

International Section Briefing

時間：114年11月22日(星期六)10:15-11:25

Time: 10:15-11:25, 22-Nov-2025

地點：台中林酒店3樓環球廳

Place: 3F Universal Ballroom, The Lin Hotel

主持人：國立成功大學醫學院附設醫院翁孟玉醫師/佛教慈濟醫療財團法人大林慈濟醫院黃光永醫師

Moderator: Dr. Meng-Yu Weng, National Cheng Kung University Hospital/

Dr. Kuang-Yung Huang, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation

時間	演講題目	演講者	主持人
10:15-10:20	Opening		翁孟玉醫師 國立成功大學醫學院附設醫院
10:20-10:35	GM-CSF primes osteitis and programs early microstructural damage in rheumatoid arthritis	Tsuneyasu Yoshida, M.D., Ph.D.	
10:35-10:50	Pathogenic T cell responses and interaction with non-immune stromal cells in the inflammatory microenvironment of Sjögren's disease	Saori Abe M.D., Ph.D.	
10:50-11:05	Ultrasound Response to Biologics and JAK Inhibitors in Rheumatoid Arthritis: A Retrospective Cohort Study	Soo Min Ahn, M.D., Ph.D.	黃光永醫師 佛教慈濟醫療財團法人大林慈濟醫院
11:05-11:20	Comparative Risk of Infection-Related Complications in Systemic Lupus Erythematosus Patients Treated with Anifrolumab versus Belimumab: A Target Trial Emulation	許登傑醫師	
11:20-11:25	Closing		

GM-CSF primes osteitis and programs early microstructural damage in rheumatoid arthritis

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Background

Osteitis on magnetic resonance imaging (MRI) and bone microstructure changes (BMC) on high-resolution peripheral quantitative computed tomography (CT) are the earliest signs of arthritis, preceding bone erosion on X-ray in rheumatoid arthritis (RA). Recently, a Janus kinase (JAK) inhibitor, baricitinib, reportedly suppresses these early changes. We aimed to elucidate the underlying molecular mechanisms of osteitis and BMC using an RA mouse model and human samples.

Methods

Osteitis and BMCs were assessed by MRI and micro-CT in zymosan-treated SKG mice. Bone marrow (BM) cells were analyzed by flow cytometry. JAK–signal transducer and activator of transcription (STAT) cytokine expression was measured by quantitative PCR. Zymosan-treated SKG mice received baricitinib, anti-granulocyte–macrophage colony-stimulating factor (GM-CSF) antibodies, or recombinant GM-CSF (rGM-CSF). rGM-CSF was also used in an in vitro osteoclast differentiation assay, including human monocytes.

Results

Osteitis and BMCs occurred prior to arthritis in SKG mice. Granulocyte–macrophage-lineage cells and osteoclast precursor cells (OCPs) expanded in inflammatory BM. Receptor activator of nuclear factor kappa-B ligand-positive osteoclasts were observed at BMC sites. The expression of GM-CSF, a JAK–STAT cytokine, was upregulated in osteitic BM. Both baricitinib and anti-GM-CSF antibodies suppressed osteitis and BMCs, whereas rGM-CSF exacerbated these changes. In vitro, adding rGM-CSF markedly increased the osteoclast number and size, especially when added late in osteoclast differentiation both in mice and humans.

Conclusions

GM-CSF drives osteitis and BMCs by expanding granulocyte–macrophage-lineage cells and OCPs and promoting osteoclast differentiation. Targeting GM-CSF is a potential therapeutic strategy to prevent early radiographic changes in RA.

Pathogenic T cell responses and interaction with non-immune stromal cells in the inflammatory microenvironment of Sjögren's disease

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Sjögren's disease (SjD) is characterized by lymphocytic infiltration of the exocrine glands and systemic autoimmunity. However, the mechanisms that initiate and sustain this chronic inflammation within the target tissue, and the links between focal and systemic immune responses, remain unclear. Our research has focused on the pathogenic role of CD4⁺ T cells, which dominate early labial salivary gland (LSG) infiltration and exhibit clonal expansion, suggesting antigen-driven activation. We previously demonstrated that M3 muscarinic acetylcholine receptor (M3R)-reactive CD4⁺IL-17⁺ cells are detected in the peripheral blood of approximately 50% of patients with primary SjD and that identical T cell clones are shared between the LSG and circulation. Further analysis of broad T cell subsets using paired blood and LSG samples revealed a significant increase in CXCR3⁺CXCR5⁺ Tfh1 cells in SjD compared with healthy controls. Investigation of the LSG microenvironment indicated that TGF- β enrichment under TCR stimulation promotes Tfh1 differentiation, suggesting that the local cytokine milieu contributes to the pathogenic CD4⁺ T cell phenotype. Building on these findings, we are currently analyzing RNA-seq data from LSG to elucidate how lymphocytic infiltration is triggered and maintained. We identified seven genes consistently upregulated in SjD LSG, most of which are associated with immunofibroblasts, key stromal cells orchestrating lymphocyte interactions within the inflamed tissues. These results collectively highlight the dynamic interplay between autoreactive T cells and non-immune cells within the inflammatory tissue in shaping chronic inflammation in SjD.

