PsA + COVID-19

Conference Highlights

FROM ACR CONVERGENCE 2020

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SPEAKERS BUREAU

AbbVie, Amgen, Janssen, Lilly, Novartis, Pfizer, UCB

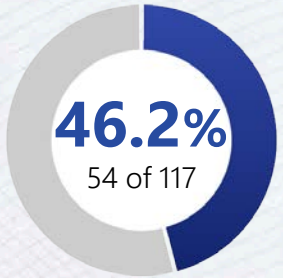
CONTRACTED RESEARCH

AbbVie, Amgen, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun Pharmaceuticals, UCB

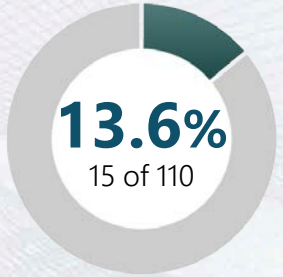
Therapy Optimization With Adalimumab or Methotrexate in Patients With Psoriatic Arthritis

245 randomized and treated patients, with prior inadequate response to an initial course of 15 mg weekly methotrexate

ACHIEVED MDA AT WEEK 16



of patients receiving adalimumab + methotrexate



of patients receiving escalated methotrexate (20-25 mg or highest tolerable dose)

ACHIEVED MDA AT WEEK 32

- Patients who achieved MDA at week 16 generally maintained MDA, despite a removal of methotrexate in the adalimumab responder group
- Patients who did not achieve MDA at week 16 modified therapy either by adding or increasing the dose frequency of adalimumab, resulting in increased proportions of patients achieving MDA

Consistent results were achieved for additional efficacy endpoints, including ACR20/50/70, resolution of enthesitis, and resolution of dactylitis.

MDA=minimal disease activity.

Mease P, et al. *Arthritis Rheumatol.* 2020;72(suppl 10): Abstract 0508.

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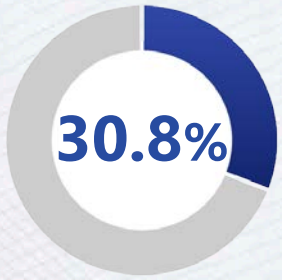
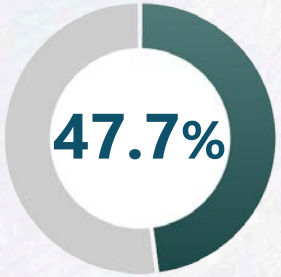
Ixekizumab in Patients With Psoriatic Arthritis With Inadequate Response to TNF Inhibitors

Patients with prior inadequate response or intolerance to 1 or 2 TNF inhibitors received ixekizumab every 4 weeks (IXEQ4W) or every 2 weeks (IXEQ2W) for 156 weeks (3 years).

IXEQ4W

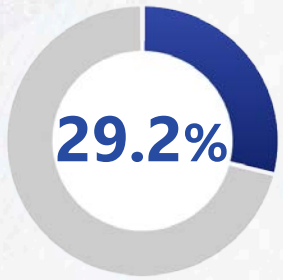


MDA

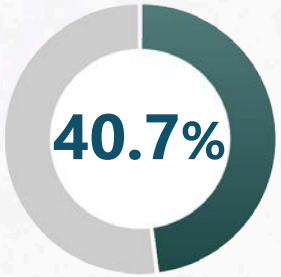


DAPSA: Low Disease Activity or Remission

IXEQ2W



MDA



DAPSA: Low Disease Activity or Remission

Sustained improvement in ACR responses and manifestations of PsA, including enthesitis, dactylitis, and skin outcomes.

DAPSA=disease activity in psoriatic arthritis.

Gratacós J, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0380.

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Tildrakizumab in Patients With Active Psoriatic Arthritis

By week 24, all 4 dose categories of tildrakizumab were significantly more efficacious than placebo in treatment of joint and skin manifestations of PsA.

Improvement in joint and skin manifestations of PsA continued through week 52.

	TILDRAKIZUMAB				Placebo → Tildrakizumab 200 mg Q12W (N=79)
	200 mg Q4W (N=78)	200 mg Q12W (N=79)	100 mg Q12W (N=77)	20-200 mg Q12W (N=78)	
MDA	47.4%	48.1%	35.1%	41.0%	36.7%
ACR20	79.5%	72.2%	67.5%	78.2%	77.2%

Tildrakizumab is an investigational drug for treatment of PsA.
P-values not shown beyond week 24.

Mease P, et al. *Arthritis Rheumatol.* 2020;72(suppl 10): Abstract 2027.

