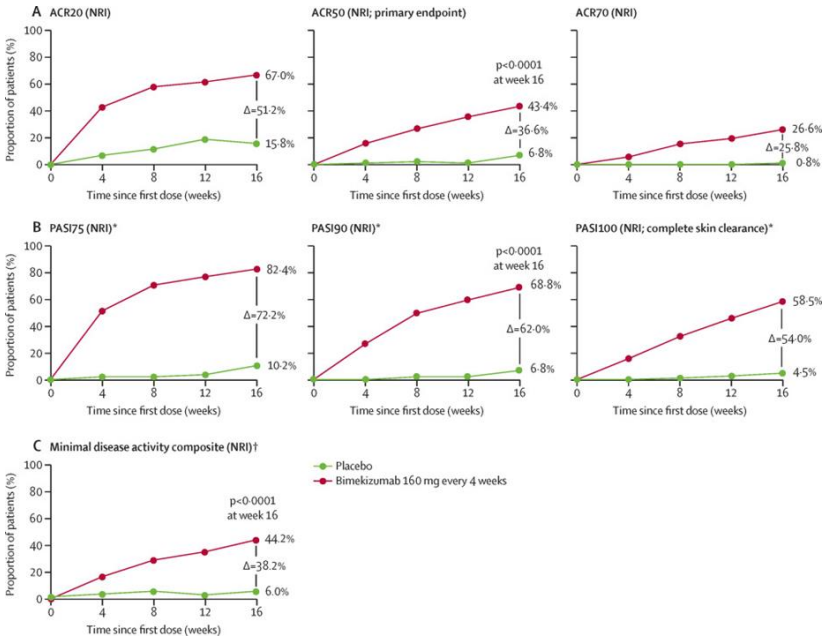


Bimekizumab – BE COMPLETE

- Patients with active PsA and previous inadequate response or intolerance to TNF-α inhibitors
- RCT, double-blind, placebo-controlled, phase 3 trial
- 18 years or older with adult-onset PsA with a history of inadequate response or intolerance to treatment with one or two TNFα inhibitors.
- Patients were randomly assigned (2:1) to receive SQ bimekizumab 160 mg every 4 weeks or placebo.
- The primary endpoint was the proportion of patients with 50% or greater improvement in ACR50 at week 16

BE COMPLETE

- 400 patients were randomly assigned to bimekizumab 160 mg every 4 weeks (n=267) or placebo (n=133).
- 116 (43%) of 267 patients receiving bimekizumab reached ACR50, vs nine (7%) of 133 patients receiving placebo
- 121 (69%) of 176 patients with psoriasis affecting at least 3% body surface area at baseline who received bimekizumab reached 90% or greater improvement in PASI90), compared with six (7%) of 88 patients who received placebo
- Treatment-emergent AEs reported in 108 (40%) of 267 patients receiving bimekizumab and 44 (33%) of 132 patients receiving placebo.
- There were no new safety signals and no deaths.
- Bimekizumab treatment led to superior improvements in joint and skin efficacy outcomes at week 16 compared with placebo in patients with PsA. The safety profile of bimekizumab was consistent with previous phase 3 studies in patients with plaque psoriasis, and studies of IL-17A inhibitors.



Lupus Biomarkers

- In a study of 232 SLE patients, high levels of sialic acid binding Ig-like lectin 1 (SIGLEC1), an IFN-1 surrogate marker had highly (92.2%) negative diagnostic value, but less sensitive positive predictive value (72.8%), suggesting that it may help to exclude SLE in suspected cases
- SIRT1 (sirtuin-1) and soluble ST2 correlated with disease activity. Also, IL-6 was higher in the plasma of patients with active SLE in comparison with quiescent cases
- Urinary IL-16 was higher in patients with active lupus nephritis and may be useful in differentiating patients with proliferative lupus nephritis from those with less severe LN subtypes and urinal SLE

OP0141 LONG TERM SAFETY AND EFFICACY OF CAR-T CELL TREATMENT IN REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS – DATA FROM THE FIRST SEVEN PATIENTS

- Previously reported that deep B cell depletion using a single infusion with autologous CD19 chimeric antigen receptor (CAR) T cells induced drug-free clinical remission in severe SLE patients with refractory disease. Long-term clinical efficacy and safety data of the first seven SLE patients receiving autologous CD19-directed CAR-T cell therapy.

