Taylor & Francis
Taylor & Francis Group

Postgraduate Medicine

ISSN: 0032-5481 (Print) 1941-9260 (Online) Journal homepage: https://www.tandfonline.com/loi/ipgm20

Long-term safety and efficacy of secukinumab in patients with psoriasis and major psychiatric disorders: a case series

Maria Esposito, Alessandro Giunta, Ester Del Duca, Valeria Manfreda, Alfonso Troisi, Luca Bianchi & Maria Concetta Fargnoli

To cite this article: Maria Esposito, Alessandro Giunta, Ester Del Duca, Valeria Manfreda, Alfonso Troisi, Luca Bianchi & Maria Concetta Fargnoli (2020) Long-term safety and efficacy of secukinumab in patients with psoriasis and major psychiatric disorders: a case series, Postgraduate Medicine, 132:2, 172-175, DOI: 10.1080/00325481.2020.1712153

To link to this article: https://doi.org/10.1080/00325481.2020.1712153

Published online: 22 Jan 2020.

POSTGRADUATE MEDICINE
2020, VOL. 132, NO. 2, 172–175
https://doi.org/10.1080/00325481.2020.1712153

Taylor & Francis
Taylor & Francis Group

CLINICAL FEATURE
LETTER TO THE EDITOR

Long-term safety and efficacy of secukinumab in patients with psoriasis and major psychiatric disorders: a case series

Maria Esposito[a], Alessandro Giunta[b], Ester Del Duca[b], Valeria Manfreda[b], Alfonso Troisi[c], Luca Bianchi[b] and Maria Concetta Fargnoli[a]

[a]Department of Dermatology, Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy; [b]Department of Dermatology, University of Rome "Tor Vergata", Rome, Italy; [c]Department of Systems Medicine, International Medical School, University of Rome "Tor Vergata", Rome, Italy

ARTICLE HISTORY Received 7 October 2019; Accepted 2 January 2020

KEYWORDS IL-17, psoriasis, psychiatric disorder, secukinumab

Dear Editor,

Psoriasis has been associated with various psychiatric disorders and its negative impact on patient's mental health has been hypothesized although a clear-cut pathophysiologic link was not established [1]. In patients with psoriasis the incidence of depression, anxiety and suicidality is 25.9, 20.9, and 0.9 per 1000 subject per year, respectively, as reported by a cohort study [2]. Moreover, in patients affected by severe psoriasis a 72% increased risk of depression has been demonstrated as compared with a control population [2]. Moreover, some cases of suicidal ideation and behavior (SIB) occurring in the context of randomized clinical trials (RCT) investigating brodalumab have risen concerns about a possible inducing role of some targeted anti-psoriatic agents [3,4]. Brodalumab is a human monoclonal IgG2 antibody directed against the IL-17 receptor (IL-17RA) that inhibits its interactions with the IL-17 family of cytokines (IL-17A, IL-17F, IL-17C, IL-17 A/F) and IL-25 [5].

For this reason, a careful assessment of patients, in particular for those reporting a history of psychiatric symptoms needing a pharmacological approach with anti-IL17 agents, is needed in routine practice.

We report here our experience regarding 3 patients affected by major psychiatric disorders and moderate-to-severe psoriasis treated with secukinumab. Secukinumab is a fully human IgG1 monoclonal antibody against IL-17A that selectively binds with the interleukin IL-17A cytokine and inhibits its interaction with IL-17 receptor [5].