Ultrasound Response to Biologics and JAK Inhibitors in Rheumatoid Arthritis: A Retrospective Cohort Study

Soo Min Ahn, M.D., Ph.D.

ABSTRACT

Objective: Comparative ultrasound data on biologic and JAK inhibitor responses in rheumatoid arthritis (RA) are limited in real-world settings.

Methods: This retrospective cohort study included 135 patients with RA who initiated tumor necrosis factor inhibitors (TNFi, n=45), JAKi (n=28), tocilizumab (n=39), or abatacept (n=23) between January 2023 and December 2024. Synovitis was assessed at baseline and 6 months using grayscale (GS) and power Doppler (PD) ultrasound in 22 joints, including bilateral wrists, 1st–5th metacarpophalangeal joints, 2nd–5th proximal interphalangeal joints, and 1st interphalangeal joints. Clinical disease activity was evaluated using the 28-joint Disease Activity Score (DAS28), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). Ultrasound response was defined as a $\geq 20\%$ reduction in GS or PD scores. Group comparisons and post-hoc pairwise analyses (vs. TNFi) were performed using the Kruskal–Wallis and Fisher's exact tests.

Results: At 6 months, the proportion achieving $\geq 20\%$ improvement in PD did not significantly differ across groups (p=0.083); however, response rates were numerically highest in TNFi (53.3%), followed by JAKi (50.0%), tocilizumab (48.7%), and abatacept (21.7%). In post-hoc analysis, abatacept showed significantly lower PD response than TNFi (p=0.019), while JAKi (p=0.814) and tocilizumab (p=0.827) did not differ. GS improvement showed similar trends (p=0.331). ESR and CRP differed among groups, with lowest values in tocilizumab.

Conclusion: TNFi and JAKi showed higher synovitis improvement than abatacept, underscoring ultrasound's value beyond clinical indices.

Table 1. Baseline Characteristics

Characteristic	Total	TNFi	JAKi	Tocilizumab	Abatacept	P-value
Female, n (%)	96 (71.1%)	32 (71.1%)	19 (67.9%)	27 (69.2%)	18 (78.3%)	0.853
Biologic-naïve, n (%)	98 (72.6%)	40 (88.9%)	18 (64.3%)	23 (59.0%)	17 (73.9%)	0.014
Age (years)	59.9 (49.9–65.2)	59.0 (48.8–63.1)	58.0 (49.8–61.8)	60.6 (54.2–68.2)	64.2 (51.9–68.9)	0.138
DAS28	5.3 (5.2–5.8)	5.3 (5.2–5.6)	5.3 (5.2–5.9)	5.3 (5.2–5.8)	5.3 (5.2–5.5)	0.629
ESR (mm/h)	26.0 (11.5–50.0)	26.0 (8.0–53.0)	32.5 (12.5–51.3)	32.0 (16.0–49.5)	15.0 (8.5–28.5)	0.154
CRP (mg/dL)	0.35 (0.10–1.32)	0.39 (0.10–1.45)	0.44 (0.10–1.34)	0.56 (0.12–1.37)	0.11 (0.10–0.64)	0.277
GS score	6.00 (4.00–9.00)	7.00 (4.00–10.00)	7.00 (5.75–9.00)	6.00 (3.00–8.00)	6.00 (3.00–8.00)	0.162
PD score	1.00 (0.00–2.00)	1.00 (0.00–2.00)	1.00 (0.00–3.00)	1.00 (0.00–2.00)	0.00 (0.00–2.00)	0.512

Data are presented as median (Q1–Q3) and mean \pm standard deviation for continuous variables, and number (%) for categorical variables.

P-values were calculated using Kruskal–Wallis test for medians, one-way ANOVA for means, and chi-square test for categorical comparisons.

Abbreviations: TNFi = tumor necrosis factor inhibitor; JAKi = Janus kinase inhibitor; DAS28 = Disease Activity Score 28; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; GS = grayscale; PD = power Doppler.

