Archives of Dermatological Research (2019) 311:421–424
https://doi.org/10.1007/s00403-019-01907-y

CONCISE COMMUNICATION

Successful intra-class switching among IL-17 antagonists: a multicentre, multinational, retrospective study

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Received: 13 December 2018 / Revised: 14 February 2019 / Accepted: 1 March 2019 / Published online: 16 March 2019

Abstract

IL-17 blockers are among the newer anti-psoriatic treatment options and little is known about the interclass switching. We have thus initiated a multi-center, multi-national, retrospective study to assess the treatment response of patients who were switched from one IL-17 blocker to another. Analysis consisted of data from patients with moderate-to-severe psoriasis who did not respond satisfactorily to one of the available IL-17 blockers (secukinumab, ixekizumab, brodalumab) and were subsequently switched to another drug of this class. After 12 weeks of treatment, patients' PASIs were evaluated. Treatment success was defined as reaching PASI 75 after 12 weeks. Topical treatment was allowed and used in all patients. 26 patients were included (13 male, 13 female) and 29 switches were evaluated. Overall, 29 switches in 21 patients were evaluated. 18 patients changed their therapy from secukinumab to ixekizumab, or in 7 cases to brodalumab. Brodalumab was used in 3 cases after failure of treatment with ixekizumab. Only in one case, non-response of brodalumab resulted in a therapy switch to secukinumab. In 15 (52%) cases, PASI 75 was reached. In 6 (20%) patients, the switch led to a PASI 50 response. No success of treatment was seen among 8 (28%) participants. When patients fail to respond or do not tolerate an IL-17 blocker, switching to another anti-IL-17A/RA is a promising viable option. Larger studies are needed to confirm our results.

Keywords Interleukin-17 · IL-17 · IL-17A · IL-17 receptor blocker · Secukinumab · Ixekizumab · Brodalumab

Introduction

Interleukin (IL)-17 plays an important role in the pathogenesis of psoriasis [1]. It is highly expressed by TH17 cells subsequent to their polarization by dendritic cell-derived

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IL-23. The IL-17 blockers are among the newer anti-psoriatic treatment options. Neutralization of the cytokine IL-17A or its receptor by anti-IL-17A/RA shows improvement of the clinical and histological features of psoriasis [2]. Secukinumab and ixekizumab inhibit IL-17A, while brodalumab blocks the alpha chain of the IL-17 receptor [3].

In general, biologics are highly efficacious in psoriasis, especially the IL-17 antagonists. However, some patients do not respond to treatment and switching of therapy is required. So far, little is known about the outcomes of drug switching on the anti-psoriatic efficacy of the newer biologics [4, 5]. Thus, it remains unclear whether non-responders to an IL-17 blocker should be switched to another IL-17 or whether a class switch to IL-23 or TNF antagonism is more appropriate. No guidelines exist and physicians and patients are left without clear recommendations.

Georgakopoulos et al. have recently published a case series of 17 patients with moderate-to-severe plaque psoriasis that did not respond to secukinumab and thus were switched to ixekizumab. 15 out of the 17 patients responded to ixekizumab and reached a 75% reduction of the Psoriasis Area and Severity Index (PASI 75) within 12 weeks [6]. No data exists on switching from or to brodalumab or to secukinumab.

We have thus initiated a multi-center, multi-national, retrospective study to assess the treatment response of patients with moderate-to-severe psoriasis who were switched from one IL-17 blocker to another.

The aim of our study was to evaluate whether an intra-class switching of IL-17 antagonists can lead to treatment response, and therefore, is worth considering in daily practice. We hypothesized that if IL-17 blockers were not successful initially, switching to another IL-17 antagonist is not advisable.

Methods

Patients

To evaluate the efficacy of anti-IL-17 switching, we conducted a multinational retrospectively collaborative study on the outcome of anti-IL-17 switching.

Each institution, namely University of Zurich, Innsbruck, Hamburg, Kiel, Munich, Barcelona, Linz and Graz contributed local patients with moderate-to-severe psoriasis who did not respond (reach PASI 75) or lost response to any of the available IL-17 blockers (secukinumab, ixekizumab, brodalumab) and were switched to another drug of this class. The decision for the change of treatment and the choice of drugs was performed by the treating physician.

Patients signed an informed consent as by the ethics commission requirement (BASEC-Nr. ID 2018-00884). All patients meeting the inclusion criteria that presented to our departments until 31st of March 2018 were included. Inclusion criteria were a PASI ≥ 10 at baseline, a non-response to an IL-17 blocker and consecutively being switched to another IL-17 blocker. If patients received two systemic therapies or UV-therapy simultaneously, they were excluded from our cohort.

