Psoriatic arthritis: A comprehensive review for the dermatologist—Part II: Screening and management

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Learning objectives

After completing this learning objective, the reader will be able to better discuss this aspect of the literature.

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The editors involved with this CME activity have reported no relevant financial relationships with commercial interest(s).

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Psoriatic arthritis (PsA) is a common comorbidity of psoriasis occurring in up to one-third of patients. Dermatologists hold an essential role in screening patients with psoriasis for PsA, since as many as 85% of patients develop psoriasis before PsA. Early detection and treatment of PsA are important for both short- and long-term patient outcomes and quality of life. Many factors must be weighed when selecting the appropriate therapy for PsA. One must consider the 'domains of disease' that are manifested, the disease severity, patient comorbidities, patient preferences (routes of dosing or frequency, as examples) as well as factors often outside of patient-physician control, such as access to medications based on insurance coverage and formularies. As many patients will have involvement of multiple domains of psoriatic disease, selecting the therapy that best captures the patient's disease is required. In this review, we will address PsA screening, diagnosis, therapeutic approach to psoriatic disease, comorbidity considerations, and comanagement. (J Am Acad Dermatol 2025;92:985-98.)

Key words: psoriasis; psoriatic arthritis.

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Abbreviations used:

ACR:	American College of Rheumatology
AS:	ankylosing spondylitis
DMARD:	disease modifying antirheumatic drug
FDA:	Food and Drug Administration
GRAPPA:	Group for Research and Assessment of Psoriasis and Psoriatic Arthritis
IBD:	inflammatory bowel disease
IL:	interleukin
JAK:	janus kinase
MTX:	methotrexate
MDA:	minimal disease activity
NPF:	National Psoriasis Foundation
PEST:	Psoriasis and Epidemiology Screening Tool
PsA:	psoriatic arthritis
TNFi:	tumor necrosis factor inhibitor

PSORIATIC ARTHRITIS SCREENING

- The mnemonic PSA, representing joint pain, stiffness/swelling/sausage digit, and axial involvement, is a method to facilitate the recognition of psoriatic arthritis (PsA) disease features.
- Validated screening tools include the Psoriasis and Epidemiology Screening Tool (PEST), the Psoriatic Arthritis Screening and Evaluation, and the Toronto Psoriatic Arthritis Screening.

A mnemonic, "PSA" (Fig 1) is a simple method to remind providers to ask about PsA and recognize the specific characteristics of PsA.[1] Formal screening or referral may follow.

Several screening tools were developed and validated, including the PEST, the Psoriatic Arthritis Screening and Evaluation, and the Toronto Psoriatic Arthritis Screening.[2-6] These self-reported questionnaires can be given to patients with psoriasis before or during office visits. While initially showing good sensitivity and specificity in validation studies, subsequent research in different populations yielded mixed results; there is no consensus on which tool performs best.[7,8]

The PEST, which is available in the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) mobile app and has been translated into multiple languages, is particularly simple and easy to use (Fig 2).

Screening is recommended every 6 months by the National Psoriasis Foundation (NPF) since treatment delays of >6 months have been associated with worse outcomes.[9] The authors, however, recommend screening at every visit. Studies regarding electronic health record reminders and patient mailings for PsA screening are ongoing.

MANAGEMENT

Treat-to-target and minimal disease activity/remission

- A treat-to-target approach to achieve minimal disease activity (MDA) may improve patient outcomes and result in less disease progression.

Treat-to-target approaches allow physicians and patients to set targets for improved health outcomes.[10] A proposed "target" of disease treatment specific for PsA is MDA. Like many outcome measures, MDA may not be clinically practical but does serve as a stringent measure that sets a high bar of improvement and is patient-centered.[11]

In the TICOPA trial, treatment-naïve PsA patients were randomized to receive either treatment with tight control of their PsA, in which regimens were re-examined every 4 weeks, or standard care, in which patients were re-examined every 12 weeks. The primary endpoint, ACR20, was more likely to be achieved in the tight control group than the standard therapy group, suggesting that a treat-to-target approach can result in improved patient outcomes and reduced disease progression.[12] The International Dermatology Outcome Measures has provided a similar framework that may guide treatment decisions (Fig 3).[13]

While MDA serves as an endpoint for the treatment of PsA, in patients with concomitant psoriasis, optimal improvements in health-related quality of life are dependent upon the treatment of both joint and skin symptoms.[14] Other tools exist to define remission and treatment success in PsA, including the Disease Activity in Psoriatic Arthritis, but these are not discussed here.[15]

Of note, these endpoints are distinct from the ACR20, which is commonly used as a primary endpoint in clinical trials, in being more PsA-specific.[16]

Comanagement, dermatology, and rheumatology

- Dermatologists are encouraged to adopt interdisciplinary strategies, including combined clinic models.

