ORIGINAL

SWITCHING TO GUSELKUMAB IN MODERATE-TO-SEVERE PSORIASIS: ROLE OF PATIENT-REPORTED OUTCOMES AND HOSPITAL PHARMACISTS

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ABSTRACT

Objective: The study objective was to assess the value of patient-reported outcomes (PRO) in guiding the switching of biological agents in patients with moderate-to-severe psoriasis attending hospital pharmacy clinics.

Method: At the suggestion of hospital pharmacists, 45 patients completed the Psoriasis Symptoms and Signs Diary with seven-day recall (PSSD_7D). Those with a PSSD_7D score of ≥20 were referred to the dermatology service for switching to guselkumab. The PSSD_7D score was reassessed after one, six and 12 months of guselkumab therapy.

Results: Fourteen patients had a PSSD_7D score of ≥20. All were accepted for switching to guselkumab at standard doses. An improvement in the mean PSSD_7D score was already clear within the first month of guselkumab therapy. After 12 months, the score was 83.4% lower than at baseline.

Conclusions: A PRO instrument could be useful in clinical practice to guide biological therapy in patients with psoriasis.

Drug Switching – Guselkumab - Patient-Reported Outcomes – Psoriasis

RESUMEN

Objetivos: El objetivo del estudio fue investigar el valor de los resultados percibidos por los pacientes (PRO) para guiar el cambio de fármacos biológicos en pacientes con psoriasis de moderada a grave que acuden a una consulta de farmacia hospitalaria.

Método: A sugerencia de los farmacéuticos hospitalarios, 45 pacientes completaron el instrumento Diario de los signos y síntomas de la psoriasis durante siete días (PSSD_7D por sus siglas en inglés). A los pacientes con una puntuación igual o superior a 20 se les remitió al Servicio de Dermatología para su evaluación y cambio de tratamiento a guselkumab. La puntuación del PSSD_7D se evaluó después de uno, seis y doce meses de tratamiento.

Resultados. Catorce pacientes tuvieron una puntuación del PSSD-7D igual o superior a 20; todos ellos fueron aceptados para cambiar a guselkumab a dosis estándar. La puntuación del PSSD_7D mejoró desde el primer mes de tratamiento. Después de 12 meses, la puntuación fue un 83,4% inferior a la puntuación inicial.

Conclusiones. Un instrumento PRO podría ser útil en la práctica clínica para guiar el tratamiento biológico en pacientes con psoriasis moderada a grave.

Cambio de fármaco – Guselkumab – Resultados percibidos por el paciente – Psoriasis

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INTRODUCTION

Biological agents are used to treat moderate-to-severe psoriasis that does not respond to conventional local and systemic therapies or when those treatments are not well tolerated. Assessment of disease improvement is usually made by the treating physicians using instruments such as the Psoriasis Area and Severity Index (PASI). However, psoriasis is a multifaceted disease that requires a multidisciplinary approach, with the collaboration of different hospital services and outpatient clinics. In addition, patient-reported outcomes (PRO) provide a wider view of the disease. Skin clearance as assessed by physicians does not correlate exactly with the feelings of patients[1] or with increases in quality of life.[2]

The aim of this study was to assess a PRO-driven switching strategy for the treatment of moderate-to-severe psoriasis with the collaboration of hospital pharmacists and dermatologists.

METHOD

This was a single-center, open-label, prospective study. In July and August 2019, we assessed psoriasis control by means of the Psoriasis Symptoms and Signs Diary (PSSD) in all patients with moderate-to-severe psoriasis that was being treated with biological or targeted immunomodulatory agents and who were attending our hospital pharmacy clinics.

PSSD is a PRO instrument for assessing disease severity. Patients rate five cutaneous symptoms (itching, tightness, burning, stinging, and pain) and six skin signs (dryness, cracking, scaling, shedding or flaking, redness, and bleeding) from 0 (absence) to 10 (worst imaginable). Total PSSD score can range between 0 (best) and 110 (worst); higher scores mean more severe disease. Patients complete a daily or weekly online diary requiring 24-hour recall or seven-day recall (PSSD_7D), respectively.[3] In this study, patients completed the PSSD_7D online.

There is no established threshold for PSSD scores to suggest that switching therapy would be beneficial. For this reason, an expert panel of pharmacists and dermatologists from our hospital agreed to set this threshold at 20 points. We therefore proposed switching patients with a PSSD_7D score of ≥20 to another biological agent with a different therapeutic target, i.e. to guselkumab. If they agree, we referred them to the dermatology department, where they were assessed for their suitability for switching to guselkumab. If switching was approved, guselkumab therapy was initiated the same day or within the following week.