After 12 weeks of treatment, patients' PASIs were evaluated. Treatment success was defined as reaching PASI 75 after 12 weeks. Psoriasis type, age, gender, duration of therapy and PASI were measured. In accordance to the international treatment recommendations, treatment was continued, if PASI 50 was reached and the patient had a DLQI ≤ 5 [7]. Topical treatment, including steroids, Vitamin D derivates and urea-containing moisturizers, was allowed and used in all patients. If patients received all three IL-17 blockers consecutively, up to two switching events were analysed.

The reason for termination of the initial IL-17 therapy was either primary failure of response, if the patient never responded to therapy, or secondary failure, which was defined as primary response, but loss of response over time. Additionally, patients terminating treatment due to side effects, end of study and noncompliance were included.

Results

All patients suffered from plaque psoriasis, one showed additional changes on the palms and two also suffered from psoriasis inversa. One patient was diagnosed of psoriatic arthritis and nail psoriasis. Thirteen patients were male, 13 female. About one-third of all patients had a positive family history for psoriasis. The mean age of the participants was 53, while the average age of onset was 23 years. With the exception of one participant, all patients were Caucasian. The mean PASI before switch was 13.6 ± 7.1. Secondary failure (62%) was the most common reason for discontinuation of IL-17 treatment. 5 patients never responded to the primary therapy (Table 1).

Overall, 29 switches in 21 patients were evaluated. In 15 (52%) cases, PASI 75 was reached. In 6 (20%) patients, the switch lead to a PASI 50 response. No success of treatment was seen among 8 (28%) participants (Fig. 1).

In 18 cases, secukinumab was switched to ixekizumab. PASI 75 was reached in 9 (50%) cases and PASI 50 was reached in 4 (22%). Overall, after 12 weeks 13 (72%) of the 18 patients were still under ixekizumab. The average PASI change was 69%. When secukinumab was switched to brodalumab (7 patients), in 4 cases (57%) PASI 75 was reached, one (14%) patient reached PASI 50 and no success was seen in 2 (28%) patients. Ixekizumab was switched to brodalumab in 3 cases: 2 patients (66%) reached PASI 75 and in 1 patient (33%) the treatment was considered to be

Table 1 Patient characteristics, reason for discontinuation of initial IL-17 treatment and efficacy

Variables	Value
Gender, *n*	
Male	13
Female	13
Family history, *n* (%)	10 (38.5%)
Mean age, years ± SD	53 ± 18.4
Mean age of onset, years ± SD	27.2 ± 10.4
Mean PASI at baseline ± SD	15.2 ± 7.9
Reason for discontinuation of IL-17 treatment	
Primary failure	5
Secondary failure	18
Low response	3
Non-compliant	1
End of study	1
Side effects	1
Efficacy	
Secukinumab → Ixekizumab, *n*	18
Mean treatment duration before switch (months)	14.5 ± 8.5
Mean interval between switch (months)	3.5
Mean PASI at baseline	12.6
≥ PASI 75, *n* (%)	9 (50%)
Secukinumab → Brodalumab, *n*	7
Mean treatment duration before switch (months)	18.4
Mean interval between switch (months)	1.9
Mean PASI at baseline	11.6 (9.7) ± 5.9
≥ PASI 75, *n* (%)	3 (50%)
Brodalumab → Secukinumab, *n*	1
Mean treatment duration before switch (months)	29
Mean interval between switch (months)	1
Mean PASI at baseline	Not available
≥ PASI 75, *n* (%)	0
Ixekizumab → Brodalumab, *n*	3
Mean treatment duration before switch (months)	21.5
Mean interval between switch (months)	16.7
Mean PASI at baseline	13.5 (2.7) ± 3
≥ PASI 75, *n* (%)	2 (67%)

unsuccessful. Brodalumab was changed to secukinumab in one case, with eventual PASI worsening. There were no instance of ixekizumab to secukinumab or brodalumab to ixekizumab switches.

Discussion

Our study aim was to evaluate whether an intraclass IL-17 can lead to treatment response, and therefore, is worth considering in daily practice. We hypothesized that if IL-17 blockers were not successful initially, switching to another IL-17 antagonist is not advisable. However, our data showed several patients were an intraclass switch was successfully performed.

Shortcomings and limitations of this study include its retrospective design, the limited number of patients and the subjectivity of the PASI assessment that might lead to variation between centres and countries. As brodalumab is not commercially available in most countries, which might account for the relative scarcity of switching reports, it yielded the least data.

