

# Secukinumab in the treatment of psoriasis: patient selection and perspectives

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**Abstract:** Secukinumab is a human monoclonal antibody targeting IL-17A that has been approved for three indications: moderate-to-severe plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis. In Phase III clinical trials for each of these three indications, secukinumab has proven to be both highly efficacious and well-tolerated. However, several biologic medications are currently approved for the treatment of moderate-to-severe plaque psoriasis, and many demonstrate excellent efficacy and safety. Due to this wide selection, it is often unclear how to choose biologics for specific patients. Important considerations in biologic selection include clinical efficacy, safety, cost, convenience, onset of action, and management of comorbid disease. This article aims to outline the key considerations in patient selection for the treatment of plaque psoriasis with secukinumab.

**Keywords:** secukinumab, IL-17 inhibitor, IL-17A, biologics, psoriasis, patient selection

## Introduction

Psoriasis vulgaris is associated with significant comorbidity including depression,<sup>1-3</sup> increased risk of cardiovascular events,<sup>4,5</sup> diminished quality of life,<sup>6</sup> as well as overall increased mortality.<sup>7</sup> Furthermore, up to 40% of psoriasis patients have or will develop comorbid psoriatic arthritis in their lifetime.<sup>8</sup> Effective treatment of this chronic, immune-mediated systemic inflammatory disease is necessary to improve quality of life and possibly decrease the risk of comorbid disease in psoriasis patients.<sup>9-11</sup>

Biologic medications currently approved for the treatment of moderate-to-severe plaque psoriasis include TNF- $\alpha$  inhibitors (adalimumab, etanercept, infliximab), IL-17 pathway inhibitors (ixekizumab, brodalumab, secukinumab), IL-12/IL-23 inhibitors (ustekinumab), and IL-23 inhibitors (guselkumab, tildrakizumab). Each medication has its own unique efficacy and safety profile. Dermatologists are fortunate to now have so many options available in the therapeutic armamentarium for moderate-to-severe psoriasis patients, but it can be difficult to select specific biologics for individual patients. This article outlines key considerations in patient selection for the treatment of plaque psoriasis with secukinumab.

## Practical considerations

Secukinumab (Cosentyx<sup>®</sup>, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA) is a recombinant human monoclonal IgG1 antibody that specifically binds to IL-17A that has been approved for the treatment of adult patients with moderate-to-severe

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plaque psoriasis, active psoriatic arthritis, or active ankylosing spondylitis.<sup>12</sup>

The recommended dosing for secukinumab differs for psoriasis as compared to psoriatic arthritis and ankylosing spondylitis. Recommended dosing for plaque psoriasis patients is 300 mg administered subcutaneously at weeks 0, 1, 2, 3, and 4 (loading dose), and every 4 weeks thereafter (maintenance).<sup>12</sup> However, a lower dosage of 150 mg may also be used to improve tolerability. Patients with psoriatic arthritis or ankylosing spondylitis may use secukinumab with or without a loading dose. With a loading dose, 150 mg secukinumab is administered at weeks 0, 1, 2, 3, and 4 (loading dose), and every 4 weeks thereafter (maintenance). Without a loading dose, 150 mg secukinumab is administered every 4 weeks. If patients continue to have active psoriatic arthritis, they may benefit from increasing the dose to 300 mg. Patients with both psoriatic arthritis and moderate-to-severe psoriasis are advised to use the dosing recommendations for plaque psoriasis.

Secukinumab is supplied as single-use 1 mL autoinjector pens and 1 mL prefilled syringes with a 27-gauge fixed ½-inch needle, each containing a 150 mg dose of the medication. Secukinumab can also be reconstituted from a lyophilized powder by a health care professional, with each vial containing 150 mg of the medication.

Secukinumab is contraindicated in patients with a hypersensitivity reaction to secukinumab or to any of its excipients. It is recommended to evaluate patients for tuberculosis

infection prior to initiating treatment with secukinumab. Secukinumab should be avoided in patients with preexisting inflammatory bowel disease (IBD). Secukinumab may increase the risk for infection, and live vaccines should not be given to patients treated with secukinumab.