The management of psoriatic disease can be complex as multiple disease domains can be affected. Dermatologists should consider interdisciplinary management, ranging from facilitated communication among specialists to more formal combined clinic models. Resources to help determine when and how to refer are made available by the Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network (www.

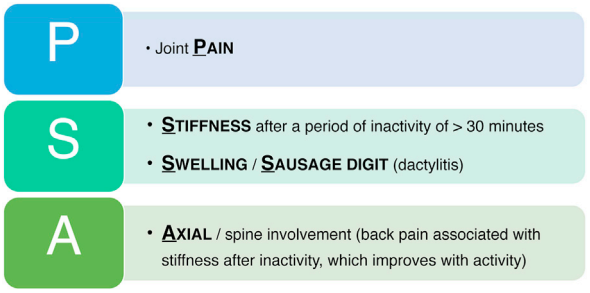

Fig 1. Psoriatic arthritis. PSA mnemonic. The psoriatic arthritis (PsA) mnemonic was developed to promote awareness of the clinical manifestations of psoriatic arthritis. The clinical manifestations of the disease include joint pain, stiffness, "sausage digit," and/or axial spine involvement. Any 2 features (P, S, and/or A) may suggest psoriatic arthritis. Stiffness (S) and axial involvement (A) may suggest axial PsA. If PsA is suspected, the patient should be formally screened for PsA and/or referred to a rheumatologist.

Psoriasis Epidemiology Screening Tool (PEST)	YES (1)	NO (0)
Have you ever had a swollen joint (or joint)?		
Has a doctor ever told you that you had arthritis?		
Do your fingernails or toenails have holes or pits?		
Have you experienced pain in your heel?		
Have you had a finger or toe that was completely swollen and painful for no apparent reason?		
Total		

A score of ≥3 suggests a potential risk of psoriatic arthritis, and a rheumatology referral may be considered.

Fig 2. Psoriatic arthritis. The Psoriasis Epidemiology Screening Tool (PEST) questionnaire. The PEST is a patient self-assessment tool that consists of 5 binary questions. Each positive answer is assigned 1 point. Scoring ≥3 is considered a positive screen that should be further evaluated. Of note, patients may additionally indicate the locations of stiff, swollen, or painful joints on a manikin (not shown). While indicating the locations of affected joints on the manikin does not contribute to the overall score, it may allow the physician to promptly identify problematic joints, making the referral process easier if necessary. Modified from Ibrahim et al.[3]

PPACMAN.org), a nonprofit organization that represents dermatology-rheumatology collaboration.

Treatment algorithms

Several organizations published treatment guidelines, including the GRAPPA, the European League Against Rheumatism (EULAR), and the American College of Rheumatology (ACR) and NPF in collaboration.[17,18] GRAPPA recommendations are organized to cover the domains of PsA, including peripheral arthritis, axial disease, enthesitis, dactylitis, skin psoriasis, and nail psoriasis, as well as inflammatory bowel disease (IBD) and uveitis. Fig 4 highlights classes of medications commonly used to treat PsA and their efficacy on domains of psoriatic disease with relevant comorbidities also addressed. The information presented is up-to-date at the time of this publication and may serve as a resource for practicing dermatologists when selecting an optimal treatment plan.

Treatment guidelines are challenged by the constant emergence of new data and therapeutics. Furthermore, while evidence-based guidelines follow rigorous methodology, they are often insufficiently prescriptive to support practical clinical use, especially in more complex real-world contexts. Another limitation includes the limited number of head-to-head trials that directly compare the efficacy of PsA treatments, particularly within individual domains of PsA.

TREATMENT

- While methotrexate (MTX) was historically considered first-line therapy, data to support its use in PsA are mixed.
- Tumor necrosis factor inhibitors (TNFis) effectively treat all domains of psoriatic disease.
- Agents targeting interleukin (IL)-17, IL 12/23, and IL23 demonstrate efficacy in treating PsA, with generally higher skin efficacy and less frequent dosing than TNFis.
- Janus Kinase (JAK) inhibitors and phosphodiesterase 4 inhibitors demonstrate efficacy in PsA.