When patients fail to respond or are intolerant to any IL-17 blocker, switching to another anti-IL-17A/RA is common, despite lack of evidence about its benefits.

IL-17 switching is controversial as, with the exception of a case series of Georgakopoulos et al. very little is known. Having today several efficient biological treatment options (TNF-alpha, IL-12/23, IL-17, and IL-23) the controversy if an intraclass switch should be performed exists.

Our data suggest that switching within IL-17 blockers is possible and can lead to satisfactory results. To our knowledge, there is no mechanism why intraclass switching works in many patients. The proportion of patients that were successfully switched from secukinumab to ixekizumab was lower than previously reported [6]. Taken together, intraclass switching is a promising option as confirmed by us and others. In regard to our data we conclude that intraclass switching should be considered in daily practice, when an IL-17 antagonist does not reach PASI 75.

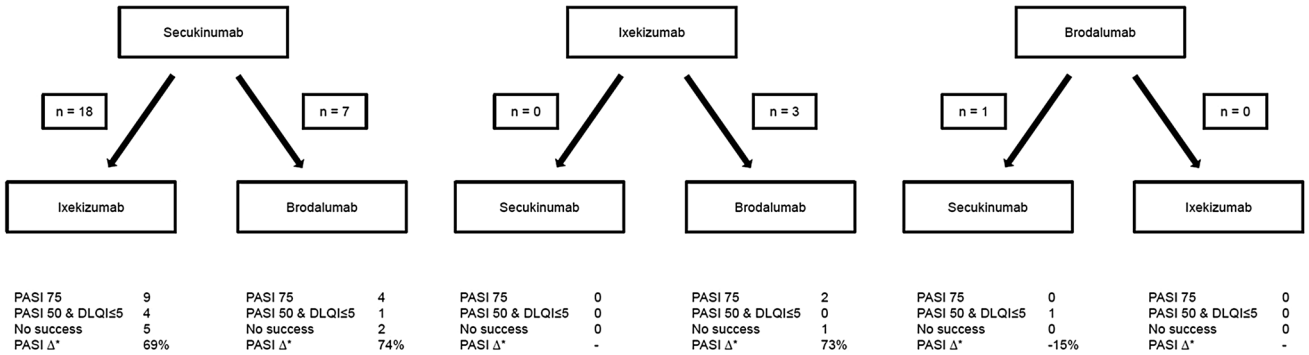

Fig. 1 Overview of IL-17 switches including the number of patients reaching treatment response. *Average change of PASI

References

1. Durham LE, Kirkham BW, Taams LS (2015) Contribution of the IL-17 pathway to psoriasis and psoriatic arthritis. Curr Rheumatol Rep 17(8):55
2. Krueger JG, Fretzin S, Suarez-Farinas M, Haslett PA, Phipps KM, Cameron GS et al (2012) IL-17A is essential for cell activation and inflammatory gene circuits in subjects with psoriasis. J Allergy Clin Immunol 130(1):145 e9–154 e9
3. Tausend W, Downing C, Tyring S (2014) Systematic review of interleukin-12, interleukin-17, and interleukin-23 pathway inhibitors for the treatment of moderate-to-severe chronic plaque psoriasis: ustekinumab, briakinumab, tildrakizumab, guselkumab, secukinumab, ixekizumab, and brodalumab. J Cutan Med Surg 18(3):156–169
4. Blauvelt A, Papp KA, Griffiths CEM, Puig L, Weisman J, Dutronc Y et al (2018) Correction to: efficacy and safety of switching to ixekizumab in etanercept non-responders: a subanalysis from two phase III randomized clinical trials in moderate-to-severe plaque psoriasis (UNCOVER-2 and-3). Am J Clin Dermatol 19(3):457
5. Damiani G, Conic RRZ, de Vita V, Costanzo A, Regazzini R, Pigatto PDM et al (2018) When IL-17 inhibitors fail: real-life evidence to switch from secukinumab to adalimumab or ustekinumab. Dermatol Ther 2018:e12793
6. Georgakopoulos JR, Phung M, Ighani A, Yeung J (2018) Efficacy and safety of switching to ixekizumab in secukinumab non-responders with plaque psoriasis: a multicenter retrospective study of interleukin 17A antagonist therapies. J Am Acad Dermatol 79(1):155–157
7. Mrowietz U, Kragballe K, Reich K, Spuls P, Griffiths CE, Nast A et al (2011) Definition of treatment goals for moderate to severe psoriasis: a European consensus. Arch Dermatol Res 303(1):1–10