## Efficacy in plaque psoriasis

Two pivotal randomized, controlled, double-blind Phase III trials evaluated the efficacy of secukinumab in patients with moderate-to-severe plaque psoriasis: ERASURE and FIXTURE.<sup>13</sup> In all Phase III clinical trials for secukinumab for moderate-to-severe plaque psoriasis, patients in the treatment arm were dosed with 300 mg secukinumab administered once weekly for 5 weeks, then every 4 weeks thereafter (Table 1).

Secukinumab was compared with placebo in ERASURE and placebo or etanercept in FIXTURE.<sup>13</sup> The coprimary efficacy endpoints in both studies were the proportion of patients treated with secukinumab who achieved  $\geq 75\%$  reduction in Psoriasis Area and Severity Index (PASI 75) and Investigator's Global Assessment (IGA) 0/1 at week 12 as compared to placebo. Both trials achieved these coprimary endpoints, with a significantly greater proportion of patients at week 12 achieving PASI 75 on secukinumab (ERASURE: 81.6%, FIXTURE: 77.1%) compared to placebo (ERASURE: 4.5%, FIXTURE: 4.9%) or etanercept (FIXTURE: 44.0%), and a significantly greater proportion of patients achieving IGA 0/1 on secukinumab (ERASURE: 65.3%, FIXTURE: 62.5%) compared to placebo (ERASURE: 2.4%, FIXTURE:

**Table 1** Summary of key Phase III clinical trial results of secukinumab for the treatment of plaque psoriasis at week 12

Trial	Year	n	Treatment (n)	IGA 0/1 <sup>a</sup>	PASI 75	PASI 90	PASI 100
ERASURE <sup>13</sup>	2014	738	Secukinumab, 300 mg (245)	65.3%	81.6%	59.2%	28.6%
			Secukinumab, 150 mg (245)	51.2%	71.6%	39.1%	12.8%
			Placebo (248)	2.4%	4.5%	1.2%	0.8%
FIXTURE <sup>13</sup>	2014	1,306	Secukinumab, 300 mg (327)	62.5%	77.1%	54.2%	24.1%
			Secukinumab, 150 mg (327)	51.1%	67.0%	41.9%	14.4%
			Etanercept (326)	27.2%	4.0%	20.7%	4.3%
			Placebo (326)	2.8%	4.9%	1.5%	0.0%
CLEAR <sup>14</sup>	2015	676	Secukinumab, 300 mg (337)	80.8%	91.0%	72.8%	38.9%
			Ustekinumab (339)	65.1%	79.1%	53.4%	25.7%
SCULPTURE <sup>16</sup>	2015	966	Secukinumab, 300 mg (484)	—	90.1%	—	—
			Secukinumab, 150 mg (482)	—	84.4%	—	—
FEATURE <sup>18</sup>	2014	177	Secukinumab, 300 mg (59)	69.0%	75.9%	60.3%	43.1%
			Secukinumab, 150 mg (59)	52.5%	69.5%	45.8%	8.5%
			Placebo (59)	0.0%	0.0%	0.0%	0.0%
JUNCTURE <sup>19</sup>	2014	182	Secukinumab, 300 mg (60)	73.3%	86.7%	55.0%	26.7%
			Secukinumab, 150 mg (61)	53.3%	71.7%	40.0%	16.7%
			Placebo (61)	0.0%	3.3%	0.0%	0.0%

**Notes:** <sup>a</sup>With  $\geq 2$ -grade improvement from baseline; PASI 100, 100% improvement in PASI from baseline; PASI 75,  $\geq 75\%$  improvement in PASI from baseline; PASI 90,  $\geq 90\%$  improvement in PASI from baseline.

**Abbreviations:** IGA, Investigator's Global Assessment; PASI, Psoriasis Area and Severity Index.

2.8%) or etanercept (27.2%). Additionally, secukinumab demonstrated significantly improved PASI 90 (ERASURE: 59.2%, FIXTURE: 20.7%) and PASI 100 (ERASURE: 28.6%, FIXTURE: 24.1%) responses at week 12 as compared to placebo (PASI 90: 1.2%, 1.5%; PASI 100: 1.2%, 0.0%) and etanercept (PASI 90: 20.7%; PASI 100: 4.3%).