Complete data on approval year, dose approved for PsA, formulation, pivotal trial, ACR20, 50 and 70, and placebo data for each currently approved medication are available in Tables I and II. Notably, placebo rates in PsA trials have increased over the past several decades. Several factors may contribute to this, including background medication use and/or adherence in the context of a trial, populations enrolled, and complexities of composite outcome measures.

We review the evidence for MTX, the most commonly used classical disease-modifying antirheumatic drug (DMARD), as well as biologics, and targeted synthetic oral small molecules. We note that other DMARDs, such as hydroxychloroquine, leflunomide, and sulfasalazine are used to treat PsA.

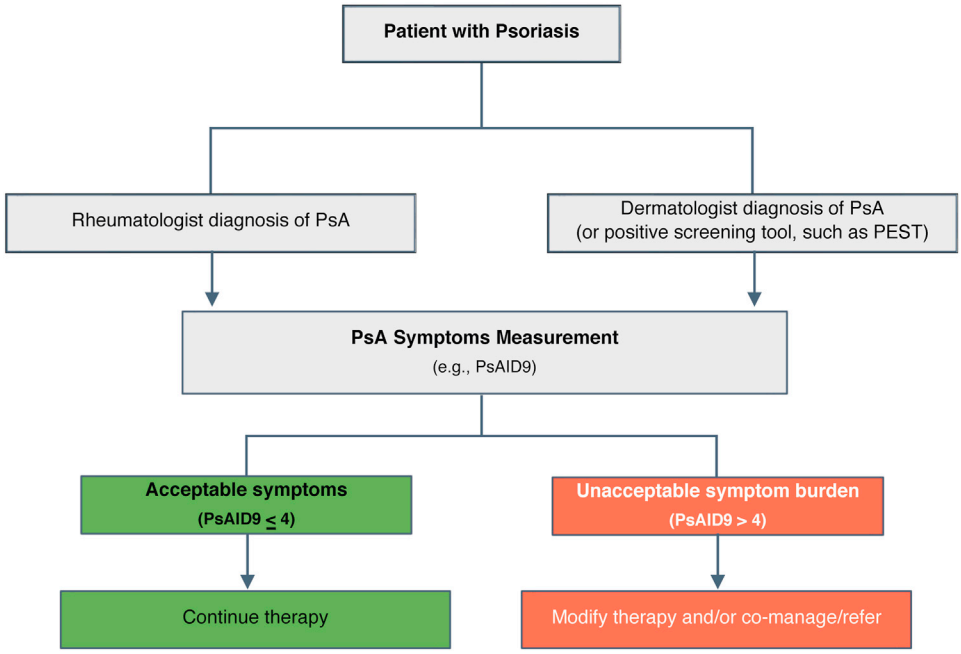

Fig 3. Psoriatic arthritis. Framework for treatment decisions and management.[13] Modified from Perez-Chada et al.[13] with author permission.

Given their lack of efficacy in psoriasis, we will not focus on these medications herein, but point the readers to society guidelines that outline where these may be applicable.

MTX

Although MTX is considered a first-line therapy of PsA in some treatment algorithms,[20] evidence to support MTX in PsA has been mixed and largely observational, although several interventional studies have evaluated its efficacy.[21,22] The MIPA study, a placebo-controlled trial of MTX found no advantage of MTX over placebo.[23] However, the TICOPA study in which MTX was used without a placebo suggested its benefit.[12] The open-label RESPOND trial which compared infliximab plus MTX to MTX monotherapy found an ACR20 response in the MTX arm of 66.7%, although combination therapy was significantly more effective.[24] Furthermore, in the SEAM-PsA study, at 48 weeks there was a trend toward more radiographic progression of disease among those treated with MTX compared to etanercept; however, there was no placebo control.[25] Other studies have shown lack of efficacy of MTX toward inhibition of radiographic progression.[26] Given the mixed data on MTX monotherapy, the 2018 ACR/NPF PsA treatment guidelines recommend TNFi over MTX in patients with active, treatment-naïve PsA.[17]

MTX may be utilized to treat peripheral arthritis, enthesitis, and dactylitis.[18] An important limitation of MTX is its lack of efficacy in treating axial spondyloarthritis.[27] Of note, a recent trial evaluated the efficacy and tolerability of MTX and leflunomide; the study found greater efficacy in treating PsA with combination than monotherapy, although with higher rates of adverse events.[19] MTX also has a poorer safety profile when compared to many newer targeted agents, particularly among psoriatic patients with fatty liver disease.[28,29] Moreover, its less favorable tolerability profile contributes to reduced adherence and worse outcomes.[21,30]

TNFis

Food and Drug Administration (FDA) approved TNFis for the treatment of PsA include etanercept, infliximab, adalimumab, certolizumab, and golimumab. TNFis have good coverage against all domains of PsA disease and inhibit radiographic progression of disease.[31] All TNFi are approved for ankylosing spondylitis (AS), from which efficacy toward axial PsA has been extrapolated. As such, TNFi have been largely considered a gold-standard and first-line treatment for PsA among rheumatologists.