Table 2. Six-Month Clinical and Ultrasound Outcomes by Treatment Group

Variable	Total	TNFi	JAKi	Tocilizumab	Abatacept	P-value
6-month DAS28	2.70 (2.30–3.00)	2.80 (2.40–3.00)	2.90 (2.48–3.10)	2.40 (2.20–2.80)	2.80 (2.45–3.05)	0.018
6-month ESR	11.0 (3.0–27.0)	15.0 (7.0–33.0)	15.0 (6.8–26.2)	3.0 (2.0–7.5)	18.0 (8.5–41.5)	<0.001
6-month CRP	0.1 (0.1–0.2)	0.1 (0.1–0.3)	0.1 (0.1–0.2)	0.1 (0.1–0.1)	0.1 (0.1–0.2)	0.001
6-month GS score	4.0 (2.0–6.5)	5.0 (2.0–7.0)	5.0 (3.0–7.0)	4.0 (2.0–5.0)	4.0 (2.0–6.5)	0.450
6-month PD score	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–1.0)	0.057
Δ DAS28	-2.90 (-3.20–-2.45)	-2.70 (-3.20–-2.20)	-2.85 (-3.30–-2.57)	-3.00 (-3.40–-2.65)	-2.70 (-3.20–-2.25)	0.087
Δ ESR	-9.0 (-31.0–0.0)	-5.0 (-25.0–3.0)	-8.0 (-36.8–1.8)	-27.0 (-40.5–-14.0)	0.0 (-6.0–7.5)	<0.001
Δ CRP	-0.17 (-1.17–0.00)	-0.16 (-1.27–0.00)	-0.14 (-1.17–0.00)	-0.46 (-1.27–0.00)	0.00 (-0.49–0.00)	0.171
Δ GS score	-1.00 (-3.00–0.00)	-2.00 (-3.00–-1.00)	-1.50 (-3.00–-0.75)	-1.00 (-3.00–0.00)	-1.00 (-2.50–0.00)	0.375
Δ PD score	0.00 (-2.00–0.00)	-1.00 (-2.00–0.00)	-0.50 (-3.00–0.00)	0.00 (-2.00–0.00)	0.00 (0.00–0.00)	0.097
GS \geq 20% improvement, n (%)	81 (60.0%)	31 (68.9%)	15 (53.6%)	24 (61.5%)	11 (47.8%)	0.331
PD \geq 20% improvement, n (%)	62 (45.9%)	24 (53.3%)	14 (50.0%)	19 (48.7%)	5 (21.7%)	0.081

All continuous variables are presented as median (interquartile range).

P-values were calculated using the Kruskal-Wallis test for continuous variables and the chi-square test for categorical variables.

Table 3. Post-hoc Comparison of PD Improvement (TNFi vs Other Treatments)

Comparison	PD responder rate (\geq 20%) (n, %)	p-value	GS responder rate (\geq 20%) (n, %)	p-value
TNFi vs JAKi	24 (53.3%) vs 14 (50.0%)	0.814	31 (68.9%) vs 15 (53.6%)	0.219
TNFi vs Tocilizumab	24 (53.3%) vs 19 (48.7%)	0.827	31 (68.9%) vs 24 (61.5%)	0.500
TNFi vs Abatacept	24 (53.3%) vs 5 (21.7%)	0.019	31 (68.9%) vs 11 (47.8%)	0.117

Values are expressed as number and percentage of patients achieving \geq 20% reduction in ultrasound scores from baseline to 6 months.

Comparisons were made between TNF inhibitor (TNFi) and each treatment group using Fisher's exact test.

Comparative Risk of Infection-Related Complications in Systemic Lupus

Erythematosus

Patients Treated with Anifrolumab versus Belimumab: A Target Trial Emulation

Anifrolumab 與 Belimumab 治療 SLE 患者之感染相關併發症風險比較：一項目標試驗模擬研究

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Abstract

Background

Anifrolumab and belimumab are biologic agents approved for systemic lupus erythematosus (SLE), yet their comparative safety profiles, particularly regarding infection risks, remain inadequately characterized in real-world settings.

Methods

We conducted a retrospective cohort study using data from the TriNetX research network. Patients diagnosed with SLE between January 1, 2000, and June 30, 2024, with at least two diagnoses were included. We identified new users of anifrolumab or belimumab between August 1, 2021, and June 30, 2024, excluding patients with infection before the index date, patients hospitalized within 6 months before the index date, and patients who died before the index date. Propensity score matching was employed to control for confounding factors. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI), and Kaplan-Meier analysis was used to assess cumulative infection probabilities. The primary outcome was infection occurrence (including herpes zoster, influenza, pneumonia, tuberculosis, sepsis, urinary tract infection, and COVID-19), while secondary outcomes included mortality and hospital inpatient services utilization.