In the randomized, double-blind, controlled Phase III trial CLEAR, the clinical efficacy of secukinumab for psoriasis was evaluated head-to-head against ustekinumab.<sup>14</sup> The primary endpoint for this study was the proportion of patients treated with secukinumab achieving PASI 90 at week 16 as compared to ustekinumab. This study met the primary endpoint, with secukinumab demonstrating a superior PASI 90 response at week 16 compared to ustekinumab (79.0% vs 57.6%). Patients' clinical responses to secukinumab at 12 weeks were notably higher than the clinical responses observed at the same time point in ERASURE and FIXTURE, with 91.0% achieving PASI 75, 72.8% achieving PASI 90, and 38.9% achieving PASI 100 (Table 1). The clinical response to secukinumab was sustained at week 52, with superior efficacy as compared to ustekinumab noted in PASI 75 (92.5% vs 79.5%), PASI 90 (76.2% vs 60.6%), and PASI 100 (45.9% vs 36.7%).<sup>15</sup>

Another randomized, double-blind controlled Phase III trial was conducted to assess the optimal dosing for secukinumab in plaque psoriasis. In this study, SCULPTURE, secukinumab retreatment-as-needed was compared to a fixed-interval regimen.<sup>16</sup> Patients achieving PASI 75 response at week 12 were randomized 1:1 to fixed-interval dosing of secukinumab every 4 weeks or retreatment-as-needed every 4 weeks upon loss of PASI 75 response plus loss of more than 20% maximal PASI improvement. The primary endpoint for this study was non-inferiority of retreatment-as-needed compared to fixed-interval dosing for maintaining PASI 75, but this primary endpoint was not achieved, as significantly more patients on fixed-interval maintained PASI 75 compared to retreatment-as-needed (78.2% vs 67.7%). On 5-year follow-up of the SCULPTURE study, patients demonstrated sustained responses to secukinumab, with 79.2% achieving PASI 75, 59.5% achieving PASI 90, and 37.5% achieving PASI 100.<sup>17</sup>

The clinical efficacy of secukinumab for psoriasis was evaluated with secondary endpoints assessing the usability and tolerability of a prefilled syringe in FEATURE, a randomized, double-blind, placebo-controlled Phase III trial.<sup>18</sup> The coprimary endpoints for this study were the proportions of patients achieving PASI 75 and IGA 0/1 at week 12 as compared to placebo. These coprimary endpoints were met, with significantly more patients treated with secukinumab

achieving PASI 75 (75.9% vs 0%) and IGA 0/1 (69.0% vs 0%) response as compared to placebo. Additionally, 60.3% and 43.1% of patients treated with secukinumab achieved PASI 90 and PASI 100 at 12 weeks, respectively.

The clinical efficacy of secukinumab for psoriasis was evaluated with secondary endpoints assessing the usability and tolerability of an auto-injector pen in JUNCTURE, another randomized, double-blind, placebo-controlled Phase III trial.<sup>19</sup> The coprimary endpoints for this study were the proportions of patients achieving PASI 75 and IGA 0/1 at week 12 as compared to placebo. These coprimary endpoints were achieved, with significantly more patients treated with secukinumab achieving PASI 75 (86.7% vs 3.3%) and IGA 0/1 (73.3% vs 0%). Additionally, 55.0% and 26.7% of patients achieved PASI 90 and PASI 100 at 12 weeks, respectively. Patients demonstrated sustained responses to secukinumab at week 52, with 81.4% achieving PASI 75, 64.1% achieving PASI 90, and 38.8% achieving PASI 100.<sup>19</sup>

In its Phase III trials, secukinumab has demonstrated efficacy for plaque psoriasis similar to other IL-17 inhibitors (Table 2). Notably, it has shown superiority over both etanercept and ustekinumab in head-to-head comparisons. Secukinumab offers a highly efficacious treatment option for patients with moderate-to-severe psoriasis, and may be a preferred treatment option for patients who have disease recalcitrant to treatment with TNF- $\alpha$  inhibitors or IL-12/23 inhibitors.