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Safety of Adalimumab, Ixekizumab, and Tildrakizumab in Patients With Psoriatic Arthritis

Ixekizumab, 3-year results: 38 out of 337 (5.9%) patients discontinued due to AEs. The most common TEAEs were infections (IR=33.1) and injection site reactions (IR=5.4). 3 deaths occurred. Safety profile was consistent with previous studies.[1]

Adalimumab: Serious adverse events across all groups were <5%. 2 malignancies were reported: one each in the adalimumab responder and adalimumab nonresponder groups. Safety profile was consistent with previous studies.[2]

Ixekizumab vs adalimumab: The frequency of TEAEs was similar between 2 groups. Compared with ixekizumab, patients with PsA treated with adalimumab had significantly more SAEs (4.2% vs 12%; $P<0.001$); and the time to develop the first SAE was significantly shorter for adalimumab ($P<0.001$). Safety profiles were consistent with previous studies.[3]

Tildrakizumab: 64.5% patients had a TEAE; the most common were nasopharyngitis (8.4%) and upper respiratory tract infection (6.4%). Serious TEAEs were observed in 13 (3.3%) patients. No deaths or major adverse cardiac events occurred.[4]

Tildrakizumab is an investigational drug for treatment of PsA.

AE=adverse event. TEAE=treatment-emergent adverse event. SAE=serious adverse event. IR=incidence rate.

1. Gratacós J, et al. *Arthritis Rheumatol.* 2020;72(suppl 10): Abstract 0380. 2. Mease P, et al. *Arthritis Rheumatol.* 2020;72(suppl 10): Abstract 0508.
3. Mease P, et al. *Arthritis Rheumatol.* 2020;72(suppl 10): Abstract 0346. 4. Mease P, et al. *Arthritis Rheumatol.* 2020;72(suppl 10): Abstract 2027.

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Guselkumab in Patients With Psoriatic Arthritis

LITERATURE REVIEW[1]

24 phase 3 studies were included in a network meta-analysis.

Conclusion:
GUS provides joint arthritis efficacy (ACR responses and modified vdH-S score), physical function (HAQ-DI score), and safety outcomes comparable to most targeted PsA treatments.

For PASI outcomes, GUS was considered better than most other targeted PsA treatments.

DISCOVER-1 and DISCOVER-2 (Biologic-Naïve Patients)
Phase 3 Trials in Adults With Active PsA Despite Standard Treatment

Trial Endpoint(s)	Conclusions
WPAI	Improvement in overall work productivity greater with GUS vs PBO among patients with moderate-to-severe PsA (at W24, $P<0.001$).[2]
LEI	In patients with PsA with dactylitis or enthesitis at baseline, GUS improved dactylitis or LEI scores vs PBO by W8; treatment differences were significant at W16 and W24. Resolution of dactylitis or enthesitis was significantly associated with clinically meaningful improvements in PsA joint and skin symptoms. Improved dactylitis scores correlated with improved skin symptoms and mental health; improved LEI scores correlated with improved physical function.[3]
ACR 50, IGA	Benefits of GUS 100 mg Q4W and Q8W in substantially improving signs and symptoms of active PsA appeared consistent irrespective of baseline characteristics assessed.[4]
BASDAI score	Improvements in axial symptoms were maintained for a full year in GUS-treated patients with active PsA who had imaging-confirmed sacroiliitis.[5]
FACIT-Fatigue	In 2 phase 3 trials, GUS treatment improved fatigue when compared to PBO ($P\leq0.003$ at W24) and maintained improvements through 1 year of treatment.[6]
Safety at W24, W52	GUS safety in PsA was similar at W24 and W52 and consistent with GUS safety in psoriasis. Regarding efficacy in biologic-naïve patients with active PsA, GUS was associated with sustained improvements in joint and skin symptoms; slowed disease progression, and improvements in quality of life and composite indices through W52.[7]
Safety of Q8W, Q4W schedules	GUS regimens of Q8W and Q4W were well tolerated in patients with PsA through 1 year of treatment. There were no meaningful differences between incidences of AEs reported in the Q8W and Q4W groups. The safety profile of GUS in patients with PsA is generally comparable with the previously established safety profile of GUS.[8]

AEs=adverse events. BASDAI=Bath ankylosing spondylitis disease activity index. FACIT=Functional Assessment of Chronic Illness. GUS=guselkumab. HAQ-DI=Health Assessment Questionnaire Disability Index. IGA=Investigator Global Assessment. LEI=Leeds Enthesitis Index. PASI=Psoriasis Area and Severity Index. PBO=placebo. PsA=psoriatic arthritis. Q8W=every 8 weeks. vdH-S=van der Heijde Modified Sharp score. WPAI=Work Productivity and Impairment questionnaire.

1. Mease P, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0334. 2. Curtis J, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0332.
3. McGonagle D, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0895. 4. Deodhar A, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0908.
5. Mease P, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 2025. 6. Rahman P, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0347.
7. McInnes I, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0506. 8. Ritchlin C, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0349.

