Perspective

International Journal of Clinical Rheumatology

How can the key findings from the GO-REVEAL study be translated to the clinic?

Psoriatic arthritis (PsA) is a chronic systemic inflammatory condition of unknown etiology affecting the skin, peripheral joints, axial spine and entheses. Five TNF-inhibitors (TNF-Is) are approved for the treatment of PsA and are considered first line biological agents for the treatment of moderate-to-severe psoriasis and PsA. This paper focuses on golimumab and the results from its pivotal clinical trial: GO-REVEAL. Golimumab resulted in similar improvements in the ACR20/50/70, PASI and radiographic scores as other TNF-Is. The clinical response was maintained through 5 years. With similar efficacy and safety profile, decision to choose one TNF-I over another may depend on cost, mode of delivery and patient preference.

Keywords: golimumab • GO-REVEAL • psoriasis • psoriatic arthritis • safety • treatment

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Psoriatic arthritis (PsA) is a chronic systemic inflammatory condition of unknown etiology, typically affecting the skin, peripheral joints as well as the spine, entheses and other tissues. It affects men and women equally with peak incidence between 15 and 45 years of age. Skin disease precedes joint disease in 80% of the cases with PsA occurring in 10–30% of patients with psoriasis [1]. PsA is seronegative for rheumatoid factor and anti-citrullinated peptide antibody in the majority of patients, although these autoantibodies are detected in PsA patients more often than in the general population. PsA can be quite heterogeneous and present in various clinical forms [1–3]. Left untreated, it can cause periarticular bony erosions, periostitis, osteolysis, spondylitis, impaired functional status and decreased quality of life [4–7,9].

Psoriatic arthritis: immunology, disease metrics & approved drugs

PsA shares similar immunopathogenesis and clinical features with other seronegative spondyloarthropathies such as ankylosing spondylitis (AS). Both are characterized by overexpression of several key cytokines and signaling molecules: IL-12, IL-17A, IL-23, JAK2, TYK2 and STAT3 [10]. Psoriatic plaques are rich in IL-23, which in turn stimulates Th17 cells to produce IL-17, TNF-α, IL-21 and IL-22 [5,7–8]. PsA synovium also has proinflammatory cytokines often found in rheumatoid arthritis (RA): TNF-α, IL-1-β, IL-6 and IL-18 [5,7–8]. Despite the overlap, PsA appears to share greater similarity to other spondyloarthropathies than to RA as demonstrated by clinical response to agents targeting IL-17A, IL-12/23 and IL-6. Inhibition of IL-17 and IL-12/23 appears to be effective in AS [11] and PsA, whereas IL-6 inhibition is only effective in RA [12,13].

There are several disease metrics used in PsA to assess efficacy and to facilitate treat to target (T2T) strategy with the goals of reaching disease remission/minimum disease activity (MDA): Composite Psoriatic Disease Activity Index (CPDAI), Disease Activity Index for Psoriatic Arthritis (DAPSA), Disease Activity Score in 28 Joints (DAS28), Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Psoriatic Arthritis Response Criteria (PsARC), Psoriasis Area Severity Index (PASI) and American College of Rheumatology response criteria. These

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indices measure some combination of tender/swollen joint count (TJC/SJC), enthesitis, dactylitis, axial disease, psoriasis, patient-/physician-global assessment, patient-reported pain, physical function and acute phase reactants. DAS28 and ACR metrics are the most commonly used indices in clinical trials but these indices do not assess for dactylitis, enthesitis or skin/nail changes. Regardless, all indices appear to correlate highly to each other [14]. While the benefit of T2T has been well established in RA, the long-term impact of T2T in PsA remains to be seen.

With the success of biological agents in RA and some similar pathologic findings in RA and PsA, many agents used in RA have been studied in and subsequently found to be effective in PsA. Five TNF-inhibitors (TNF-Is) are available for the treatment of PsA worldwide: infliximab, etanercept, adalimumab, golimumab and certolizumab pegol. All except for certolizumab are also approved for psoriasis [15]. TNF-Is are considered first line biological agents for the treatment of moderate-to-severe psoriasis and PsA. Most recently, apremilast, a PDE4 inhibitor, has been added to a growing list of therapeutic agents for PsA. Two additional biologicals have been approved for the treatment of moderate to severe psoriasis: ustekinumab, an IL-12/23 inhibitor and secukinumab, an IL-17A inhibitor. This paper will focus on golimumab and its potential use in the treatment of PsA, with a special emphasis on the results of its pivotal clinical trial: GO-REVEAL (Golimumab-A Randomized Evaluation of Safety and Efficacy in Subjects with Psoriatic Arthritis Using a Human Anti-TNF Monoclonal Antibody).