In the seminal trial of etanercept, 59% of patients achieved ACR20 at week 12.[32] Etanercept was shown to improve enthesitis and dactylitis.[33]

Mechanism of Action	Skin and Nail Disease	Peripheral Arthritis	Axial Disease[1]	Dactylitis	Enthesitis	Inflammatory Bowel Disease	Uveitis
Conventional Synthetic DMARDs							
MTX	✓✓ (skin) ✓ (nails)	✓✓	✕✕	✓	✓	✓	✓
NSAIDs/Glucocorticoids							
NSAIDs		✓	✓✓	✓	✓	✕✕ *	
Intra-articular glucocorticoids		✓	✓	✓			
Oral glucocorticoids		✓					
Targeted Synthetic DMARDs							
Apremilast	✓✓	✓✓	✕	✓✓	✓✓	?	
JAKi [2,3]	✓✓ (skin) [4] ✓ (nails) [4]	✓✓ [2]	✓✓	✓✓	✓✓	✓ *	
TYK2i [5]	✓✓ *	? *		? *	? *		
Biologic DMARDs							
TNFi [2]	✓✓	✓✓ [2]	✓✓	✓✓	✓✓	✓✓ (ETN=?)	✓✓ (ETN=✕)
IL-12/23i	✓✓	✓✓	?	✓✓	✓✓	✓✓	?
IL-23i	✓✓	✓✓	?	✓✓	✓✓	✓✓	
IL-17i [2]	✓✓	✓✓ [2]	✓✓ [6]	✓✓	✓✓	✕✕	?
CTLA4-Ig		✓		✓	✓		

Fig 4. Psoriatic arthritis. Treatment of Psoriatic Arthritis by Domains of Disease and Comorbidities. Courtesy of Joseph F. Merola, MD, MMSc. ✓✓, Strong recommendation for; ✓, conditional recommendation for; ✕ ✕; strong recommendation against; ✕, conditional recommendation against; *?*, insufficient or conflicting evidence; *CTLA4-Ig*, cytotoxic T-lymphocyte–associated antigen 4 immunoglobulin infusion protein; *DMARD*, disease-modifying antirheumatic drug; *ETN*, etanercept; *IL-12/23i*, interleukin 12/23 inhibitors; *IL23i*, interleukin 23 inhibitors; *IL17i*, interleukin 17 inhibitors; *JAKi*, Janus kinase inhibitor; *MTX*, methotrexate; *NSAID*, non-steroidal anti-inflammatory drug; *TNFi*, tumor necrosis factor inhibitor; *TYK2*, tyrosine kinase inhibitor; . The strength of recommendation was adapted from the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) treatment guidelines[19]; any ratings that differ from GRAPPA guidelines are indicated with (*) and reflect an update by the authors based upon recent literature published since GRAPPA guidelines were released. [1]Based on data from ankylosing spondylitis trials, used as a surrogate for axial psoriatic arthritis (PsA). [2]More than 1 in class has inhibition of radiographic progression in the label. [3]Indication reserved for adults with active PsA who have had an inadequate response or intolerance to 1 or more TNFi. [4]JAKi have not been approved by the Food and Drug Administration (FDA) for treating psoriasis. [5]Approved for psoriasis skin and nail disease. Efficacy in peripheral arthritis, dactylitis, and enthesitis was demonstrated in phase 2 studies, phase 3 studies are pending. [6]Dedicated axial PsA study (MAXIMISE).