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Secukinumab and Bimekizumab in Patients With Psoriatic Arthritis

SECUKINUMAB
FUTURE 5, 2-Year Phase 3 Trial, Patients With Active PsA

"48-62% and 19-36% of all SEC-treated groups, respectively achieved sustained LDA (DAPSA LDA+REM or MDA) and sustained REM (DAPSA REM or VLDA) in at least three visits."[1]

"Initiation of SEC as a first-line biologic in patients with PsA resulted in early, statistically significant, and clinically meaningful improvements in PROs across all doses, and significant and meaningful improvements in TNFi-IR patients as later-line therapy."[2]

"A higher level of disease burden was observed in patients with dactylitis compared to patients without dactylitis. SEC 300 mg was associated with a faster time to resolution of dactylitis, higher resolution of dactylitis irrespective of severity and higher responses on skin and joints."[3]

BIMEKIZUMAB
BE ACTIVE, Phase 2b Dose-Ranging Study, Patients With Active PsA

"This BKZ-treated population, who achieved high levels of disease control as early as 12 weeks (including ACR50, MDA, VLDA, BSA 0% and DAPSA remission), demonstrated a consistent maintenance of response rate around 80% across both joint and skin outcomes."[5]

"This patient population with active PsA demonstrated rapid and sustained improvements in patient-reported physical function and psychological wellbeing over 48 weeks of BKZ treatment."[6]

"BKZ treatment was associated with improvements in BASDAI [Bath Ankylosing Spondylitis Disease Activity Index] total and single question scores related to fatigue and neck, back and hip pain in patients with PsA."[7]

SECUKINUMAB AND ADALIMUMAB
Head-to-Head, Phase-3b Trial

"A comparable proportion of patients achieved LDA and/or REM at week 24 across the two treatment groups with further improvements in response/targets at Week 52."[4]

Bimekizumab is an investigational drug for treatment of PsA.

BKZ=bimekizumab. BSA=body surface area. LDA=low disease activity. REM=remission. SEC=secukinumab. VLDA=very low disease activity.

1. Coates L, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0353. 2. Strand V, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 1363.
3. Kirkham B, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 1374. 4. McInnes I, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0909.
5. Merola J, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 1352. 6. Gossec L, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0356.
7. Deodhar A, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0906.

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Upadacitinib in Patients With Psoriatic Arthritis

UPADACITINIB[1]
Post-Hoc Analysis From Select-PsA 1 and Select-PsA 2 Phase 3 Studies; 2345 Patients

At Week 12	SELECT-PsA 1 (Non-Biologic DMARD-IR)			SELECT-PsA 2 (Biologic DMARD-IR)		
	UPA 15 mg QD (N=429)	UPA 30 mg QD (N=423)	PBO (N=423)	UPA 15 mg QD (N=211)	UPA 30 mg QD (N=218)	PBO (N=212)
MDA	24.7%	35.5%	6.4%	16.6%	22.9%	4.2%
VLDA	6.1%	10.4%	0.7%	3.8%	6.4%	0%
DAPSA LDA	34.5%	44.0%	11.1%	25.1%	37.6%	7.5%
PASDAS LDA	28.4%	37.4%	8.5%	19.4%	31.2%	4.2%

P-value ≤0.05 for UPA 15 mg and UPA 30 mg vs PBO. Treatment with UPA also resulted in higher rates of remission/low disease activity at week 24 compared with PBO.

- Higher rates of response for remission/low disease activity were with upadacitinib 30 mg QD vs adalimumab in nonbiologic DMARD-IR patients (*P*≤0.003 at week 24); response rates were similar between the upadacitinib 15 mg QD and adalimumab
- In all treatment groups, the most common reasons for patients not achieving MDA were failure to achieve patient-reported outcomes

UPADACITINIB[2]
SELECT-PsA 2 (Biologic DMARD-IR)

- Upadacitinib 15 mg and 30 mg QD demonstrated significant improvements across all PsA domains vs placebo at week 24
- No new safety concerns were identified compared with findings from studies of upadacitinib in patients with rheumatoid arthritis

Upadacitinib is an investigational drug for treatment of PsA.
IR=inadequate response.

1. Mease P, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 1355. 2. Genovese M, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0504.

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Filgotinib and Deucravacitinib in Patients With Psoriatic Arthritis

FILGOTINIB[1]
EQUATOR2, Phase 2 Trial, Patients With Active Moderate-to-Severe PsA

"By week 52 of the EQUATOR2 OLE, the proportion of patients with clinical resolution of enthesitis had increased from that seen at the end of the EQUATOR study, with the majority of patients who had baseline enthesitis achieving clinical resolution, regardless of treatment in the core 16-week study."

DEUCRAVACITINIB[2]
Phase 2 Trial, Patients With Active PsA (Late-Breaking)

Patients had failed or inadequate response to NSAIDs, corticosteroid, conventional synthetic DMARD, or one TNF inhibitor.