Golimumab for the treatment of psoriasis & psoriatic arthritis: GO-REVEAL

GO-REVEAL clinical results

Golimumab is a human anti-TNF-α monoclonal antibody that binds with high affinity and specificity to soluble and transmembrane TNF. It received US FDA approval in 2009 for RA, PsA and AS. It is given 50 mg subcutaneously every 4 weeks. GO-REVEAL was a Phase III, randomized double-blind placebo controlled trial through week 24, with an early escape at week 16, followed by an open label extension up to 5 years. Patients with less than 10% improvement in their SJC and TJC at week 16 could 'early escape' from placebo to golimumab 50 mg or from golimumab 50 mg to golimumab 100 mg. Beginning with the week 24, all patients still receiving placebo corssed over to receive golimumab 50mg. After week 52, all patients entered open-labeled portion of the study with golimumab 50 or 100 mg injections every 4 weeks. The doses of golimumab could be changed at the discretion of the investigators. Four hundred five patients were randomized (1:1.3:1.3) to receive placebo, golimumab 50 mg or golimumab 100 mg every 4 weeks. Randomization was stratified by concomitant methotrexate (MTX) use. PsA patients with ≥ 3 TJC, 3SJC and psoriasis >2 cm diameter despite disease modifying antirheumatic drugs (DMARDs) and/or nonsteroidal anti-inflammatory drugs (NSAIDs) were eligible for the study (Table 1).

At 14 weeks (primary end point), the ACR20 response was 48% in the combined golimumab group (51% in 50 mg, 45% in 100 mg) versus 9% in the placebo group. At 24 weeks, an ACR 20 was achieved in 12%/52%/61% of placebo, golimumab 50 and 100 mg group, respectively [16]. Intent to treat analysis including those patients with early escape was used for all analysis after 24 weeks due to lack of control group and all patients receiving golimumab. At 52 weeks, the placebo, golimumab 50 mg and golimumab 100 mg group achieved an ACR20 66%/67%/71%, respectively; an ACR50 39%/49%/51%, respectively; and an ACR70 20%/36%/30%, respectively [17]. This was maintained through 5 years with an ACR 20/50/70 response rates of 63–70%/43–50%/30–35% for each group [18]. Similarly, DAS28-CRP improvement was greater among golimumab groups versus placebo at week 24 (-1.43 to -1.56 vs -0.12 from baseline, respectively) with 75–85% achieving DAS28-CRP good/moderate response at week 256 (Table 2) [18]. A total of 126/405 (31%) discontinued the trial through week 252, mainly due to adverse events (AEs) and/or unsatisfactory clinical response. Fewer patients (10 vs 1.8%) on concomitant MTX developed antibodies to golimumab but neither MTX use nor presence of antigolimumab antibody affected overall clinical response rate [16–18].

GO-REVEAL radiographic results

Golimumab provided radiographic protection with less mean changes in PsA-modified Sharp/van der Heijde score (SHS) from baseline: -0.22 ± 1.64 versus 0.22 ± 1.38 for golimumab and placebo group, respectively at week 52 [18]. Greater proportion of patients on golimumab without baseline erosions and joint space narrowing remained free of radiographic progression compared with placebo at week 24 [16]. Radiographic protection was maintained through year 5 for all groups with mean change of 0.1 to 0.3 from baseline, including placebo group patients who switched to golimumab between weeks 16 and 24. Unlike clinical response, concomitant MTX use was associated with less radiographic progression compared with golimumab monotherapy at week 256 [18].