## Efficacy in difficult-to-treat areas of psoriasis

Secukinumab has also demonstrated efficacy for psoriasis located in difficult-to-treat areas, including the scalp, palms and soles, and the nails.<sup>20,21</sup> In a randomized, double-blind, placebo-controlled Phase III trial of patients with scalp psoriasis, treatment with 300 mg secukinumab for 12 weeks improved scalp disease severity as compared to placebo with respect to  $\geq 90\%$  reduction in Psoriasis Scalp Severity Index (52.9% vs 2.0%) and scalp only IGA 0/1 (56.9% vs 5.9%).<sup>22</sup> In the randomized, double-blind, placebo-controlled GESTURE study of patients with non-pustular palmoplantar psoriasis, treatment with 300 mg secukinumab for 16 weeks resulted in significant improvements in palmoplantar psoriasis disease severity, as measured by Palmoplantar Investigator's Global Assessment 0/1 (33.2% vs 1.5%).<sup>23</sup> In the randomized, double-blind, placebo-controlled Phase III trial of patients with nail psoriasis, TRANSFIGURE, treatment with 300 mg secukinumab for 16 weeks significantly decreased Nail Psoriasis Severity Index as compared to

**Table 2** Clinical efficacy of biologic treatments for plaque psoriasis in pivotal Phase III trials

Drug/Trial	Dose	Frequency	Contraindications	PASI 75 <sup>a</sup>	PASI 90 <sup>a</sup>	PASI 100 <sup>a</sup>
<b>IL-23 inhibitors</b>						
Ustekinumab	45 mg	12 weeks	None			
PHOENIX I				67%	42%	13%
PHOENIX 2				67%	42%	18%
ACCEPT				68%	36%	16%
Guselkumab	100 mg	8 weeks	None			
VOYAGE I				91%	73%	37%
VOYAGE II				86%	70%	34%
Tildrakizumab	100 mg	12 weeks	None			
RESURFACE I				64%	35%	14%
RESURFACE 2				61%	39%	12%
Risankizumab <sup>b</sup>	150 mg	12 weeks	None			
ultIMMa-1				–	75%	36%
ultIMMa-2				–	75%	51%
IMMvent				–	72%	40%
IMMhance				89%	73%	47%
<b>IL-17 inhibitors</b>						
Brodalumab	210 mg	2 weeks	Crohn's disease			
AMAGINE-1				83%	70%	42%
AMAGINE-2				86%	–	44%
AMAGINE-3				85%	–	37%
Secukinumab	300 mg	4 weeks	Hypersensitivity to drug			
ERASURE				82%	59%	29%
FIXTURE				77%	54%	24%
Ixekizumab	80 mg	4 weeks	Hypersensitivity to drug			
UNCOVER-1				83%	65%	34%
UNCOVER-2				78%	60%	31%
UNCOVER-3				84%	65%	35%

**Notes:** Adapted from Yang et al (2018).<sup>46</sup> <sup>a</sup>Measured at 12 weeks, except guselkumab and risankizumab which were measured at 16 weeks. <sup>b</sup>Not currently approved for the treatment of plaque psoriasis. PASI 100,  $\geq 100\%$  improvement in PASI from baseline; PASI 75,  $\geq 75\%$  improvement in PASI from baseline; PASI 90,  $\geq 90\%$  improvement in PASI from baseline.

**Abbreviation:** PASI, Psoriasis Area and Severity Index.

placebo (–45.4% vs –11.2%).<sup>24</sup> Additionally, in a single-arm, open-label Phase III trial of patients with generalized pustular psoriasis, treatment with 150 mg secukinumab with up-titration to 300 mg as needed, resulted in treatment success in 83.3% of patients as measured by Clinical Global Impression.<sup>25</sup> Secukinumab may benefit patients with isolated scalp, palmoplantar, or nail psoriasis.

