Artículo de Investigación

Guselkumab in moderate-to-severe plaque psoriasis: Effectiveness in real clinical practice

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Resumen

Introducción: La psoriasis es una enfermedad cutánea inflamatoria crónica inmunomediada que afecta a casi el 1-2% de la población mundial. El tratamiento biológico de la psoriasis moderada a grave ha cambiado el paradigma de manejo de la enfermedad, permitiendo un mejor control de la misma.

Métodos: Se llevo a cabo un estudio observacional retrospectivo que incluyó a pacientes con psoriasis moderada a grave que fueron tratados durante al menos 36 semanas con guselkumab. La eficacia se evaluó mediante la estimación de pacientes que alcanzaron las respuestas PASI 75, PASI 90 y PASI 100 en las semanas 16, 24 y 36. Se utilizó la prueba T de Student para muestras pareadas para determinar la significación estadística entre PASI al inicio y respuesta PASI en las semanas 16, 24 y 36.

Resultados: Se incluyeron 22 pacientes, 14 mujeres (63, 6%), con una edad media de 48, 7 ± 15, 5 años. El tratamiento con guselkumab redujo el PASI medio de 10, 3 ± 6 al inicio del estudio a 2, 4 ± 2 (p = 0,003), 1, 3 ± 1, 8 (p = 0,001) y 0, 3 ± 0, 6 (p = 0,001) a las 16, 24 y 36 semanas, respectivamente.

Discusión: El primer fármaco en unirse al arsenal terapéutico anti-IL23 fue guselkumab. La eficacia obtenida fue superior a la observada en estudios fase III para PASI 90 y 100 a la semana 36. Existen algunos estudios que han evaluado la eficacia a corto plazo de guselkumab en la práctica clínica real; sin embargo, este fármaco se ha comercializado recientemente, limitando la posibilidad de evaluación durante períodos de tiempo más prolongados.

Conclusión: Guselkumab presenta buenos resultados en el manejo de la psoriasis en adultos. La práctica clínica real a medio y largo plazo será fundamental, con un mayor tamaño muestral y período de seguimiento.

Palabras claves: Biológico; Dermatología; Eficacia; Guselkumab; Soriasis.

Summary

Introduction: Psoriasis is a chronic immune-mediated inflammatory skin disease that affects nearly 1–2% of the population worldwide. Biologic treatment of moderate-to-severe psoriasis has changed the disease management paradigm, allowing for better disease control.

Methods: A retrospective observational study including patients with moderate-to-severe psoriasis who were treated for at least 36 weeks with guselkumab. Efficacy was evaluated by estimating the proportion of patients achieving PASI 75, PASI 90 and PASI 100 responses at weeks 16, 24 and 36. The Student t-test for paired samples was used to determine the significant difference in outcome of patients between PASI at baseline and PASI response at weeks 16, 24 and 36.

Reslts: 22 patients were included, 14 women (63.6%), with mean age of 48.7±15.5. Guselkumab treatment decreased mean PASI from 10.3±6 at baseline to 2.4±2 (p=0.003), 1.3±1.8 (p=0.001) and 0.3±0.6 (p=0.001) at 16, 24 and 36 weeks, respectively.

Discussion: The first anti-IL23 drug family to join the therapeutic arsenal is guselkumab. The efficacy obtained is higher than that observed in phase III studies for PASI 90 and 100 at week 36. There are some studies that have evaluated the short-term effectiveness of guselkumab in real clinical practice; however, this drug has only recently been marketed, limiting the possibility of as yet longer treatment periods.

Conclusion: Guselkumab shows great results in the management of psoriasis in adults. Medium- and long-term real clinical practice will be essential, with a larger sample size and longer follow-up period.

Key words: Biologic; Dermatology; Effectiveness; Guselkumab; Psoriasis.

Psoriasis is a chronic immune-mediated inflammatory skin disease that affects nearly 1–2% of the population worldwide[1]. Approximately 20% of patients have a moderate-to-severe form of the disease[2,3]. It is associated with serious comorbidity, including increased risk for depression, psoriatic arthritis, metabolic disease, major adverse cardiac events (MACEs), diminished quality of life, and overall increased mortality[4].

Over the past two decades, biologic treatment of moderate-to-severe psoriasis has changed the disease management paradigm, allowing for better disease control[5]. Tumor necrosis factor alpha (TNF-α) inhibitors (adalimumab, etanercept, infliximab, and certolizumab pegol), IL-17 pathway inhibitors (ixekizumab, brodalumab, and secukinumab), IL 12/23 inhibitors (ustekinumab), and IL-23 inhibitors (guselkumab, tildrakizumab, risankizumab and mirikizumab) are available for the treatment of moderate-to-severe psoriasis. Guselkumab is a fully human immunoglobulin G1 λ (IgG1λ) monoclonal antibody that binds to the p19 subunit of IL-23[6].