GO-REVEAL: psoriasis, dactylitis, enthesitis & patient reported outcomes

Golimumab was effective for psoriasis with 56 and 66% of patients on golimumab 50 and 100 mg, respectively achieving at least 75% improvement in a Psoriasis Area and Severity Index (PASI75) at week 24 versus 1% on placebo [16–18]. This was maintained through year 5 with 60–72% achieving the PASI75. Interestingly, no significant difference was noted among patients with or without concomitant MTX [18]. Approximately 78% of patients had enthesitis at baseline. At 24 weeks, significantly smaller proportion of patients treated with golimumab had enthesitis (50 vs 69%) and had greater improvement in PsA-modified MASES enthesitis score (60–67 vs 12%) compared with placebo. For patients with dactylitis at baseline (~35%), the proportion with dactylitis remained similar at 24 weeks in both golimumab and placebo groups (14–22%), but golimumab treated patients had a greater improvement in dactylitis severity score (100 vs 42%). These improvements in enthesitis and dactylitis were maintained through year 5 [16–18].

Golimumab treated patients also had significant improvements in patient reported outcomes: physical function (as measured by Health Assessment Questionnaire [HAQ] disability index [DI] score), Health Related Quality of Life (HRQOL as measured by 36-Short Form Health Survey mental component summary [MCS] and physical component summary [PCS]) and productivity (as measured self-reported 10 cm VAS). HAQ DI improved 0.33–0.39 ± 0.5 at 24 weeks [16–18] with 52–58% maintaining this improvement through week 256. The mean HAQ-DI score ranged from 0.6 to 0.7 at week 256 [16–18]. Similarly, improvements in productivity and health related quality of life as measured by SF-36 PCS (0.63 ± 8.72 vs 7.83 ± 9.41) and MCS (-0.60 ± 12.13 vs 3.84 ± 10.79) at 24 weeks were greater in both golimumab dose groups compared with placebo group [16–18]. In general, improvements in work productivity and SF-36 PCS correlated closely to an ACR 20 response whereas improvements in SF-36 MCS correlated more with an ACR 20 rand PASI75 response. Interestingly, despite significant improvements in dactylitis and enthesitis scores (67–85% and 40–60%, respectively), these correlated only weakly with HRQOL, physical function and work productivity [16–18].

Table 1. Baseline characteristics of GO-REVEAL.

	Placebo (n = 113)	Golimumab 50 mg (n = 146)	Golimumab 100 mg (n = 146)	Combined (n = 292)
Men; n (%)	69 (61)	89 (61)	86 (59)	175 (60)
White; n (%)	110 (97)	141 (97)	142 (97)	283 (97)
Age (years)	47.0 ± 10.6	45.7 ± 10.7	48.2 ± 10.9	47.0 ± 10.9
PsA duration (years)	7.6 ± 7.9	7.2 ± 6.8	7.7 ± 7.8	7.5 ± 7.3
No. of swollen joints (range 0–66)	13.4 ± 9.8	14.1 ± 11.4	12.0 ± 8.5	13.0 ± 10.1
No. of tender joints (range 0–68)	21.9 ± 14.7	24.0 ± 17.1	22.5 ± 15.7	23.3 ± 16.4
CRP level (mg/dl)	1.3 _± 1.6	1.3 ± 1.6	1.4 ± 1.8	1.3 ± 1.7
HAQ DI score (range 0–3)	1.03 ± 0.55	0.98 ± 0.65	1.05 ± 0.62	1.02 ± 0.64
SF-36 PCS score (range 0–100)	31.9 ± 9.3	33.0 ± 10.7	32.8 ± 8.9	32.9 ± 9.8
SF-36 MCS score (range 0–100)	47.6 ± 10.7	45.4 ± 12.2	45.0 ± 11.7	45.2 ± 12.0
DAS28-CRP score	4.9 ± 1.0	5.0 ± 1.1	4.9 ± 1.1	4.9 ± 1.1
PASI score (range 0–72)†	8.4 ± 7.4	9.8 ± 8.6	11.1 ± 9.5	10.4 ± 9.1
Patients with fingers/toes with dactylitis; n (%)	38 (34)	50 (34)	49 (34)	99 (34)
Patients with enthesitis; n (%)‡	88 (78)	109 (75)	115 (79)	224 (77)
Productivity score (0–10-cm VAS)	5.3 ± 2.8	5.3 ± 2.9	5.3 ± 2.6	5.3 ± 2.8

Values are the mean ± SD unless otherwise indicated.
†In patients with ≥3% of body surface area with psoriasis skin involvement.
‡As determined using the PSA-modified Maastricht Ankylosing Spondylitis Enthesitis Score index.
CRP: C-reactive protein; DAS28-CRP: 28-joint Disease Activity Score using the CRP level; HAQ: Health Assessment Questionnaire SF-36:36-item Short Form health survey; DI: Disability index; MCS: Mental component summary; PASI: Psoriasis Area and Severity Index; PCS: Physical component summary; PsA: Psoriatic arthritis; VAS: Visual analog scale.
Adapted with permission from [17].