In the seminal trial of infliximab, 65% of patients achieved ACR20 at 16 weeks.[34] Infliximab is administered intravenously and is weight-based. A concern with the use of infliximab is the production of neutralizing antidrug antibodies. Concurrent administration of low-dose MTX may help sustain response and increase serum levels of infliximab.[24,35] In the authors' opinion, the weight-based and off-label

Table I. Characteristics of biologic therapies approved for the treatment of psoriatic arthritis

Biologic therapy	FDA approval year	FDA approved dose	Pivotal phase III trial	Primary endpoint week	Primary endpoint efficacy (ACR20) for FDA approved dose	Placebo rate	ACR 50 (Placebo)	ACR 70 (Placebo)
TNF inhibitors								
Etanercept	2002	50 mg weekly (SC)	12-wk study	12	59%	15%	38% (5%)	10% (1%)
Infliximab	2005	5 mg/kg at 0, 2 and 6 wk, then every 8 wk (IV)	IMPACT	16	65%	10%	46% (0%)	29% (0%)
Adalimumab	2005	40 mg every other week (SC)	ADEPT	12	58%	14%	36% (4%)	20% (1%)
Certolizumab pegol	2013	400 mg at weeks 0, 2 and 4, then 200 mg every other week	RAPID-PsA	12	58%	24%	36% (11%)	25% (3%)
Golimumab	2009	50 mg every 4 wk (SC); 2 mg/kg at weeks 0 and 4, then every 8 wk (IV)	GO-REVEAL; GO-VIBRANT	14	51% (SC); 75% (IV)	9% (SC); 14 (IV)	29% (1%) (SC); 54% (6%) (IV)	10% (1%) (SC); 33% (3%) (IV)
IL-12/23 inhibitor								
Ustekinumab	2013	45 mg at weeks 0 and 4, then 45 mg every 12 wk (SC)	PSUMMIT-1	24	42% (45 mg); 50% (90 mg)	23%	25% (9%)	12% (2%)
			PSUMMIT-2*	24	44% (45 mg); 44% (90 mg)	20%	20% (7%)	8% (3%)
IL-23 inhibitors								
Guselkumab	2020	100 mg at weeks 0 and 4, then 100 mg every 8 wk (SC)	DISCOVER-1*	24	52%	22%	30% (9%)	12% (6%)
			DISCOVER-2	24	64%	33%	31% (14%)	19% (4%)
Risankizumab	2022	150 mg at weeks 0 and 4, then 150 mg every 12 wk (SC)	KEEPsAKE-1	24	57%	33%	33% (11%)	15% (5%)
			KEEPsAKE-2*	24	51%	27%	26% (9%)	12% (6%)

IL-17 inhibitors								
Secukinumab†	2016	With a loading dose: 150 mg weekly at weeks 0, 1, 2, 3 and 4, then 150 mg every 4 wk (SC) Without a loading dose: 150 mg every 4 wk (SC)	FUTURE-1*	24	50%	17%	35% (7%)	21% (1%)
Ixekizumab†	2017	160 mg at week 0, then 80 mg every 4 wk (SC)	SPIRIT-P1	24	58%	30%	40% (15%)	23% (6%)
			SPIRIT-P2*	24	53%	19%	35% (5%)	22% (0%)
Costimulatory blockade								
Abatacept	2017	125 mg weekly (SC) 500 mg (<60 kg), 750 mg (60-100 kg), 1000 mg (>100 kg) at weeks 0, 2 and 4, then every 4 wk (IV)	ASTRAEA	24	39%	22%	19% (12%)	10% (7%)

Listed dosing is for psoriatic arthritis. Dosages may differ for psoriasis and other indications such as inflammatory bowel disease.
ACR, American College of Rheumatology; *FDA*, Food and Drug Administration; *IL*, interleukin.
*Trials that included patients with inadequate response or intolerance to bDMARDs.
†Per label, the dosing regimen for adult patients with plaque psoriasis is recommended for patients with psoriatic arthritis with concomitant moderate-to-severe plaque psoriasis. However, the authors recommend considering psoriasis dosing in all psoriatic arthritis patients where available.

Table II. Characteristics of targeted small molecules approved for the treatment of psoriatic arthritis

Small molecules targeted therapies	FDA approval year	FDA approved dose	Pivotal phase III trial	Primary endpoint week	Primary edpoint efficacy (ACR20) for FDA approved dose	Placebo rate	ACR 50 (Placebo)	ACR 70 (Placebo)
PDE4 inhibitor								
Apremilast	2014	Dosage titration from days 1-5, then 30 mg twice a day from day 6 on	PALACE-1	16	40%	19%	16% (6%)	4% (1%)
JAK inhibitors								
Tofacitinib	2017	Immediate release: 5 mg twice a day (PO)*	OPAL Broaden	12	50%	33%	28% (10%)	17% (5%)
		Extended release: 11 mg daily	OPAL Beyond†	12	50%	24%	30% (15%)	17% (10%)
Upadacitinib	2021	Extended release: 15 mg daily*	SELECT-PsA 1	12	71%	36%	38% (13%)	16% (2%)
			SELECT-PsA 2†	12	57%	24%	32% (5%)	9% (1%)