Capsule summary

- Biologic treatment of moderate-to-severe psoriasis has changed the disease management paradigm.
- This original article shows guselkumab as a drug to consider in the management of psoriasis in adults.
- We aim to help the reader to know effectiveness of guselkumab in real clinical practice.

In 2017, the USA's Food and Drug Administration (FDA) and the European Medicines Agency (EMA) approved guselkumab for treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for either systemic therapy or phototherapy[8], based on the phase III clinical trials VOYAGE 1, VOYAGE 2, NAVIGATE and ECLIPSE.

To date, there are only limited post-marketing data available on its effectiveness and tolerance, for that reason, the efficacy of guselkumab in patients with moderate–severe chronic plaque psoriasis is now being evaluated.

Methods and materials

Patients and Study Design

A retrospective observational study including patients with moderate-to-severe psoriasis treated with guselkumab for at least 36 weeks in outpatient consultation at the Pharmacy Department of the Juan Ramón Jiménez University Hospital, in Huelva (Spain). Patients were candidates to receive guselkumab because of contraindications, intolerance or if they had had an inadequate response to conventional systemic treatments (i.e., methotrexate, cyclosporine, or acitretin), or phototherapy (ultraviolet B, psoralen plus ultraviolet A) and failure or intolerance of TNF-α inhibitors. Patients who had not received at least 4 doses of guselkumab were excluded. Patients' data regarding the demographic characteristics (age, sex), comorbidities, previous systemic and/or biological therapies were extracted from the University Hospital's digital database.

Outcome Measures

The Psoriasis Area Severity Index (PASI) was used to assess the severity of plaque psoriasis; its values were recorded at baseline and at weeks 12, 16, 24, 28 and 36 of treatment.

Moderate-to-severe psoriasis was defined as PASI >10 or involvement of sensitive areas such as the face, scalp, hands, or genital areas.

Efficacy was evaluated by estimating the proportion of patients achieving PASI 75 (at least a 75 percent reduction in the PASI score), PASI 90 (at least a 90 percent reduction in the PASI score) and PASI 100 (complete clerarance) responses at weeks 16, 24 and 36.

Statistical Analysis

Descriptive statistics were gathered for each variable, means and standard deviations were used for the description of numerical variables, and absolute and relative frequencies were used for categorical variables. The Student t-test for paired samples was used to determine the significant difference in outcome of patients between PASI at baseline and PASI response at weeks 16, 24 and 36. For the measurement of significant difference in outcome, a confidence interval of 95% was deemed acceptable. Data were analyzed using IBM® SPSS Statistics® v 19.0.

Results

Patient Demographic and Clinical Characteristics

This analysis included 22 patients, 14 of whom were women (63.6%), with a mean age of 48.7±15.5 years. The demographic and clinical features of the study population are summarized in Table 1. All patients had chronic plaque psoriasis. Hypertension, dyslipidemia and depression were the most frequent comorbidities observed (59.1%, 50% and 50%, respectively). Most patients had previously undergone systemic therapy (90%), with methotrexate and cyclosporine being the most prescribed drugs. Most patients had previously been treated with a biologic drug (90%, n=20); nine patients received one biologic, six patients received two biologics and five patients received three or more biologics. Adalimumab, ustekinumab and certolizumab were the most frequent biologic therapies prescribed (45.5%, 40.9% and 40.9%, respectively).

PASI Response

Mean PASI at baseline was 10.3±6.Nineteen patients received guselkumab in a standard dosing regimen (Induction phase: 100 mg subcutaneously at weeks 0 and 4, and a maintenance dose every 8 weeks thereafter) and three patients received guselkumab at week 0 and a maintenance dose every 8 weeks thereafter, without induction phase. Guselkumab treatment decreased mean PASI from 10.3±6 at baseline to 2.4±2 (p=0.003), 1.3±1.8 (p=0.001) and 0.3±0.6 (p=0.001) at 16, 24 and 36 weeks, respectively. Figure 1 shows the evolution of the PASI score. At 16 weeks, PASI 75, 90 and 100 response was achieved in 50%, 31.8% and 22.7% of patients, respectively, at 24 weeks, PASI 75, 90 and 100 response was achieved in 86.4%, 54.5% and 40.9%, respectively, whereas at 36 weeks, PASI 75, 90 and 100 response was achieved in 100%, 77.3% and 72.7% of patients, respectively. Figure 2 shows the evolution of the percentage of patients achieving the PASI 75, 90 and 100 responses.