Table 2. Clinical and radiographic results of the GO-REVEAL study.

	Placebo (early escape starting at week 14)	Golimumab 50 mg	Golimumab 100 mg	Golimumab 50 + 100 mg
Number of randomized patients	113	146	146	292
ACR 20				
Week 14	9%	51%*	45%*	48%*
Week 24	12%	52%*	61%*	
Week 24 (early escape patients)	47%			
Week 52	65.5%	67.1%	71.2%	69.2%
Week 104	62.8%	67.1%	69.9%	
Week 256	62.8%	65.8%	68.9%	
ACR 50				
Week 24 (early escape patients)	14%			
Week 52	38.9%	48.6%	50.7%	49.7%
Week 104	46%	46.6%	51.4%	
Week 256	43.4%	47.9%	50.7%	
ACR 70				
Week 24 (early escape patients)	6%			
Week 52	19.5%	35.6%	30.1%	32.9%
Week 104	31%	28.8%	35.6%	
Week 256	32.7%	30.8%	35.6%	
DAS28 – CRP (% EULAR good/moderate responders)				
Baseline score	4.9 ± 1.0	5.0 ± 1.1	4.9 ± 1.1	
Week 24	-0.12 ± 0.97	-1.43 ± 1.34	-1.56 ± 1.10	
Week 52	-1.67 ± 1.19	-2.02 ± 1.34	-1.20 ± 1.21	-2.01 ± 1.28
Week 104	2.9 (2.0, 4.1)	2.6 (1.8, 3.7)	2.6 (1.7, 3.6)	
Week 256	3.0 ± 1.4	2.8 ± 1.2	2.8 ±1.2	
PSA mSHS (mean change ± SD from baseline)				
Week 52	0.22 ± 1.38	-0.22 ± 1.64****	-0.14 ± 1.53*****	-0.18 ± 1.59
Week 104	0.08 ± 3.19	-0.39 ± 2.04	-0.32 ± 1.87	
Week 256	0.3 ± 3.8	0.3 ± 4.2	0.1 ± 2.7	
PASI 75 (%)				
Week 24	1	56*	66*	
Week 52	48.1	62.4	68.5	65.4
Week 104	55.7%	63.3%	72.2%	
Week 256	60.8%	61.5%	72.2%	

ACR20/50/70:American College of Rheumatology Proportions of patients achieving at least 20%/50% and 70% improvement according to the American College of Rheumatology criteria; BSA: Body surface area; CRP: C-reactive protein; DAS28-CRP: Disease Activity Score in 28 joints using the CRP level (intend to treat analysis); HAQ: Health Assessment Questionnaire; JSN: Joint space narrowing; MCS: Mental component summary; mMASES: Modified Maastricht Ankylosing Spondylitis Enthesitis Score; PASI: Psoriasis Area and Severity Index; PCS: Physical component summary; PsA: Psoriatic arthritis; SF-36: Short Form 36; SHS: Sharp/van der Heijde score.
*p < 0.001 vs placebo; **p < 0.05 vs placebo; ***p less 0.01 vs placebo; ****p less 0.011 vs placebo; *****p =0.086 vs placebo.

Table 2. Clinical and radiographic results of the GO-REVEAL study.