JAK, Janus kinase; *PDE4*, phosphodiesterase-4.
*Tofacitinib is approved for those with an inadequate response or intolerance to methotrexate or other disease-modifying antirheumatic drugs, and upadacitinib is for those with an inadequate response or intolerance to 1 or more Tumor necrosis factor inhibitor.
†Trials that included patients with inadequate response or intolerance to bDMARDs.

dose flexibility of infliximab makes it of particular use in higher weight patients, and more severe and resistant/difficult to treat disease.

The efficacy of adalimumab was established in the ADEPT trial; 58% of patients achieved ACR20 at 12 weeks.[36,37] The effects of adalimumab may decrease over time due to antidrug antibodies, which can be ameliorated by concurrent use of MTX.[38,39] Adalimumab is the only TNFi approved for the treatment of noninfectious uveitis, a potential comorbidity.

The efficacy of certolizumab was demonstrated in the RAPID-PsA trial. At 12 weeks, 59% of patients achieved ACR20; sustained benefits across all domains of PsA were also observed.[40] Benefit exists with respect to certolizumab and pregnancy; it does not cross the placenta and is not excreted in breast milk, making it particularly suited to pregnancy and lactation, if clinically indicated, in discussion with the patient's obstetrics providers.[41]

In the pivotal trial of subcutaneous golimumab, 45% of patients achieved ACR20 at 14 weeks.[42] Subsequent studies showed benefit on enthesitis, dactylitis, and radiographic progression of disease.[43] A recent study evaluating its intravenous formulation revealed ACR20 achievement of 75% at 14 weeks.[44] Of note, golimumab is not FDA approved for psoriasis.

Patients should be screened for latent tuberculosis and hepatitis B/C prior to initiation of TNFis. Infliximab should likely be avoided in patients with New York Heart Association heart failure class III/VI. TNFi therapy should be avoided in patients with a personal history of demyelinating disease. These medications should be used with caution in patients with certain malignancies or severe, chronic and/or recurrent infections.[20] TNFi are approved for IBD and 1 for uveitis, which may factor into decisions for patients with these comorbidities.

IL 12/23 inhibitor

Ustekinumab is a fully human monoclonal antibody that binds to the common p40 subunit of IL-12 and IL-23. Ustekinumab was assessed in the PSUMMIT-1 and 2 trials, with PSUMMIT-2 including approximately 60% previously treated with TNFi. In PSUMMIT-1, ACR20 was achieved in 42% of patients receiving 45 mg and 50% of patients receiving 90 mg. Patients with previous TNFi exposure achieved ACR20 of 36.7% on 45 mg, 34.5% on 90 mg, and 14.5% on placebo.[45,46]

Ustekinumab has not demonstrated efficacy in treating axial disease[47] or inhibiting the radiographic progression of disease.[48] Ustekinumab is FDA-

approved in IBD and thus a consideration for patients with this comorbidity.

IL23 inhibitors

Guselkumab and risankizumab are p19 inhibitors of IL23 that are FDA approved for PsA. Tildrakizumab, which is approved for plaque psoriasis, has shown promising phase IIb data with ACR20 between 71% and 80% (50.6% response in placebo).[49] Phase III clinical trials are ongoing.

In the DISCOVER-1 and 2 trials, 52% to 64% of patients who received guselkumab 100 mg every 8 weeks after 2 starter doses achieved ACR20, with similar responses in those previously treated with TNFi. Benefit was also seen in enthesitis and dactylitis.[50,51] Unlike ustekinumab, post-hoc analysis of the 2 DISCOVER trials demonstrated potential benefit in axial disease symptoms among a subset with spondyloarthritis features.[52] At the US-approved 8 weeks dose, guselkumab did not meet its radiographic inhibition endpoint, however every 4 weeks dosing in the DISCOVER-2 trial yielded significantly less radiographic progression.[53] Ongoing trials are evaluating the effect of guselkumab on axial disease and radiographic progression inhibition.