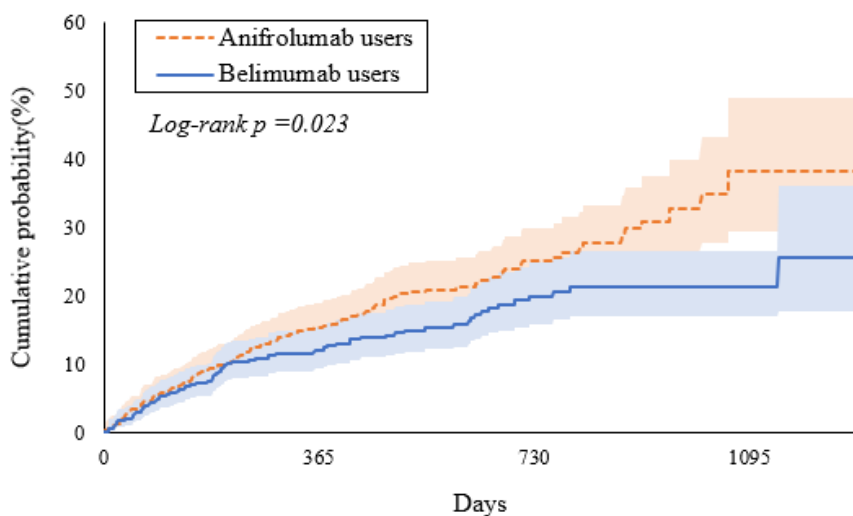
Results

After applying exclusion criteria and propensity score matching, the final analytic cohort included 481 patients in each treatment group. After matching, anifrolumab users showed a significantly higher risk of infection compared to belimumab users (HR 1.40, 95% CI: 1.05-1.88), with 3-year cumulative infection rates of 38.3% and 21.3%, respectively. Analysis of specific infections revealed significantly increased risks of herpes zoster (HR 3.944, 95% CI: 1.111-13.996) and COVID-19 (HR 1.663, 95% CI: 1.042-2.653) associated with anifrolumab use. Subgroup analysis showed significantly higher infection risk in White patients receiving anifrolumab (HR 1.64, 95% CI: 1.09-2.48). Time-dependent analysis suggested that certain infection risks, such as herpes zoster, may develop or intensify with longer treatment duration. No significant differences in mortality or hospital inpatient services utilization were observed between the treatment groups.

Conclusion

Anifrolumab use in SLE is associated with a higher risk of specific infections, particularly herpes zoster and COVID-19, compared to belimumab, especially with prolonged exposure. These findings underscore the need for vigilant infection monitoring, region-specific preventive strategies, and further research to optimize biologic therapy safety across diverse populations.

Figure 2. Kaplan-Meier curves of cumulative probability (%) of Infection, comparing Anifrolumab group and Belimumab groups.



Supplementary Table 2. Hazard ratio and 95% CIs for the risk of various Infection

	Patients cohort	Patients in	Patients with outcome	Hazard ratio* (95% CI)
Herpes Zoster				
Anifrolumab user	481		12	3.944(1.111, 13.996)
Belimumab user	481		10	reference
Influenza				
Anifrolumab user	481		<10	1.719(0.576, 5.133)
Belimumab user	481		<10	reference
Pneumonia				
Anifrolumab user	481		24	1.624(0.840, 3.139)
Belimumab user	481		14	reference
TB				
Anifrolumab user	481		<10	0.951(0.059, 15.210)
Belimumab user	481		<10	reference
Sepsis				
Anifrolumab user	481		15	2.017(0.822, 4.949)
Belimumab user	481		10	reference
UTI				
Anifrolumab user	481		39	1.135(0.714, 1.805)
Belimumab user	481		33	reference
COVID-19				
Anifrolumab user	481		48	1.663(1.042, 2.653)
Belimumab user	481		28	reference

*Hazard ratio for outcomes among Anifrolumab users group compared to Belimumab users group subjects (after propensity score matching).

*95% CI, 95% confidence interval.

*propensity score matching include Age at index, Sex, Ethnicity, Race, BMI, Medical utilization, Socioeconomic, Lifestyle, and Comorbidities.

* If the patients count is 1–10 or less, the results indicate a count of 10.