	Placebo (early escape starting at week 14)	Golimumab 50 mg	Golimumab 100 mg	Golimumab 50 + 100 mg
Enthesitis (m MASES Score)				
Baseline score	5.0 ± 4.1(n = 88)	5.7 ± 4.0 (n = 109)	6.1 ± 4.1 (n = 115)	
Week 104	40.4 ± 92.7	59.5 ± 70	56 ± 72.7	
Dactylitis				
Baseline score	3.1 ± 2.1 (n = 38)	6.3 ± 6.1 (n = 50)	5.4 ± 6.7 (n = 49)	
Week 104	67.4 ± 63.9	83 ± 36.4	85.3 ± 38.5	
Week 256	1.2 ± 2.3	1.3 ± 4.9	0.8 ± 2.1	
HAQ (improvement from baseline)				
Week 14	0.04 ± 0.44	0.31 ± 0.50*	0.38 ± 0.51*	0.35 ± 0.50*
Week 24	-0.01 ± 0.49	0.33 ± 0.55*	0.39 ± 0.50*	0. 36 ± 0.53*
Week 52	0.37 ± 0.56	0.41 ± 0.53	0.43 ± 0.53	0.42 ± 0.53
Week 104	0.36 ± 0.58	0.43 ± 0.56	0.45 ± 0.55	044 ± 0.55
Week 256 (% with >0.3 unit improvement)	54.0%	52.7%	58.9%	
SF-36 MCS (improvement from baseline)				
Week 14	0.40 ± 11.39	2.79 ± 10.27**	3.56 ± 12.06**	3.18 ± 11.20**
Week 24	-0.60 ± 12.13	3.37 ± 10.55***	4.20 ± 11.03***	3.87 ± 10.79*
Week 52	3.69 ± 11.23	3.95 ± 11.73	4.84 ± 11.60	4.40 ± 11.7
Week 104	2.99 ± 11.08	4.71 ± 11.35	4.69 ± 12.21	4.70 ± 11.77
SF-36 PCS (improvement from baseline)				
Week 14	0.63 ± 7.68	6.53 ± 8.88*	7.85 ± 9.55*	7.19 ± 9.23*
Week 24	0.67 ± 8.72	7.42 ± 9.17*	8.22 ± 9.64*	7.83 ± 9.41*
Week 52	8.25 ± 10.50	9.87 ± 9.51	9.19 ± 10.29	9.53 ± 9.90
Week 104	8.76 ± 11.41	8.70 ± 9.56	8.50 ± 10.45	8.60 ± 10.00
Week 256	8.1 ± 10.9	8.8 ± 11.1	8.8 ± 11	9.53 ± 9.90

ACR20/50/70:American College of Rheumatology Proportions of patients achieving at least 20%/50% and 70% improvement according to the American College of Rheumatology criteria; BSA: Body surface area; CRP: C-reactive protein; DAS28-CRP: Disease Activity Score in 28 joints using the CRP level (intend to treat analysis); HAQ: Health Assessment Questionnaire; JSN: Joint space narrowing; MCS: Mental component summary; mMASES: Modified Maastricht Ankylosing Spondylitis Enthesitis Score; PASI: Psoriasis Area and Severity Index; PCS: Physical component summary; PsA: Psoriatic arthritis; SF-36: Short Form 36; SHS: Sharp/van der Heijde score.
*p < 0.001 vs placebo; **p < 0.05 vs placebo; ***p less 0.01 vs placebo; ****p less 0.011 vs placebo; *****p =0.086 vs placebo.

GO-REVEAL: disease remission & minimum disease activity

The ability to reach minimum disease activity (MDA) and its impact on clinical and radiographic outcome of patients treated with golimumab were assessed at year 5 using *post hoc* analysis. The Outcome Measures in Rheumatology Clinical Trials (OMERACT) group defined MDA is "that state of disease activity deemed a useful target of treatment by both the patient and physician, given current treatment possibilities and limitations," and encompasses both remission and low disease activity. In accordance to this definition, GO-REVEAL used previously validated PsA MDA criteria where five of the seven components must be met: TJC ≤1; SJC ≤1; PASI ≤1 or body surface area ≤3; patient pain visual analog score (VAS) ≤15; patient global disease activity VAS ≤20; HAQ ≤0.5; tender entheseal points ≤1 [16–20].

The MDA at ≥ 3 visits were achieved more frequently among golimumab treated patients (28.1% vs 7.7 and 42.4% vs 30.2% at week 24 and 52, respectively). Through 5 years, approximately 50% of patients achieved MDA at least once. Lower baseline HAQ score but not baseline MTX use was associated with higher likelihood of achieving MDA. Similar to other studies supporting T2T strategy, the achievement of MDA, irrespective of treatment group, was associated with less

radiographic progression, better functional improvement and patient global assessment of disease. The delay in active treatment among the placebo group was associated with twice the amount of radiographic damage, though still minimum overall. However, the achievement of MDA did not lead to improved skin symptoms [17]. In fact, while patients who achieved MDA on concomitant MTX had less radiographic progression, they had less improvements in PASI score at week 256 [16–18].