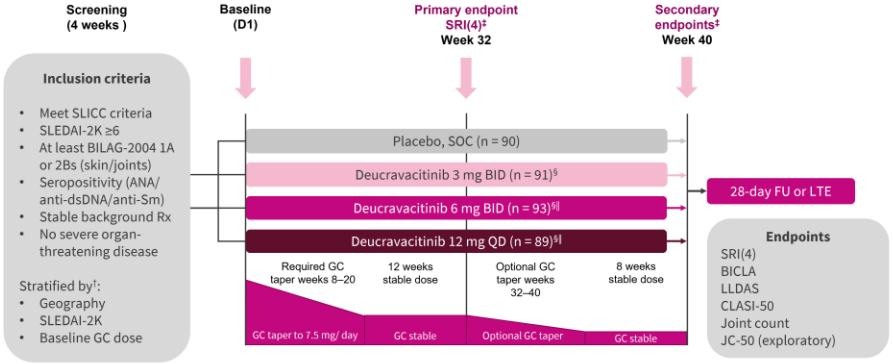
- **Methods**: Severe active SLE showing organ involvement and resistance to multiple immune suppressive treatments. Patients received autologous $1x10^6$ CD19-CAR-T cells/kg by single infusion after standard conditioning therapy

- **Results** As of January 2023, seven SLE patients had been treated with CD19 CAR-T cells. Patients had active disease with a median SLEDAI of 10 (range: 8-16), with a median of 4 organs involved (range: 8-16) and a median number of 7 failed treatments (range: 4-15). All patients had active kidney disease. In addition, involvement of the heart, lungs, pleura, joints, skin, muscles and bone marrow were documented. All patients experienced drug-free remission as assessed by DORIS remission criteria and met lupus low activity state (LLDAS) usually within the first three months after CAR T cell therapy. Furthermore, seroconversion with loss of dsDNA antibodies and other autoantibodies was observed. To date, no SLE flare occurred despite complete cessation of treatment.

- **Conclusion** Taken together, these data suggest that CD19 CAR T-cell therapy can abrogate disease and delete autoimmunity in patients with severe SLE. After CD19 CAR T-cell therapy SLE patients remain in drug free-remission of SLE even if B cells recur. This remission can be long-lasting as the longest disease -free observation period is now 22 months.

PAISLEY STUDY: Deucravacitinib Phase 2 in SLE

- DEAU: oral, selective TYK inhibitor
- Phase 2, 48 wk DBRCT in active SLE on SOC; 363 pts with SLE
  - PBO vs DEUC 3mg, 6mg, 12mg
  - Oral GC tapering to 7.5 mg/day required
- +ANA/anti-DNA or anti-Sm
- Primary endpoint % pts achieving SRI-4 at Wk 32
- Safety: increased rash on 12mg- no signal for SAE, infections, malignancy, MACE, VTE
- Results: appears effective in MSK and MC manifestations



SLE-BRAVE 1 and SLE-BRAVE 2

- In a 24-week phase 2 study in patients with systemic lupus erythematosus (SLE), baricitinib 4 mg significantly improved SLE disease activity compared with placebo. In this Article, we report the evaluation of efficacy and safety of baricitinib in patients with SLE in a 52-week phase 3 study.
- Methods: In this phase 3 double-blind, randomised, placebo-controlled study, SLE-BRAVE-II, patients (aged ≥18 years) with active SLE receiving stable background therapy were randomly assigned 1:1:1 to baricitinib 4 mg, baricitinib 2 mg, or placebo once daily for 52 weeks. The primary endpoint was the proportion of patients with an SLE Responder Index (SRI)-4 response at week 52 in the baricitinib 4 mg treatment group compared with placebo. Glucocorticoid tapering was encouraged but not required per protocol. The primary endpoint was assessed by logistic regression analysis with baseline disease activity, baseline corticosteroid dose, region, and treatment group in the model.
- Findings: 775 patients were randomly assigned and received at least one dose of baricitinib 4 mg (n=258), baricitinib 2 mg (n=261), or placebo (n=256). There was no difference in the primary efficacy outcome of the proportion of SRI-4 responders at week 52 between participants who received baricitinib 4mg (121 [47%]; odds ratio 1·07 [95% CI 0·75 to 1·53]; difference with placebo 1·5 [95% CI –7·1 to 10·2]), 2 mg (120 [46%]; 1·05 [0·73 to 1·50]; 0·8 [–7·9 to 9·4]) and placebo (116 [46%]). None of the major secondary endpoints, including glucocorticoid tapering and time to first severe flare, were met.
- Interpretation: Although phase 2 data suggested baricitinib as a potential treatment for patients with SLE, which was supported in SLE-BRAVE-I, this result was not replicated in SLE-BRAVE-II.