PSSD_7D scores were measured after one, six and 12 months of guselkumab therapy, and at each visit, we asked patients about any potential adverse events. In addition, we assessed quality of life at baseline and after six months of guselkumab therapy. For this purpose, we used the Spanish version of the EuroQoL five dimension (EQ-5D) instrument, a short, generic, patient-rated questionnaire. Patients answered items for five domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and completed a visual analogue scale of health status from 0 (worst) to 100 (best). The EQ-5D index was calculated, with index value ranges between 1 (best health status) and 0 (death).[4]

Descriptive statistical analysis was performed using IBM® SPPS® Statistics 26.0 (IBM, Armonk, NY, USA).

The study was approved by the Pharmacy and Therapeutics Committee of our hospital as a therapeutic protocol based on efficacy, safety and cost criteria.

RESULTS

Forty-five patients with moderate-to-severe psoriasis that was being treated with biological agents attended our hospital pharmacy clinics. Hospital pharmacists assessed them all using the PSSD_7D instrument and found 14 patients (31.1%) to have a PSSD_7D score of ≥20. Compared with the whole group, these patients were slightly older (52 ±14.1 years vs 50 ±13.8 years), included a lower percentage of women (20% vs 37.8%), had slightly more severe psoriasis (PASI score 11.3 ±4.6 vs 9.3 ±6.74), and had shorter disease duration (8.8 ±5.2 years vs 10.1 ±7.4 years). The mean PSSD score was higher (48.5 ±21 vs 11.3 ±4.6) (Tables 1 and 2).

All patients (No. = 14) had previously used topical therapy, and almost 80% of them had previously received conventional systemic therapy (methotrexate, cyclosporine or acitretin). Moreover, they had all had at least one previous biological agent. Nine patients (64.3%) had had one previous biological agent: ustekinumab (USK; No. = 7), adalimumab (ADA; No. = 1) or secukinumab (SEC; No. = 1). Other four patients (28.6%) had had two previous agents: ADA and USK (No. = 2), etanercept (ETN) and USK (No. = 1), or ADA and SEC (No. = 1). Only one patient had had three previous agents (ADA, USK and ixekizumab [IXE]). Therefore the most used agent was USK (No. = 10), followed by ADA (No. = 4), SEC (No. = 2), and IXE and ETN (both No. = 1). (Table 2).

Hospital pharmacists explained the proposal of switching therapy to these patients. All of them agreed and signed the informed consent form. They were then assessed by dermatologists and accepted for switching to guselkumab, which was prescribed and administered on the same day or within the following week. Patients received the standard dose of guselkumab: 100 mg by subcutaneous injection at Week 0, Week 4, and then every eight weeks thereafter. No patient discontinued guselkumab during the study period and all patients were still being treated with guselkumab as of 30 November 2020.

Mean PSSD score decreased throughout the 12-month study in such way that the final score was more than 80% lower than the score at baseline. The improvement was already clear within the first month of therapy (Fig. 1).

At 12 months, the EQ-5D index had increased from 0.86 at Visit 0 to 0.91 at Visit 6. The visual analogue scale value was also higher compared with baseline, increasing from 81.4 at Visit 0 to 90 at Visit 6.

In addition, mean PASI score at 12 months was 2.3 ±1.3. This difference of 9 points from baseline score accounted for an 80% reduction. Furthermore, psoriasis severity was

TABLE 1. Demographic and clinical characteristics of patients with psoriasis in our center.

Characteristics	*No. (%)*
Patients	45
Age (years), mean ±SD	50 ±13.8
Women	17 (37.8)
BMI (kg/m^2), mean ±SD	23.3 ±5.14
Weight (kg), mean ±SD	77.4+18.2
Psoriasis disease duration (years), mean ±SD	10.1±7.4
PASI score (0-72), mean ±SD	9.3 ±6.74
Previous treatments	45 (100)
Topical therapies	45 (100)
Phototherapy	0
Conventional systemic drugs	39 (86.6)
Biologic agents	40 (88)
— 0	5 (11.1)
— 1	21 (46.67)
— 2	13 (28.89)
— 3	4 (8.89)
— 4	1 (2.2)
— 5	1 (2.2)
PSSD score at study onset (0-100 points), mean ±SD	21.1 ±23

TABLE 2. Demographic and clinical characteristics of the study population.

Characteristics	*No. (%)*
Patients	14
Age (years), mean ±SD	52 ±14.1
Women	2 (20)
BMI (kg/m^2), mean ±SD	22.9 ±5.5
Weight (kg), mean ±SD	79.13 ±22.1
Psoriasis disease duration (years), mean ±SD	8.8 ±5.2
PASI score (0-72), mean ±SD	11.3 ±4.6
Previous treatments	14 (100)
Topical therapies	14 (100)
Phototherapy	0
Conventional systemic drugs	11 (78.6)
Biologic agents	14 (100)
— 1[a]	9 (64.3)
— 2[b]	4 (28.6)
— 3[c]	1 (7.1)
PSSD score at study onset (0-100 points), mean ±SDn	50.14 ±21.9

a: Ustekinumab (USK; No. = 7), adalimumab (ADA; No. = 1) and secukinumab (SEC; No. = 1);
b: ADA and USK (No. 2), etanercept (ETN) and USK (No. 1), and ADA and SEC (No. 1);
c: ADA, USK and ixekizumab (No. = 1).

categorized as moderate-to-severe at baseline (PASI >10),[5] but at the end of the study mean PASI score was very low.