Risankizumab was evaluated in the KEEPSAKE 1 and 2 trials. At 24 weeks, 51.3% to 57.3% of patients who received risankizumab achieved ACR20. Similar responses were observed in those previously treated with biologics. Resolution of enthesitis and dactylitis were more likely to be achieved in the treatment group.[54,55] Previous trials of risankizumab in the treatment of AS were disappointing.[56] Furthermore, risankizumab did not achieve its specified endpoint regarding inhibiting radiographic progression. Risankizumab obtained FDA approval for the treatment of Crohn's disease, making it an option for patients with this comorbidity.

ANTI-IL 17 AGENTS

Secukinumab and ixekizumab are approved for the treatment of psoriasis and PsA. Brodalumab is approved for psoriasis but not PsA in the US (PsA approval in Japan). Bimekizumab, an inhibitor targeting IL17A/F, has been granted FDA approval for treating psoriasis, with pending approval for its use in PsA in the US.[57,58] Sonelokimab, an IL17A/F nanobody, recently demonstrated efficacy in a phase II study for PsA; phase III is ongoing.

Secukinumab's efficacy was evaluated in 2 phase III trials. In these studies, 30% to 35% of patients had previously been on TNFi. ACR20 responses were achieved in approximately 50% of patients receiving 150 mg and 54% receiving 300 mg. Secondary endpoints, including improvement in enthesitis, dactylitis, and inhibition of radiographic progression were greater in the treatment arms.[59-61] Secukinumab's efficacy on axial disease was evaluated in the MAXIMISE study, demonstrating significant improvement in axial disease.[62] The intravenous formulation of secukinumab was recently approved for PsA.

Ixekizumab's efficacy was evaluated in SPIRIT P1 and P2. SPIRIT P2 enrolled patients with previous inadequate response to TNFi. In these trials, ACR20 was achieved in 53% to 58% of patients receiving ixekizumab every 4 weeks. Furthermore, ixekizumab effectively inhibited radiographic progression of disease.[63,64]

The efficacy of bimekizumab for the treatment of PsA was demonstrated in the BE-OPTIMAL and BE-COMPLETE trials. In BE-OPTIMAL,[59] 44%, 10%, and 46% of patients receiving bimekizumab, placebo, and adalimumab, respectively, achieved ACR50 at week 16. Bimekizumab also led to higher improvements in skin and radiographic efficacy outcomes at week 16 compared with placebo. In BE-COMPLETE,[60] which included patients with PsA with a history of inadequate response or intolerance to TNFis, bimekizumab was also more effective than placebo in treating both joints and skin. The BE-MOBILE trial further showed improvements in efficacy outcomes among patients with axial spondyloarthritis.[65]

We caution against using anti-IL-17 agents in patients with active IBD given the potential risk of IBD exacerbation.[66,67] Furthermore, we highlight the association of candida infections (ie, thrush) in those treated with IL-17 inhibitors.[68]

Secukinumab and ixekizumab have been evaluated head-to-head with TNFi, demonstrating efficacy in joint endpoints comparable to TNFi, although with superior efficacy in skin and nails.[69,70]

Phosphodiesterase 4 inhibitors

Apremilast was evaluated in the PALACE trials. At week 16, ACR20 was achieved in 32.1% to 40.7% of patients receiving 30 mg twice daily and 18.3% to 19% receiving placebo. At 52 weeks, 52.6% to 63% of patients receiving 30 mg twice daily achieved this primary endpoint.[71-73] Apremilast 30mg twice daily was associated with improvement in enthesitis and dactylitis.[74] Evidence supporting apremilast's ability to prevent radiographic progression in PsA is

lacking, and it is not approved for treating axial disease.[71] Apremilast most recently demonstrated efficacy in the phenotypic subset of 'early oligoarticular psoriatic arthritis' in the FOREMOST trial.[75]

Apremilast may benefit patients with multiple comorbidities due to its favorable safety profile, lack of associated tuberculosis reactivation risk, and lack of laboratory monitoring requirements.[76] While effective as monotherapy, real-world (off-label) use as a combination therapy with other agents including biologics, has suggested apremilast is safe and effective.[77]

JAK inhibitors

Tofacitinib, a JAK 1 and 3 inhibitor, is approved for adult patients who have had intolerance or an inadequate response to DMARDs.[78] Tofacitinib was evaluated in OPAL Broaden, where patients had active PsA and an inadequate response to at least 1 csDMARD, and OPAL Beyond, where patients had active PsA and previous treatment with at least 1 TNFi. In OPAL Broaden, 50.5% treated with tofacitinib 5 mg twice daily achieved ACR20.[79] In OPAL Beyond, 49.9% treated with 5 mg twice daily achieved ACR20.[80] Dactylitis and enthesitis also improved. Tofacitinib is approved for the treatment of AS; trials in treating psoriatic spondyloarthritis are ongoing.[81]