OP0053 EFFICACY AND SAFETY OF BARICITINIB IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE 3 TRIAL

- Baricitinib a selective Janus kinase (JAK) inhibitors 1&2 have been recognized as a potential therapeutic option in systemic lupus (SLE); however, no JAK inhibitor studies have been conducted in lupus nephritis (LN) to date.
- Methods: The study is a RCT, double-blind, active competitor (cyclophosphamide)-controlled, phase 3, enrolled adults ≥18 years with a clinical diagnosis of LN. Pts were randomized 1:1 to receive Group 1: oral Baricitinib 4mg once daily and PBO (saline infusion monthly), Group 2: oral PBO tablet and cyclophosphamide (0.7mg/m2) infusion monthly x 6-months double-blind treatment period.
- The primary endpoint was proteinuria, response at week 12 and 24.
- Secondary endpoints at week 12 &24 included C3, anti-ds-DNA and SLEDAI-2K, and their changes from baseline

OP0053 EFFICACY AND SAFETY OF BARICITINIB IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE 3 TRIAL

- **Results** 60 enrolled in the study (Baricitinib 4mg, n=30; cyclophosphamide, n=30) and 100% received study drug through week 24. Significant reduction in proteinuria response rate at week 12 was achieved in group 1 vs group 2 (70% vs 43%; P<0.0001).
  - AEs similar between treatment groups (group 1, 48%; group 2, 46%).
  - Serious AEs leading to discontinuation were reported in 2 (6.6%) pts treated with Baricitinib and 1 (3.3%) pts treated with cyclophosphamide

Variable	Group 1 (n=30)	Group 2 (n=30)	P value
4th w	17/30, 56.6%	9/30, 30%	
8th w	20/30, 66.6%	10/30, 33.3%	
12th w	21/30, 70%	13/30, 43.3%	
24th w	23/30, 76.6%	15/30, 50%	

Conclusion

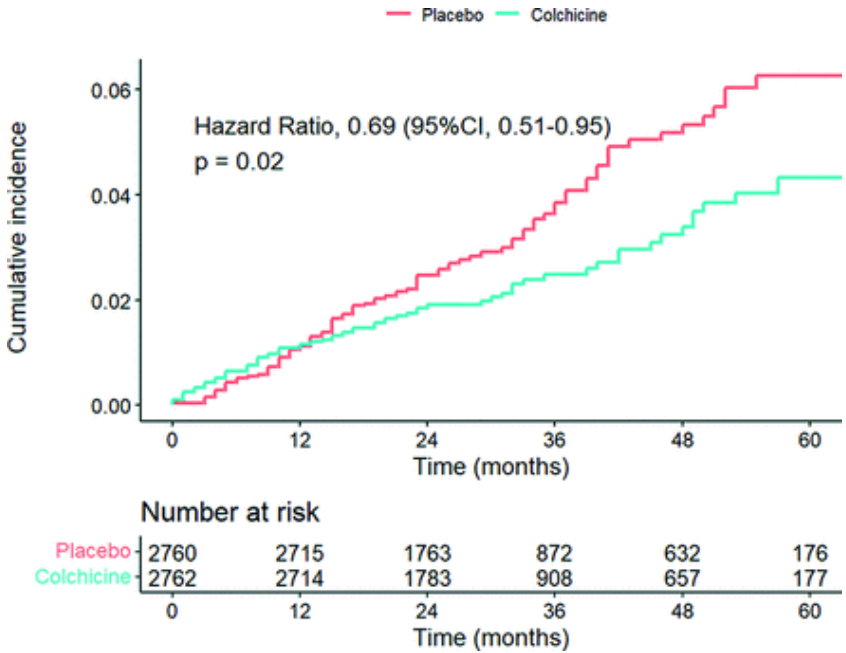
Baricitinib 4mg once daily demonstrated significantly good improvements in disease activity, proteinuria, C3, anti-ds-DNA, than cyclophosphamide after 12 &24 weeks of treatment in pts with active LN. The safety profile of Baricitinib 4mg was consistent with what has been observed with other inflammatory musculoskeletal diseases, and no new risks were identified.

Osteoarthritis

- **OP0072 LOW-DOSE COLCHICINE IS ASSOCIATED WITH LOWER INCIDENCE OF KNEE AND HIP REPLACEMENTS**
- **Objectives:** To examine years-long use of colchicine 0.5 mg daily reduces incident TKRs and THRs
- **Methods:** post-hoc analysis of data collected in the LoDoCo2 trial to determine the time to first knee or hip replacement. Colchicine 0.5 mg once daily as compared to placebo. Patients with gout were excluded at baseline or by excluding the patients who had joint surgery within the first 3 months after randomization

OP0072 – Cont.