ACR 20 response at week 16, deucravacitinib 6 mg QD, deucravacitinib 12 mg QD, and placebo: 52.9% and 62.7% vs 31.8%, respectively.

Total AEs: 65.7% deucravacitinib 6 mg or 12 mg QD; 42.4% placebo. No SAE. Treatment was well tolerated.

Filgotinib and deucravacitinib are investigational drugs for treatment of PsA.

1. Mease P, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0910. 2. Mease P, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract L03.

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Are Patients Being Treated for Rheumatic Disease at Greater Risk of Poor Outcomes From COVID-19?

NO
Conclusion
Patients with rheumatic disease had similar risk of severe COVID-19 outcomes vs comparators.[1]
Patients with IMIDs on cytokine inhibitors were not at enhanced but rather at lower risk for SARS-CoV2 infection compared to the general community and IMID patients not receiving such drugs.[2]
It is reasonable for patients with inflammatory diseases treated with biological or targeted synthetic DMARDs to continue their treatment during the COVID-19 pandemic.[3]
COVID-19 was extremely low among patients with rheumatic disease treated with biological agents or JAK inhibitors.[4]
Few of patients on biologic therapy tested positive for COVID-19 in this study, considering community spread in the area; few of those who tested positive experienced symptoms.[5]
In this systematic review, the incidence of COVID-19 was low in patients with rheumatic disease; the majority had a mild clinical course and the fatality rate was low.[6]

YES
Conclusion
Patients with inflammatory rheumatic diseases had a higher risk for hospital admission due to severe COVID-19. Researchers also found a higher risk of hospitalization in patients treated with rituximab, but not in patients treated with anti-TNF drugs or other biologics.[7]
Patients with SARDs who develop COVID-19 infection may have higher risks of end organ failure compared to matched comparators without SARDs.[8]
In patients with underlying inflammatory arthritis, COVID-19 outcomes were worse in patients receiving glucocorticoids but, not in patients on maintenance cytokine therapy.[9]
Rheumatologic patients taking targeted therapies had higher rates of COVID-19 than those seen in the general population. Admission rates observed in these patients suggested a more severe course of infection.[10]

IMID=immune-modulated inflammatory disease. JAK=Janus kinase. SARDS=systemic autoimmune rheumatic diseases.

1. Serling-Boyd N, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract L01. 2. Simon D, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0011.
3. González C, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0643. 4. Pavez Perales C, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0638.
5. Keegan Strosser J, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0435. 6. Sood A, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0008.
7. López-Gutierrez F, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0014. 8. D'Silva K, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0430.
9. Haberman R, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 1339. 10. González Fernández M, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 0642.

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COVID-19 and Patients With Rheumatic Diseases

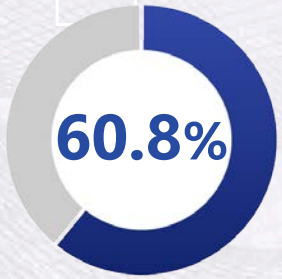
ADHERENCE TO TREATMENT[1]

"Adherence to treatment for rheumatic diseases during the COVID-19 health crisis period was very high in Madrid, despite of being one of the cities hardest hit by the SARS-CoV-2."

RISK MITIGATING BEHAVIOR IN PEOPLE WITH RHEUMATIC DISEASES[2]

(Late-Breaking)

3714 participants from 74 countries



reported shielding, the most stringent risk mitigating behavior

- Use of biologics was associated with higher shielding rates compared with no systemic therapy (odds ratio 1.65, 95% CI 1.32-2.07) and standard systemic therapy (OR 1.37, 95% CI 1.23-1.52)
- No differences in shielding was found between standard systemic therapies and no therapy

"Higher rates of shielding among people with IMIDs receiving biologics may contribute to the reported lower risk of adverse COVID-19 outcomes."

1. Castro Pérez P, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract 1477. 2. Yates M, et al. *Arthritis Rheumatol*. 2020;72(suppl 10): Abstract L02.

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Summary

CLINICAL PRACTICE

PsA is becoming more common in rheumatology practices.

Newer treatment options have allowed better clinical responses in most patients.

COVID-19 has impacted patients' views on the use of biologic therapies.

Evidence continues to build as scientists and healthcare providers study COVID-19 and its impact in patient populations.

FUTURE RESEARCH

More head-to-head trials.

Combined primary efficacy endpoints.

Combinations of targeted synthetic DMARDs with biologic DMARDs.

More data are needed on the impact of therapies on extra-articular manifestations of the diseases.

More focus on the axial domain of PsA and additional safe and effective therapies for PsA axial disease.

More data are needed from registries and other sources if COVID-19 does have a significant impact on rheumatic diseases and/or therapies.

QUESTION AND ANSWER SESSION

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