The safety of tofacitinib was evaluated in OPAL Balance, a 48-month extension study. Serious adverse events occurred in 17% of participants, with 11% discontinuing medication.[82] In ORAL Surveillance, tofacitinib vs TNFi was evaluated in a population with rheumatoid arthritis enriched for cardiovascular risk. There was a higher risk of major adverse cardiac events and malignancy in the tofacitinib group compared to TNFi, as well as a higher risk of venous thromboembolism in the 10 mg twice daily group.[83] Tofacitinib is approved for the treatment of ulcerative colitis.[84]

Upadacitinib, a JAK1 inhibitor, is FDA-approved for the treatment of PsA at 15mg once daily dosing. Its efficacy was evaluated in the SELECT-PsA 1 and 2 trials. In SELECT-PsA 1, ACR20 was achieved in 70.6% of patients receiving 15 mg of upadacitinib.[85] SELECT-PsA 2 evaluated upadacitinib in patients who failed at least 1 biologic[86]; at week 12, 56.9% in the 15 mg group achieved ACR20. Participants treated with upadacitinib additionally saw improvement in axial disease and enthesitis.[87] Although not approved for psoriasis, at the 15 mg dose, PASI 75 data was similar to that seen with adalimumab in SELECT-PsA 1.[85] The rates of adverse events were similar with placebo and upadacitinib 15 mg at week 24.

Given safety risks from these surveillance studies, prescribers may yield caution with the use of JAK inhibitors in those with a history of significant coronary artery disease, active malignancy, and history of thrombosis.

Tyrosine kinase 2 inhibition

Deucravacitinib, an oral selective tyrosine kinase 2 inhibitor approved for psoriasis, is currently being studied in phase 3 for PsA. A phase 2 trial demonstrated a dose-response relationship with 53% of participants taking 6 mg daily and 63% of participants taking 12 mg daily achieving ACR20 at week 16. In contrast, only 32% of patients in the placebo group achieved ACR 20.[88]

Costimulatory blockade

Abatacept is a CTLA4-Ig, a selective T-cell costimulation modulator approved for treating PsA, although it is not approved for psoriasis. In the pivotal phase III trial, where 60% of patients had prior exposure to TNFi, only 27% achieved PASI50 while 39% achieved ACR20 at 24 weeks.[89] Less radiographic progression and improvement in dactylitis and enthesitis were observed. Abatacept has not shown benefit in patients with axial disease.[90]

CONCLUSION

Dermatologists play a key role as the frontline health care professionals for PsA screening, referral, and management. Appropriate psoriasis treatment requires knowledge of PsA presence. Choice of effective treatment is based the domain(s) of the disease involved, presence of comorbidities and patient preferences within a collaborative, shared decision-making framework.

Conflicts of interest

Drs Perez-Chada and Elman declare no conflicts of interest. Dr Armstrong has received honoraria as consultant for Almirall, Arcutis, ASLAN, Beiersdorf, EPI Health, Nimbus, Sun Pharma, speaker for Abbvie, Sanofi Genzyme; advisory board member for Incyte, Regeneron, and UCB; investigator for Abbvie, BMS, Demira, Dermavant, Eli Lilly, Galderma, Janssen, LEO Pharma, Modernizing Medicine, Novartis, Ortho Derm, Pfizer, Sanofi Genzyme, and UCB; and Data Safety and Monitoring for Board member for Boehringer Ingelheim and Parexel. Dr Gottlieb has received honoraria as an advisory board member and consultant for Amgen, AnaptypsBio, Avotres Therapeutics, Boehringer Ingelheim, Bristol-Myers Squibb, Dice Therapeutics, Eli

Lilly, Janssen, Novartis, Sanofi, UCB, and Xbiotech. She has also received research/educational grants from AnaptypsBio, Moonlake Immunotherapeutics AG, Novartis, Bristol-Myers Squibb, and UCB Pharma (all paid to Mount Sinai School of Medicine). Dr Merola is a consultant and/or investigator for Amgen, Astra-Zeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Abbvie, Dermavant, Eli Lilly, Incyte, Moonlake, Novartis, Janssen, UCB, Sanofi-Regeneron, Sun Pharma, Biogen, Pfizer and Leo Pharma; board positions of PPACMAN, GRAPPA, IDEOM, NPF.

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