- **Results** 5522 participants, 2762 received colchicine and 2760 placebo during a median duration of follow-up of 28.6. During the trial, TKR/ THR was performed in 68 patients (2.5%) in the colchicine group and in 97 patients (3.5%) in the placebo
- **Conclusion** Use of colchicine 0.5 mg daily was associated with a reduced risk of TKR/ THR. Further investigation of long-term therapy with colchicine to slow disease progression in osteoarthritis is warranted.



OA – Colchicine Twice a Day for Hand Osteoarthritis (COLOR): A Double-Blind, Randomized, Placebo-Controlled Trial

- Methods: single-centre, double-blind, RCT, placebo-controlled trial. adults with symptomatic hand osteoarthritis and finger from an outpatient clinic in Denmark. Participants were randomly assigned (1:1) to 0.5 mg colchicine or placebo taken orally twice a day for 12 weeks.
  - The primary endpoint was change from baseline to week 12 in target hand finger pain, assessed on a 100 mm VAS.
- Findings: Jan 15, 2021-March 3, 2022, 100 were randomly assigned to receive colchicine (n=50) or placebo (n=50). The mean change from baseline to week 12 in finger pain were –13.9 mm in the colchicine group and –13.5 mm in the placebo group.
  - In the colchicine group, there were 76 adverse events in 36 (72%) of 50 participants and one serious adverse advent (migraine attack leading to hospital admission).
  - In the placebo group, there were 42 adverse events in 22 (44%) of 50 participants and two serious adverse events (cholecystitis and elevated LFTs concentrations, in the same patient).
- Interpretation: In people with painful hand OA, treatment with 0.5 mg of colchicine twice day for 12 weeks did not effectively relieve pain, and treatment with colchicine was associated with more adverse events.

Antidepressants for Pain Management in Adults With Chronic Pain: A Network Meta-Analysis

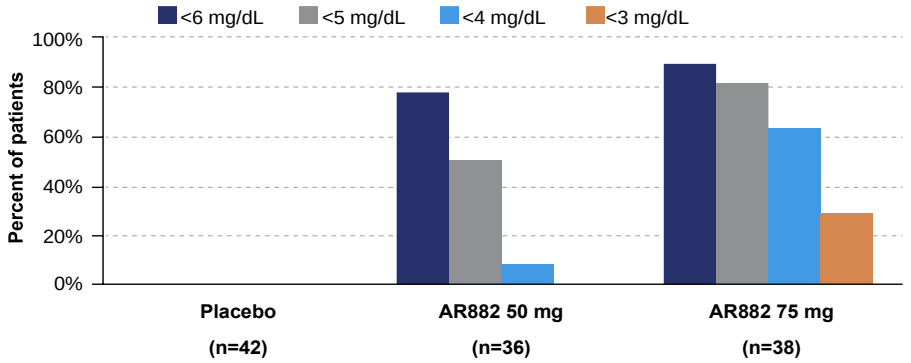
- **Search methods:** searched CENTRAL, MEDLINE, Embase, CINAHL, LILACS, AMED and PsycINFO databases, and clinical trials registries, for RCTs of antidepressants for chronic pain conditions in January 2022.
- **Main results:** included 176 studies with a total of 28,664 participants. The majority of studies were placebo controlled. The most common pain conditions examined were fibromyalgia (59 studies); neuropathic pain (49 studies) and musculoskeletal pain (40 studies
  - Duloxetine was consistently the highest-ranked antidepressant with moderate- to high-certainty evidence. Primary efficacy outcomes Duloxetine standard dose (60 mg) showed a small to moderate effect for substantial pain relief
  - Milnacipran standard dose (100 mg) also showed a small effect (SMD -0.22, 95% CI -0.39 to 0.06; 4 studies, 1866 participants; moderate-certainty evidence).
- **Conclusions**: the only antidepressant certain about for the treatment of chronic pain is duloxetine. Duloxetine was moderately efficacious across all outcomes at standard dose. There is also promising evidence for milnacipran, although further high-quality research is needed to be confident in these conclusions.