Guselkumab was well tolerated, with only adverse event reported being mild headache in two patients. No moderate or severe adverse events were reported.

DISCUSSION

In this study, we highlighted the value of PRO for the therapeutic decision-making process in psoriasis management. We also restated the relevance of the collaboration between professionals of different specialties for the care of patients with psoriasis.

The use of PRO instruments in patients with psoriasis is of growing importance. Some instruments are general, such as the EQ-5D and the 36-item short form survey, while others are disease-specific, such as the dermatology life quality index, the psoriasis disability index, and the impact of psoriasis on quality of life.[6] We chose the PSSD mainly for two reasons. First, it was developed according to the recommendations outlined in the US Food

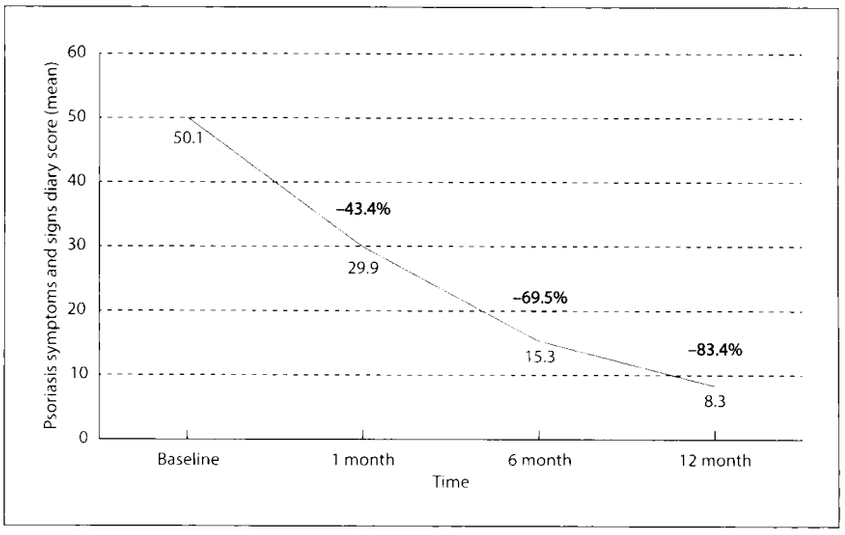

FIG. 1. Evolution of PSSD score in 14 patients with moderate-to-severe psoriasis treated with guselkumab for 12 months.

and Drug Administration's PRO guidance. Second, it has been used in clinical trials of guselkumab, which was the study drug. In addition, we preferred the seven-day recall version, which is more suitable for clinical research than the 24-h recall version.[3] Furthermore, in the VOYAGE 1 and VOYAGE 2 trials of guselkumab, a correlation was observed between PSSD and PASI scores, although there were differences between patients and physicians regarding total clearance.[1]

With regard to the choice of the biological agent for switching, we preferred guselkumab because it has been found to be effective and safe in long-term treatment [7, 8] and is cost-effective.[9] Several recent studies have assessed the use of guselkumab in real-life settings and have shown it to be effective and well tolerated.[10-12] However, switching to guselkumab in these studies was based only on physicians' criteria, i.e. PASI scores. Furthermore, guselkumab is used in our hospital.

Improvement in PSSD scores was consistent throughout the study period. After only one month of guselkumab therapy, the mean PSSD score was reduced by almost 45%, with a 70% reduction after six months, and a reduction of more than 80% after 12 months. The difference between mean baseline and final PSSD scores was greater than 40 points, indicating clinically meaningful improvement.[13]

This outcome probably reflects the benefit of switching to a therapy that uses an agent with a different therapeutic target. Previous biological agents were targeted to tumor necrosis factor (ADA and ETN), interleukin (IL)-12 and IL-23 (USK), and IL-17A (SEC and IXE). After switching to guselkumab, which selectively inhibits the p19 subunit of IL-23, patients reported an improvement in symptoms and signs of psoriasis. Moreover, quality of life increased from baseline.

The improvement in PRO results was accompanied by an 80% reduction in PASI score from baseline. A reduction of 50% is already considered clinically significant [14] and the psoriasis guidelines consider that a minimal response criterion is a 50% or greater reduction in baseline disease severity (expressed by PASI response).[5, 15] Furthermore, a PASI score lower than five indicates an appropriate response in the long term.[5] The 80% reduction in PASI and the mean score of 2.3 confirmed the efficacy of guselkumab.