GO-REVEAL: safety considerations

Golimumab was well tolerated with no significant differences between the 50 and 100 mg golimumab dose except for increased infections in the latter group (33 vs 41%) [18]. Through week 24, the most frequently reported AEs were nasopharyngitis and upper respiratory tract infections, occurring 59% in placebo and 65% in golimumab groups [16]. Through week 256, 15 patients developed serious infections with opportunistic infections occurring only in the 100 mg group. Five patients died: two from accidents, one unknown and two nonskin cancers. Twenty-one patients developed malignancies (10 non-melanoma skin cancers and 11 non-lymphoma cancers) with standard incidence ratio of 0.57–1.85 compared with general US population. Serious AEs leading to drug discontinuation occurred in 12.4% of the patients and included: basal cell carcinoma (BCC), increased asparate- and alanine-aminotransferase, breast cancer, PsA and accidental death. Antibodies with golimumab occurred in 1.8% of patients on MTX and 10.0% without MTX. However, the presence of antigolimumab antibody did not impact the clinical response or frequency of AEs (e.g., injection site reactions) [16–18].

GO-REVEAL: study limitations

This study represents the longest available clinical data for any TNF-I for the treatment of PsA. While it provides unprecedented long-term data on efficacy and safety of golimumab among PsA patients with high retention rate, it does have several limitations. These patients were relatively treatment naive with no prior history of biological agents and with only about half of the patients on baseline MTX. Investigators were allowed to escalate the dose once at week 52 at their discretion but no data are available on the frequency of dose escalation.

Clinical application from GO-REVEAL: comparison of TNF-Is

To date, there are no studies directly comparing the efficacy and safety of five approved TNF-Is. Several studies have performed meta-analysis of randomized controlled trials for the treatment of PsA comparing efficacy of adalimumab, etanercept, golimumab and infliximab. These studies were published prior to the approval of certolizumab in 2013 for the treatment of PsA [21,22]. All TNF-Is were comparable in efficacy as measured by PsARC response, HAQ and ACR20/50/70. Certolizumab had similar ACR response to other TNF-Is when compared with placebo with ACR 20/50/70 of 58/42/26% at week 24 [22]. All TNF-Is also were equally effective in delaying radiographic progression [23,24]. However, monoclonal antibodies appeared to be slightly more effective than etanercept for psoriasis [21]. Similar to findings in the GO-REVEAL study, concomitant MTX did not affect the ACR response among PsA patients receiving TNF-Is [25].

With similar efficacy and safety profile, decision to choose one TNF-I over another may depend on cost, mode of delivery and patient preference. They are all quite expensive with direct cost to patients and society varying depending on their healthcare system. Infliximab is given intravenously with effective dose ranging from 5 to 10 mg/kg every 4–8 weeks. Etanercept, adalimumab, golimumab and certolizumab are all given subcutaneously (biweekly to monthly). The overall persistent rate appears to be similar at 66–68% among these agents [26]. In a large regional survey in England, the median time from diagnosis to TNF-I therapy was 4.6 years with the majority starting adalimumab first (64%) followed by etanercept (34%), infliximab (2%) and golimumab (1%) [27].

Recent development of TNF-I biosimilars offers additional options for patients who are candidates for TNF-Is. Biosimilars are highly similar to their reference products with minor differences in clinically inactive components. They do not appear to have clinically meaningful differences between the biological product and biosimilars in terms of safety, purity and potency. Several monoclonal anti-TNF antibody biosimilars have been developed and found to be effective in RA. As these agents are not identical, one cannot recommend interchangeability until their long-term efficacy and safety are tested compared with currently approved TNF-Is.