The first was a male aged 37 years; he presented with a previous diagnosis of adolescent bipolar disorder at the age of 15 years with recent delusion episodes and had been treated for many years with lithium carbonate 300 mg as monotherapy three times daily and more recently in combination with quetiapine 300 mg daily (Figure 1). The second was a male aged 43 years; he presented with a diagnosis of major depressive disorder that had been treated for 2 years with paroxetine 20 mg and delorazepam (Figure 2). Finally, the third was a female patient, aged 50 years, with a previous diagnosis of panic attack episodes, minor depressive episodes and agoraphobia, treated with valproic acid 300 mg daily; she also referred frequent use of delorazepam as needed. At baseline patients presented a severe skin involvement expressed by a Psoriasis Area and Severity Index (PASI) score of 17.5, 20.5 and 18, respectively, and a concomitant consistent impact on quality of life, as expressed by Dermatology Life Quality Index (DLQI) scores. Patients showed a rapid onset of secukinumab action and a persistence of complete skin clearance at week-52, week-104, and 156 (for 2/3 patients reaching this timepoint). No signs of disease recurrence were noted during the observation period. DLQI showed a parallel and consistent reduction. Periodic psychiatric consultations stated a long-term stability or improvement of the psychiatric disorders. Baseline characteristics, including previous treatments, and follow-up disease and quality of life evaluation of patients with results of psychiatric assessment are illustrated in Table 1. No adverse events were reported. Patients signed an informed consent allowing to extract data from clinical records for scientific purposes.

Psoriasis may strongly affect patients' physical aspect, personal image and body satisfaction resulting in social discomfort and stigmatization. Furthermore, the risk to develop anxiety, depression and suicidality among psoriatic patients has been demonstrated to be increased [1,2,6,7].

A relationship between inflammation and depression has been suggested since there are growing evidences of a causative link between inflammation and psychiatric disorders, with several pro-inflammatory cytokines sharing a role in psoriasis pathogenesis as well as in psychiatric pathological mechanisms [7,8]. High-serum IL17 levels are positively associated with depression [9]. A study explored the association of systemic IL17A with depression-like behavior, using a mice model of psoriatic inflammation as well as IL17A administration [9]. An increased expression of IL17A was found in different brain regions (hippocampus and prefrontal cortex) and in blood immune cells after induction of psoriatic inflammation, also associated with depression-like symptoms; the same study demonstrated an anti-depressant effect of the anti-IL17A antibody in mice suggesting that IL17 blockage could be beneficial for psoriasis patients with associated psychiatric symptoms [9].

CONTACT Maria Esposito maria.esposito3@univaq.it; espositomaria@virgilio.it Department of Dermatology, Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, Via Vetoio, Coppito 2, L'Aquila 67100, Italy

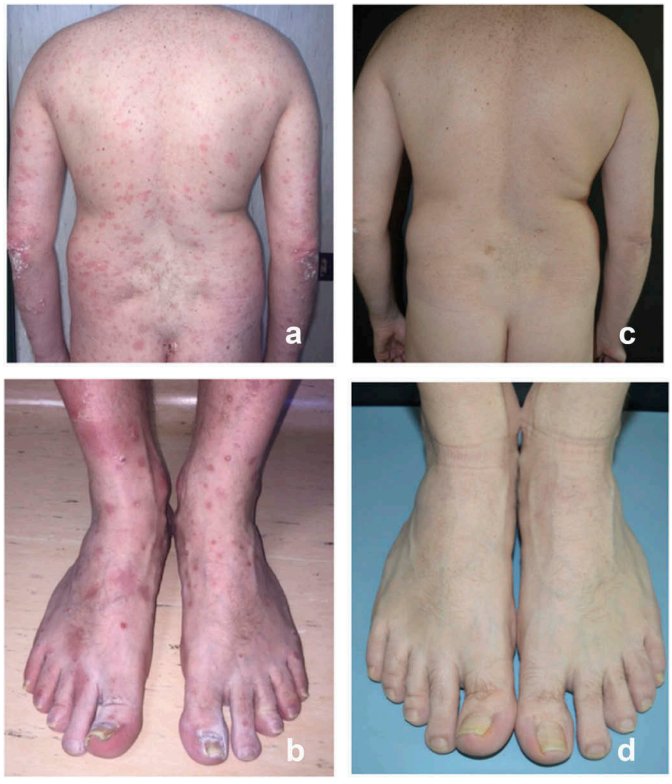

Figure 1. Clinical psoriasis aspect before (a, b) and after 156 weeks (3 years) of treatment with secukinumab (c, d) in a patient affected by bipolar disorder with delusion episodes.