This study included a small sample and did not have a control group. However, in spite of these limitations, we believe that our strategy could be easily applied to other centers.

CONCLUSION

PRO should be assessed for the management of patients with moderate-to-severe psoriasis. After 12 months of switching to guselkumab based on PSSD score, patients felt that there was a considerable improvement in their disease. The use of a PSSD could therefore be useful in clinical practice to guide biological therapy, especially when professionals of different specialties are involved.

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REFERENCES

1. Gordon KB, Han C, Li S, You Y, Song M, Fakharzadeh S, et al. Correlation of physician-assessed psoriasis area and severity index scores with patient-reported psoriasis symptoms and signs diary scores among patients with moderate-to-severe psoriasis: Results from VOYAGE 1 and VOYAGE 2 Studies. J Psoriasis Psoriatic Arthritis 2019; 4: 147-52.

2. Lacour JP, Bewley A, Hammond E, Hansen JB, Horne L, Paul C, et al. Association between patient- and physician-reported outcomes in patients with moderate-to-severe plaque psoriasis treated with biologics in real life (PSO-BIO-REAL). Dermatol Ther (Heidelb) 2020; 10: 1099-109.

3. Feldman SR, Mathias SD, Schenkel B, Colwell HH, McQuarrie K, Randazzo B, et al. Development of a patient-reported outcome questionnaire for use in adults with moderate-to-severe plaque psoriasis: The Psoriasis Symptoms and Signs Diary. J Dermatology Dermatologic Surg 2016; 20: 19-26.
4. Badia X, Roset M, Montserrat S, Herdman M, Segura A. The spanish version of EuroQol: a description and its applications. European Quality of Life scale. Med Clin (Barc) 1999; 112 (Suppl): 79-85.
5. Daudén E, Puig L, Ferrándiz C, Sánchez-Carazo JL, Hernanz-Hermosa JM. Consensus document on the evaluation and treatment of moderate-to-severe psoriasis: Psoriasis Group of the Spanish Academy of Dermatology and Venereology. J Eur Acad Dermatology Venereol 2016; 30: 1-18.
6. Otuki MF, Reis RC, Cabrini D, Prudente AS, Horinouchi CDS, Correr CJ. Patient-reported outcomes in psoriasis research and practice. Br J Dermatol 2011; 165: 1361-2.
7. Griffiths CEM, Papp KA, Song M, Miller M, You Y, Shen YK, et al. Continuous treatment with guselkumab maintains clinical responses through 4 years in patients with moderate-to-severe psoriasis: results from VOYAGE 1. J Dermatolog Treat 2020 Jul 13; 1-9.
8. Reich K, Armstrong AW, Foley P, Song M, Miller M, Shen YK, et al. Maintenance of Response Through up to 4 Years of Continuous Guselkumab Treatment of Psoriasis in the VOYAGE 2 Phase 3 Study. Am J Clin Dermatol 2020; 21: 881-90.
9. Augustin M, Wirth D, Mahlich J, Pepper AN, Druchok C. Cost per responder analysis of guselkumab versus targeted therapies in the treatment of moderate to severe plaque psoriasis in Germany. J Dermatolog Treat 2020 Jul 26; 1-7.
10. Rodriguez Fernandez-Freire L, Galán Gutierrez M, Armario Hita JC, Perez-Gil A, Ruiz-Villaverde R. Guselkumab: Short-term effectiveness and safety in real clinical practice. Dermatol Ther 2020; 33: e13344.
11. Fougerousse AC, Ghislain PD, Reguiai Z, Maccari F, Parier J, Bouilly Auvray D, et al. Effectiveness and short-term (16-week) tolerance of guselkumab for psoriasis under real-life conditions: a retrospective multicenter study. J Eur Acad Dermatology Venereol 2020; 34: e644-6.
12. Galluzzo M, Tofani L, Lombardo P, Petruzzellis A, Silvaggio D, Egan CG, et al. Use of guselkumab for the treatment of moderate-to-severe plaque psoriasis: A 1 year real-life study. J Clin Med 2020; 9: 2170.
13. Armstrong A, Puig L, Langley R, Tsai TF, Song M, Wasfi Y, et al. Validation of psychometric properties and development of response criteria for the psoriasis symptoms and signs diary (PSSD): results from a phase 3 clinical trial. J Dermatolog Treat 2019; 30: 27-34.
14. Carlin CS, Feldman SR, Krueger JG, Menter A, Krueger GG. A 50% reduction in the psoriasis area and severity index (PASI 50) is a clinically significant endpoint in the assessment of psoriasis. J Am Acad Dermatol 2004; 50: 859-66.
15. Smith CH, Yiu ZZN, Bale T, Burden AD, Coates LC, Edwards W, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update. Br J Dermatol 2020; 183: 628-37.