Conclusion

GO-REVEAL was a Phase III study assessing the safety and efficacy of golimumab for the treatment of PsA over 5 years. Golimumab 50 and 100 mg subcutaneous monthly resulted in similar improvement in the ACR20/50/70, PASI and radiographic scores as other TNF-Is. The concomitant use of MTX was associated with less radiographic progression of disease compared with golimumab monotherapy but had no synergistic effect on clinical outcomes (e.g., ACR 20/50/70, PASI, patient-reported outcomes). Higher dose of golimumab (100 mg) did not confer additional benefit compared with 50 mg but was associated with greater numbers

of more serious infections and malignancies The most common serious AEs among all golimumab users were abnormal liver function tests, infections and skin malignancies. This study affirmed that golimumab is a safe and effective therapeutic option for biologically naive PsA patients who continues to have active disease.

Future perspective

The armamentarium for the treatment of PsA and psoriasis has grown significantly in the past several decades, including many biologicals such as TNF-Is, ustekinumab, apremilast and secukinumab. The most commonly used biologicals appear to be TNF-Is either alone or in combination with DMARDs. There are no clinical trials directly comparing all TNF-Is for their effectiveness, safety and phramacoeconomics [28]. However, meta-analysis and indirect comparisons indicate that the efficacy and safety profile are similar between all TNF-Is. While GO-REVEAL provided long-term clinical data on golimumab in the treatment of PsA, many other questions remain. In RA, while TNF-Is are effective as monotherapy, concomitant DMARDs especially MTX appear to provide synergistic effect in improving both clinical and radiographic outcome. In GO-REVEAL, patients with active disease despite DMARDs or NSAIDs were eligible for the study and only MTX was allowed as background DMARD during the study. Based on this and other published studies, it remains unclear if any DMARDs provide synergistic effect in PsA.

Recent data suggest that treatment with TNF-I may be safely tapered and discontinued in RA patients who are in clinical remission but it remains to be seen if similar strategy can also be applied to PsA patients. In one study, 20% of 236 PsA patients were able to achieve remission before relapsing off all meds after mean duration of 13 months [29]. In addition, it is clear that combination biological therapy in RA increases safety concerns without providing synergistic clinical benefit. With bispecific antibodies in development for RA that block dual targets (e.g., TNF-I and IL-17), further studies are needed to assess their safety and potential synergistic role in the treatment of PsA.

A key unmet need in the management of PsA and other autoimmune is prospective identification of patients who are likely to benefit from specific therapies. For example, in RA, some patients who responded to TNF-I treatment had transcription profiles enriched for inflammatory processes and TNFα protein expression [30,31] while others had lower inflammatory cell-surface markers such as the IL-7 receptor α chain [32]. If we can identify certain patient characteristics that can predict clinical response to certain treatment, we can tailor individual treatment to optimize their safety and efficacy profile. At this time, we still do not know who is an ideal candidate for TNF-I as opposed to other mechanism of action (e.g., IL-17 inhibitor). This is an area of active research with biomarkers, imaging and genetic sequencing and soon, we hope to have some answers to guide us into this era of personalized medicine.

Financial & competing interests disclosure

A Kavanaugh conducts clinical trials sponsored by Amgen, Abbvie, Janssen and UCB. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Executive summary

Psoriatic arthritis: immunology, disease metrics & approved drugs

- Psoriatic arthritis shares similar immunogenesis and clinical features as other spondyloarthropathies with abundant IL-12, IL-17A, IL-23 and TNF-α.
- There are a growing list of medications for the treatment of psoriatic arthritis including five TNF-inhibitors (TNF-Is) (adalimumab, certolizumab, etanercept, golimumab and infliximab) and a phosphodiesterase-4 inhibitor (apremilast).
- In additional to TNF-Is, two biologicals have been approved for the treatment of psoraisis: ustekinumab and secukinumab.

Golimumab for the treatment of psoriasis & psoriatic arthritis: GO-REVEAL

- Golimumab 50 and 100 mg subcutaneous monthly resulted in similar improvement in the ACR20/50/70, PASI, radiographic scores, dactylitis, enthesitis and patient reported outcomes as other TNF-Is.
- The concomitant use of methotrexate was associated with less radiographic progression of disease compared with golimumab monotherapy but no synergistic effect on clinical outcomes.
- Golimumab was well tolerated with similar safety profile as other TNF-Is. The most common serious adverse events among all golimumab users were liver function tests, infections and skin malignancies.

Clinical application from GO-REVEAL: comparison of TNF-Is

- With similar efficacy and safety profile, decision to choose one TNF-I over another may depend on cost, mode of delivery and patient preference.

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