On the other hand, concerns regarding a potential link between IL-17R inhibition in the treatment of psoriasis and suicide have been raised due to the report of few cases of SIB events in patients treated with brodalumab in the context of RCT. However, patients with a previous history of alcohol abuse, drug abuse, depression, suicide and other psychiatric disorders were not excluded from clinical trials [3,10]. In consideration of this issue, a Risk Evaluation and Mitigation Strategies program has been developed by the US Food and Drug Administration in order to ensure that prescribers are educated about the risk of SIB observed with brodalumab and are able to counsel patients at the moment of prescription [10]. A recent study compared the incidence of psychiatric adverse events, in the context of 3 RCT, in patients treated with brodalumab, placebo, and ustekinumab, an IL12/23 inhibitor and demonstrated that the comparison with controls and the timing of events do not indicate a causal relationship between SIB and brodalumab treatment [10].

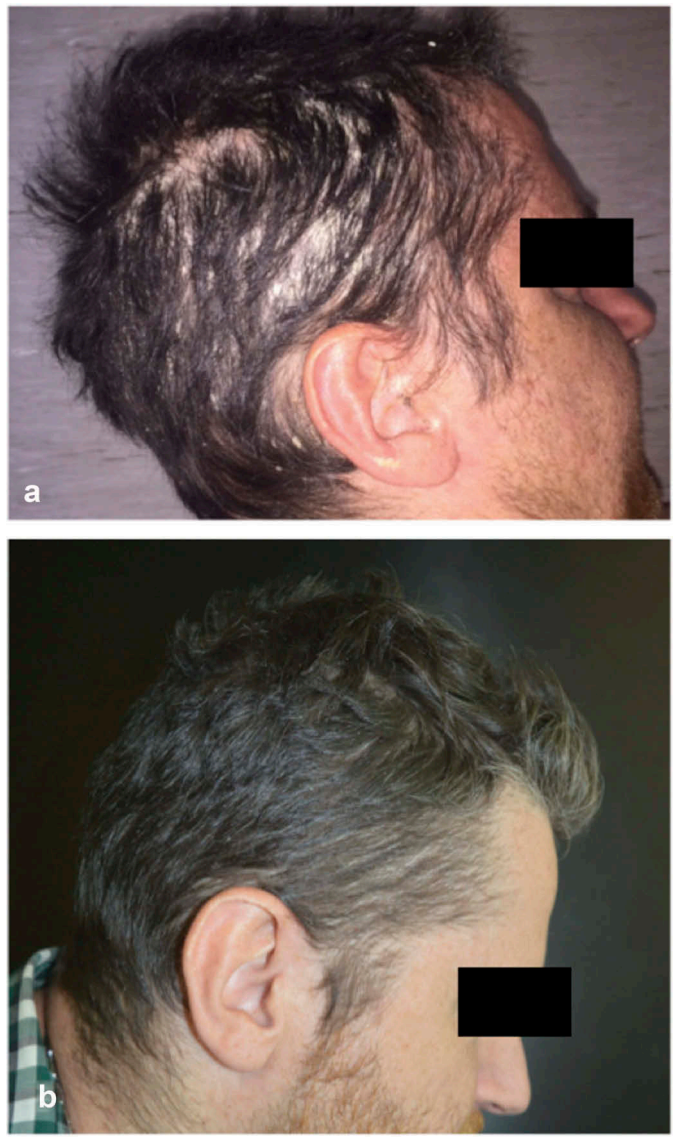

Figure 2. Severe scalp involvement before (a) and after 156 weeks (3 years) of treatment with secukinumab (b) in a patient affected by major depression.

Secukinumab is a human monoclonal antibody that selectively targets and neutralizes IL-17A, that was extensively studied in patients in a number of RCT and was the first anti-IL17 agent approved by the US Food and Drug Administration and European Medicines Agency for the treatment of adult patients with moderate-to-severe plaque psoriasis and psoriatic arthritis [11,12]. Thereafter, real-life experiences confirmed secukinumab safety and efficacy, with rapid clinical improvement and long-term maintenance of results [13].

Table 1. Baseline and follow-up disease and quality of life characteristics of patients undergoing secukinumab with concomitant results of psychiatric evaluation.