Gout: DISSOLVE I and DISSOLVE II

- SEL-212, a once-monthly, novel 2-component, sequential uricase-based infusion therapy, is designed to inhibit the formation of anti-uricase antibodies without the need for other immunosuppressant therapies.
- Phase 3 DISSOLVE clinical program consisted of two double-blind, placebo-controlled studies of SEL-212, titled in which SEL-212 was evaluated at two doses of ImmTOR (0.1 mg/kg and 0.15 mg/kg), and one dose of pegadricase (0.2 mg/kg) in both studies.
  - The primary endpoint in both studies was serum urate (SU) control during month six
  - Secondary endpoints include tender and swollen joint counts, tophus burden, patient-reported outcomes of activity limitation and quality of life and gout flare incidence.
- Response rates in the DISSOLVE I and DISSOLVE II high-dose group were 56% and 47%, respectively. The low-dose group response rates were 48% and 41%, respectively. These rates were significantly different from the placebo group ($P \leq .0015$).
- Safety: SEL-212 was observed to have a favorable safety profile and was well-tolerated across both doses of ImmTOR:
  - AEs including mild to moderate stomatitis 3.4% of the low dose group and 9.2% of the high dose group versus 0% in placebo
  - Greater number of infusion reactions at 24 hours and 1 hour after drug administration in both treatment groups versus placebo. Only 4.5% of patients receiving the low dose of SEL-212 and 3.4% at the high dose of SEL-212 had infusion reactions, evaluated 1 h post dose.

Gout: OP0295 A 12-WEEK, RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED, PHASE 2B STUDY OF SAFETY, TOLERABILITY AND EFFICACY OF AR882 IN GOUT PATIENTS

- **AR882** is a novel, potent, and selective uric acid transporter 1 (URAT1) inhibitor in development for the treatment of gout and tophaceous gout.
- Methods: Following gout flare prophylaxis for 10 days, patients received either once-daily AR882 50 mg, AR882 75 mg, or matching placebo for 12 weeks. Efficacy endpoint was the % of patients who reached sUA below 6, 5, 4, and 3 mg/dL.
- Conclusion: After 12 weeks of treatment, the median serum urate (sUA) levels were reduced from 8.6 mg/dL to 3.6 mg/dL in the AR882 75 mg cohort and 5.0 mg/dL in the AR882 50 mg group. No changes were reported in those receiving the placebo.
- AR882 was well tolerated over the 12-week treatment period and patients with comorbidities did not require any adjustments in management of the diseases while treated with AR882.



Gout – MIRROR

- MIRROR randomized, controlled trial, which resulted in the expanded FDA labeling of pegloticase to include co-administration with methotrexate (MTX) in July 2022.
- Co-administration of 15 mg of MTX weekly improved pegloticase response rates at month six (MTX 71% vs. placebo 39%, $P<0.0001$) and significantly decreased the development of infusion reactions (MTX 4% vs. placebo 31%) and anti-drug antibodies (MTX 23% vs. placebo 50%).

PMR and GCA: New Therapies

- GiACTA- TCZ in GCA
- TitAIN- Sicukinumab in GCA;
  - Sustained remission x 5 weeks; 59% vs 9% PBO
- Mavrilimumab GM-CSF receptor- alpha mAB in GCA
  - Sustained remission @ wk 26 83% vs 50%
  - Fewer flares 19% vs 46%
- SAPHYR (Sarilumab) in PMR
  - Sustained remission at wk 52: 28% vs 10%
- Tocilizumab
  - PMR-Spare: wk 16 remission; 63% vs 12%
  - SEMAPHORE: IV TCZ > PBO
- Tofacitinib
  - EAST PMR: Tofa 5mg BID (27) vs GC 15/d (25)
  - The baseline of PMR-AS was comparable in tofacitinib (19.02±5.98) and glucocorticoid group (21.38±5.52).
  - At weeks 12 and 24, all patients in both groups had PMR-AS< 10. PMR-AS, CRP, and ESR were all significantly decreased at weeks 12, and 24 in both groups.

Biosimilars

- DANBIO Biosimilar to Biosimilar switching of infliximab
- **Methods**: Observational cohort study from the DANBIO registry. Patients were classified as originator-naïve or originator-experienced. Retention rates of 1-year GP1111 treatment were explored
- **Results**: Of 1605 patients (685 RA, 314 PsA and 606 AxSpA, 1171 were originator-naïve. Retention rates at 1-year were 83% and 92% for the originator-naïve and originator-experienced, respectively. GP1111 retention rates were higher in originator-experienced compared to originator-naïve with RA and PsA, but not significantly for AxSpA. Lower disease activity was associated with higher retention. Changes in disease activity preswitch and postswitch were close to zero.
- **Conclusions**: This real-world observational study of more than 1600 patients with inflammatory arthritis showed high 1-year retention following a nationwide infliximab biosimilar-to-biosimilar switch. Retention was higher in originator-experienced and in patients with low disease activity, suggesting outcomes to be affected by patient-related rather than drug-related factors.

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