## Efficacy in psoriatic arthritis

Two pivotal randomized, double-blind, placebo-controlled Phase III trials evaluated the efficacy of 150 mg secukinumab in patients with active psoriatic arthritis, FUTURE-1 and FUTURE-2.<sup>26,27</sup> The primary endpoint for both studies was the proportion of patients achieving  $\geq 20\%$  improvement in American College of Rheumatology score 20 (ACR20) at week 24 as compared to placebo. Both trials achieved this primary endpoint, with a significantly greater proportion of patients at week 24 achieving ACR20 compared to placebo (FUTURE-1: 50.0% vs 17.3%, FUTURE-2: 51.0%

vs 15.3%) (Table 3). Patients also achieved better ACR50 response (FUTURE-1: 34.7% vs 7.4%, FUTURE-2: 35.0% vs 18.2%) and slight reductions in joint structural damage as measured by Sharp score, as compared to placebo. These improvements were sustained through 52 weeks, with 59.9% of patients treated with secukinumab reporting ACR20 response.<sup>28</sup> In the FUTURE-1 cohort, 84.3% of patients demonstrated no radiographic progression of joint damage at 2 years.<sup>29</sup>

The clinical efficacy of secukinumab for psoriatic arthritis was evaluated with secondary endpoints assessing the usability and tolerability of an auto-injector pen in FUTURE-3, a randomized, double-blind, placebo-controlled Phase III trial.<sup>30</sup> The primary endpoint for this study was the proportion of patients achieving ACR20 at week 24 as compared to placebo. This primary endpoint was achieved, with significantly more patients treated with 150 mg secukinumab achieving ACR20 (42.0% vs 16.1%). Additionally, 18.8% of patients achieved ACR50 at 24 weeks.

**Table 3** Summary of key Phase III clinical trial results of secukinumab for the treatment of psoriatic arthritis

Trial	Year	n	Treatment (n)	ACR20	ACR50	Change in HAQ-DI	Change in DAS-CRP	Change in SF-36 PCS
FUTURE-1 <sup>26</sup>	2015	606	Secukinumab, 150 mg (202)	50.0%	34.7%	−0.40	−1.62	5.91
			Secukinumab, 75 mg (202)	50.5%	30.7%	−0.41	−1.67	5.41
			Placebo (202)	17.3%	7.4%	−0.17	−0.77	1.82
FUTURE-2 <sup>27</sup>	2015	397	Secukinumab, 300 mg (100)	54.0%	35.0%	−0.56	−1.61	7.25
			Secukinumab, 150 mg (100)	51.0%	35.0%	−0.48	−1.58	6.39
			Secukinumab, 75 mg (99)	29.3%	18.2%	−0.32	−1.12	4.38
FUTURE-3 <sup>30</sup>	2018	416	Placebo (98)	15.3%	7.1%	−0.31	−0.96	1.95
			Secukinumab, 300 mg (139)	48.2%	34.5%	−0.38	−1.56	6.46
			Secukinumab, 150 mg (138)	42.0%	18.8%	−0.27	−1.24	3.42
FUTURE-5 <sup>31</sup>	2018	996	Placebo (137)	16.1%	8.8%	−0.17	−0.64	2.94
			Secukinumab, 300 mg (222)	62.6%	39.6%	−0.55	−1.49	–
			Secukinumab, 150 mg with loading dose (220)	55.5%	35.9%	−0.44	−1.29	–
			Secukinumab 150 mg without loading dose (222)	59.5%	32.0%	−0.45	−1.29	–
			Placebo (332)	27.4%	8.1%	−0.21	−0.63	–

**Notes:** Endpoints for all trials were measured at week 24, except for FUTURE-5 which were measured at week 16. ACR20, ≥20% improvement in ACR from baseline; ACR50, ≥50% improvement in ACR from baseline.

**Abbreviations:** ACR, American College of Rheumatology score; DAS-CRP, 28-joint Disease Activity Score on the basis of levels of C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; SF-36 PCS, Short Form 36-Item Physical Component Summary Score of the Medical Outcomes Survey.