			BASELINE		W52		W104		W156		
	Psychiatric Comorbidities	Previous Treatments	PASI	DLQI	PASI	DLQI	PASI	DLQI	PASI	DLQI	Psychiatric evaluation
1	Bipolar disorder/Delusion	Cs Mtx	17.5	28	0	4	0	4	0	2	Stability of the disorder
2	Major depression	Cs	20.5	20	0	4	0	4	0	4	Improvement
3	Anxiety with agoraphobia	Cs Mtx Eta	18	22	0	2	0	2	Na	Na	Improvement

Cs: ciclosporin, Mtx: Methotrexate, Eta: Etanercept.

A pooled analysis of secukinumab studies showed that the exposure-adjusted incidence rates for psychiatric disorders according to the Medical Dictionary for Regulatory Activities (MedDRA), an internationally used set of terms relating to medical conditions, were 4.17/100 patient-years, 6.15/100 patient-years, and 5.64/100 patient-years in subjects receiving secukinumab 300 mg or 150 mg, and etanercept, respectively, over 52 weeks of treatment [14]. When researching by the standardized MedDRA queries 'depression' or 'suicide/self-injury', the adjusted incidence rate was 1.20/100 patient-years, 1.85/100 patoient-years, and 2.06/100 patient-years in the secukinumab 300 mg or 150 mg, and etanercept treatment groups, respectively [14]. Furthermore, during secukinumab treatment, alleviation of anxiety and depression symptoms in patients with moderate-to-severe psoriasis has been reported in comparison to etanercept and placebo [15]. Nevertheless, after secukinumab marketing authorization, concerns were raised by a reported patient affected by psoriasis and multiple sclerosis experiencing an exacerbation of depression after starting secukinumab treatment. In this case, the disruption of the blood brain barrier due to multiple sclerosis may have led to the development of depression [16].

More recently an integrated clinical trial safety dataset included data pooled from 21 randomized controlled clinical trials of secukinumab in psoriasis, psoriatic arthritis and ankylosing spondilytis patients (N = 7355) reporting that incidences of suicidality-related adverse events were low in the psoriasis and psoriatic arthritis studies, and none emerged in the ankylosing spondilytis studies. There was no evidence to suggest that treatment with secukinumab increases the risk beyond background risk in patients with these systemic inflammatory diseases [17].

In our case series, 3 patients with a previous psychiatric diagnosis (bipolar disorder/delusion, major depression, anxiety with agoraphobia) showed an excellent long-term efficacy and safety profile during the treatment with secukinumab, despite concomitant therapies known to potentially exacerbate existing psoriasis, such as lithium and sodium valproate [18] and also demonstrating stability/improvement of the underlining psychiatric disorder.

In these 3 cases the therapeutic choice was made on the basis of the need for a rapid onset of action and potential worsening of the underlying condition was monitored with the support of psychiatric consultations. This case series highlights the importance of awareness and attention to psychiatric comorbidities as stated by the recent Joint AAD-NPF guidelines [19]. Patients with psoriasis and relatives should be educated about the association of psoriasis with anxiety and depression, and asked about signs and symptoms of anxiety and depression by their dermatologist [19]. It is also important to consider that some psychiatric agents may be causative agents for drug-induced or drug-aggravated psoriasis manifestations [18]. Besides, psoriasis patients with previous symptoms of anxiety, depression, suicidal ideation or reported stressors, should be referred to an appropriate health care professional for further assessment and management [19], considering that a multidiscplinary approach of psychiatric comorbidities may help the therapeutical choice and the long-term treatment management.

Although we presented a limited experience, these 3 cases with a long-term follow-up, highlighted an important therapeutic issue in psoriasis management and showed particularly encouraging results in terms of clinical benefits and safety for patients.

Declaration of interest

The contents of the paper and the opinions expressed within are those of the authors, and it was the decision of the authors to submit the manuscript for publication.

Maria Esposito has served as a consultant, speaker and board member for Novartis.

Luca Bianchi has served as a consultant, speaker and board member for Novartis.

Maria Concetta Fargnoli has served as a consultant, speaker and board member for Novartis.