The efficacy of secukinumab for treating the clinical signs and symptoms of psoriatic arthritis, as well as radiographic progression, was evaluated in the randomized, double-blind, placebo-controlled Phase III trial FUTURE-5.<sup>31</sup> The primary endpoint for this study was the proportion of patients achieving ACR20 response at week 16 as compared to placebo, with secondary endpoints assessing changes in the radiographic progression of the disease. This primary endpoint was achieved, with significantly more patients treated with 150 mg secukinumab achieving ACR20 (57.5% vs 27.4%). Additionally, 33.9% and 16.5% of patients on 150 mg secukinumab achieved ACR50 and ACR70, respectively. In this study, radiographic progression was significantly inhibited at week 24 as compared to placebo.

## Safety

In pooled analyses of Phase II and III trials, secukinumab was found to be well-tolerated.<sup>32,33</sup> Currently published clinical trials have demonstrated a favorable safety profile for secukinumab for up to 5 years of treatment.<sup>17,32</sup> No cases of reactivation of latent tuberculosis have been reported with secukinumab treatment in its clinical trials.<sup>33</sup> Secukinumab treatment has not been associated with any increased risk of anxiety or depression. Neutropenia was observed rarely during clinical trials of secukinumab, but most cases were transient and reversible, without association with serious infection.<sup>12,33</sup>

Common adverse effects of secukinumab treatment include headache and nasopharyngitis. Patients treated with secukinumab have been shown, in Phase II and III trials, to have an increased risk of mucocutaneous candidiasis, which can be successfully treated with oral or topical therapies and typically does not require discontinuation of secukinumab therapy.<sup>32,33</sup> Although secukinumab has not been shown to increase the risk of IBD flares, secukinumab should be avoided in patients with IBD.<sup>12</sup>

The safety profile of secukinumab is comparable to that of other IL-17 inhibitors, and continues to be well-tolerated for up to 5 years of treatment. In patients for whom the drug is not contraindicated, secukinumab is only associated with mild side effects that rarely lead to cessation of therapy. However, TNF- $\alpha$  inhibitors and ustekinumab have more safety data spanning far longer treatment durations, and may thus be a more optimal treatment option for patients concerned about the long-term safety of biologic therapies or medically-complex patients.

## Discussion

### Onset of action

Many biologics are available for the treatment of plaque psoriasis, but these therapies have varying efficacy and safety profiles (Table 1). In general, IL-17 and IL-23 inhibitors demonstrate higher efficacy than older TNF- $\alpha$  inhibitors, while sub-analyses of the onset of action of biologic therapies



demonstrated that IL-17 inhibitors act more quickly than ustekinumab and TNF- $\alpha$  inhibitors.<sup>34</sup> Of note, secukinumab resulted in PASI 75 response in 25% of patients in 3.0 weeks, and achieved an average of 50% reduction in PASI score in 3.0 weeks. Brodalumab (Siliq, Valeant Pharmaceuticals, Bridgewater, NJ, USA) had the most rapid onset of action among any biologic therapy in this analysis, with 25% of patients achieving PASI 75 at 2.1 weeks, and achieving an average of 50% reduction in PASI score at 1.8 weeks.

These data demonstrate that IL-17 inhibitors are ideal for psoriasis patients who require rapid clearance of their skin. Although a chronic disease, certain patients may benefit from more rapid response than others, such as patients with significantly impaired quality of life. Discouraged patients with recalcitrant disease may lose confidence about treatment if they do not observe efficient improvement of their skin symptoms, which can lead to poor medication adherence.<sup>35</sup> Thus, it is important to treat these patients early with rapid-acting biologic therapies, a niche that IL-17 inhibitors fill well.

Currently-approved IL-17 inhibitors – secukinumab, brodalumab, and ixekizumab – all achieve an average of 50% reduction in PASI within 2 weeks.<sup>34</sup> However, the most rapidly-acting IL-17 inhibitor, brodalumab, has a black box warning for depression. Although the actual risk for suicidality and depression with brodalumab is uncertain,<sup>36</sup> this possible risk must be discussed with patients prior to prescribing brodalumab. Secukinumab has no black box warnings that need to be discussed prior to initiating treatment, and no increased risk of depression or suicidality, as observed in its Phase III clinical trials. Thus, patients concerned about the side effect profiles of biologics are sometimes more amenable to starting on secukinumab, rather than brodalumab or TNF- $\alpha$  inhibitors, which have multiple black box warnings.