A reviewer on this manuscript has disclosed that they have had support from Novartis as well as from Abbvie, Celgene, Janssen, Leo, Lilly, Ortho and Sun. Another reviewer has disclosed that they are an employee of Mount Sinai and have received research funds from: Abbvie, Boehringer Ingelheim, Celgene, Eli Lilly, Incyte, Janssen/Johnson & Johnson, Leo Pharmaceuticals, Medimmune/Astra Zeneca, Novartis, Pfizer, Sciderm, Valeant, and ViDac. They are also a consultant for Allergan, Aqua, Boehringer-Ingelheim, LEO Pharma, Menlo, Mitsubishi, Promius and Theravance.

References

1. Rapp SR, Feldman SR, Exum ML, et al. Psoriasis causes as much disability as other major medical diseases. J Am Acad Dermatol. 1999;41:401–407.
2. Kurd SK, Troxel AB, Crits-Christoph P, et al. The risk of depression, anxiety, and suicidality in patients with psoriasis: a population-based cohort study. Arch Dermatol. 2010;146:891–895.
3. Papp KA, Reich K, Paul C, et al. A prospective phase 3, randomised, double- blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis. Br J Dermatol. 2016;175:273–286.
4. Chiricozzi A, Romanelli M, Saraceno R, et al. No meaningful association between suicidal behavior and the use of IL-17A-neutralizing or IL-17RA-blocking agents. Expert Opin Drug Saf. 2016 Dec;15:1653–1659.
5. Kaushik SB, Lebwohl MG. Review of safety and efficacy of approved systemic psoriasis therapies. Int J Dermatol. 2019 Jun;58:649–658.
6. Esposito M, Saraceno R, Giunta A, et al. An Italian study on psoriasis and depression. Dermatology. 2006;212:123–127.
7. Patel N, Nadkarni A, Cardwell LA, et al. Psoriasis, depression, and inflammatory overlap: a review. Am J Clin Dermatol. 2017;18:613–620.
8. Miller AH, Raison CL. The role of inflammation in depression: from evolutionary imperative to modern treatment target. Nat Rev Immunol. 2016;16:22–34.
9. Nadeem A, Ahmad SF, Al-Harbi NO, et al. IL-17A causes depression-like symptoms via NFκB and p38MAPK signaling pathways in mice: implications for psoriasis associated depression. Cytokine. 2017;97:14–24.
10. Lebwohl MG, Papp KA, Marangell LB, et al. Psychiatric adverse events during treatment with brodalumab: analysis of psoriasis clinical trials. J Am Acad Dermatol. 2018;78:81–89.
11. Papp KA, Langley RG, Sigurgeirsson B, et al. Efficacy and safety of secukinumab in the treatment of moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled phase II dose-ranging study. Br J Dermatol. 2013;168:412–421.
12. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis—results of two phase 3 trials. N Engl J Med. 2014;371:326–338.
13. Galluzzo M, Talamonti M, De Simone C, et al. Secukinumab in moderate-to-severe plaque psoriasis: a multi-center, retrospective, real-life study up to 52 weeks observation. Expert Opin Biol Ther. 2018;18:727–735.

14. van de Kerkhof PC, Griffiths CE, Reich K, et al. Secukinumab long-term safety experience: a pooled analysis of 10 phase II and III clinical studies in patients with moderate to severe plaque psoriasis. J Am Acad Dermatol. 2016;75:83–98.
15. Lebwohl M, Sherif B, Mollon P, et al. Secukinumab relieves pain and anxiety in psoriasis: results of two phase 3 trials. Presented at the 24th Annual Congress of the European Academy of Dermatology and Venereology; 2015 Oct 7–11; Copenhagen, Denmark.
16. Komori T, Otsuka A, Honda Y, et al. Exacerbation of depression in a psoriatic arthritis patient possibly induced by secukinumab. Eur J Dermatol. 2016;26:506–507.
17. Deodhar A, Mease PJ, McInnes IB, et al. Long-term safety of secukinumab in patients with moderate-to-severe plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis: integrated pooled clinical trial and post-marketing surveillance data. Arthritis Res Ther. 2019;21:111.
18. Basavaraj KH, Ashok NM, Rashmi R, et al. The role of drugs in the induction and/or exacerbation of psoriasis. Int J Dermatol. 2010;49:1351–1361.
19. Elmets CA, Leonardi CL, Davis DMR, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with awareness and attention to comorbidities. J Am Acad Dermatol. 2019;80:1073–1113.