## Convenience

Patient convenience should also be considered when selecting a biologic medication for psoriasis patients. IL-23 and IL-12/23 inhibitors are dosed more infrequently than IL-17 inhibitors (Table 2), and may be preferable for patients who require supervision for medication administration by a health care professional or who have issues with medication compliance. However, secukinumab is still dosed more infrequently than some TNF- $\alpha$  inhibitors that are dosed every 1–2 weeks.

The JUNCTURE and FEATURE Phase III trials demonstrated that secukinumab administered by autoinjector pen or prefilled syringe continues to be well-tolerated at 1 year under the currently-approved dosing regimen.<sup>19,37</sup> No increased risk of injection-site reactions has been reported with

secukinumab treatment with either method of administration. Patients who are able to comply with a regular monthly dosing regimen may benefit from secukinumab treatment due to its convenience over older biologic therapies, as well as for other reasons outlined in this manuscript.

## Treatment of comorbid disease

Up to 40% of psoriasis patients have or will develop psoriatic arthritis during their lifetimes, so treatment of joint symptoms in addition to skin symptoms is critical to prevent irreversible joint damage. Secukinumab is one of six biologics currently approved for the treatment of both psoriatic arthritis and psoriasis vulgaris, a group that also includes etanercept, adalimumab, infliximab, ustekinumab, and ixekizumab. Secukinumab results in excellent ACR response after 24 weeks of treatment, but this biologic also inhibits radiographic joint damage in psoriatic arthritis patients for up to 2 years.<sup>29</sup> Thus, secukinumab offers a long-term treatment option for psoriatic arthritis patients that does not just slow joint damage, but prevents further damage from occurring.

Almost half of psoriasis patients without psoriatic arthritis harbor subclinical joint inflammation, thought to be an antecedent to inflammatory arthritis.<sup>38</sup> Of these psoriasis patients with subclinical synovitis and arthralgia symptoms at baseline, 55% developed psoriatic arthritis according to Classification of Psoriatic Arthritis criteria within 1 year. Early intervention is of paramount importance for arthritis patients, as joint damage is permanent.<sup>39</sup> Thus, secukinumab treatment in patients with nonspecific joint pain may be of benefit, due to the high risk of progression to joint involvement.

## Cost-effectiveness

Biologics' cost is a primary concern for dermatologists when selecting treatment for moderate-to-severe psoriasis patients.<sup>40</sup> Current estimates of the annual cost of achieving PASI 75 response with secukinumab range from \$75,671 to \$105,131 (US\$).<sup>41,42</sup> Previous analyses from Europe have shown secukinumab to be more cost-effective than TNF- $\alpha$  inhibitors as a first-line agent due to its superior clinical efficacy, ultimately resulting in cost savings.<sup>43</sup> However, cost estimates for all biologics vary widely in the literature, and are accompanied by high levels of uncertainty.<sup>44,45</sup> Further research is needed to evaluate the cost-effectiveness of all biologics for psoriasis.

## Conclusion

Dermatologists have a plethora of options available for the treatment of patients with moderate-to-severe psoriasis, but the decision of which medication to choose is often difficult.

Secukinumab is a highly-efficacious, fast-acting biologic therapy with a relatively favorable safety profile that can be considered in patients requiring rapid clearance of their psoriasis and patients with psoriasis in difficult-to-treat areas, such as the scalp, palms and soles, or nails. Additionally, secukinumab is a preferred treatment for patients with comorbid psoriatic arthritis or arthralgia symptoms, due to its ability to inhibit progression of arthritic disease. Careful consideration of clinical efficacy, safety, cost, convenience, onset of action, and management of comorbid disease is necessary when selecting treatment for individual patients.

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