Subgroup of patients were identified, stratifying patients with PASI score > or <10 at baseline. Regarding the PASI 90 response, patients with PASI score > 10 at baseline achieved before response compared to those with PASI score < 10 at baseline; however the PASI 100 response seems to have been achieved earlier by patients with PASI

Tabla 1
Baseline clinical characteristics of psoriasis patients

	Patients (n=22)
Age (years), average ± SD	**48,7 ± 15.5**
Gender, % (n)	
Female	63.6 (14)
Male	36,4 (8)
Comorbidities, % (n)	
Depression	50 (11)
Diabetes	31.8 (7)
Dyslipidemia	50 (11)
Hypertension	59.1 (13)
Psoriatic arthritis	45.5 (10)
PASI score, average ± SD	**10.3 ± 6**
Previous bDMARD treatments, % (n)	
0	9 (2)
1	40.9 (9)
2	27.3 (6)
≥3	22.7 (5)
Previous treatments, % (n)	
NUVB	45.5 (10)
ACT	68.2 (15)
MTX	50 (11)
CyA	36.4 (8)
IFX	40.9 (9)
ETN	22.7 (5)
ADA	45.5 (10)
UST	40.9 (9)
SEC	31.8 (7)
IXE	36.4 (8)

PASI, psoriasis area and severity index; bDMARD, biologic disease modifying anti-rheumatic drugs; NUVB, narrowband UVB; ACT, acitretin; MTX, methotrexate; CyA, cyclosporin A; IFX, infliximab; ETN, etanercept; ADA, adalimumab; CER, certolizumab; UST, ustekinumab; SEC, secukinumab; IXE, ixekizumab

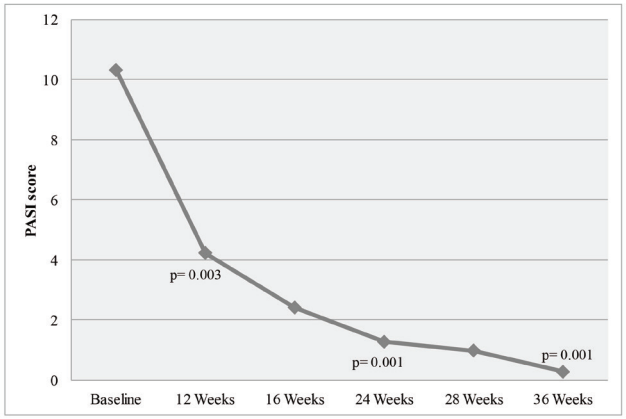

Figure 1
Evolution of the PASI score.

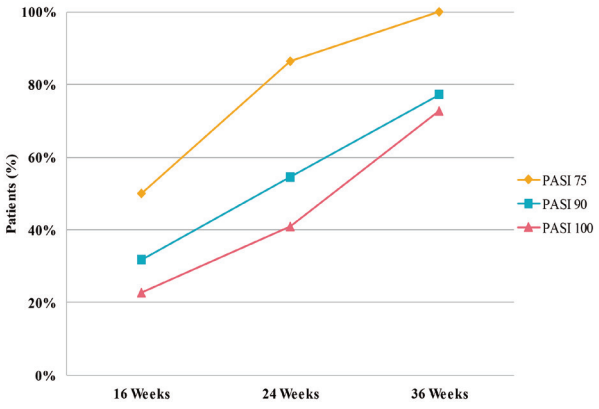

Figure 2
Evolution of the number of patients achieving PASI 75, 90 and 100 responses.

score < 10 at baseline (Figure 3). No significant differences were found between group of patients with PASI score > or <10 at baseline.

Discussion

The first anti-IL23 drug family to join the therapeutic arsenal is guselkumab. The discovery of the IL-23 axis, widely considered the most critical pathogenic pathway in the development of psoriasis, and the development of drugs targeting this pathway, have shifted the paradigm of the management of this condition[8, 9].

In this retrospective study, data were analyzed from 22 patients with moderate-to-severe psoriasis treated with guselkumab who had either not responded, or had contraindications or were intolerant, to conventional systemic treatments (i.e., methotrexate, cyclosporine, or acitretin), phototherapy (ultraviolet B, psoralen plus ultraviolet A), or who had not response (failure or intolerance) to TNF-α inhibitors.

The efficacy obtained is comparable to that observed in phase III studies regarding PASI 75 at week 24 (91.2% in VOYAGE 1 and 89.1% in VOYAGE 2)10, 11. In addition, it is higher than that observed for PASI 90 and 100 at week 36 (76.3% VOYAGE 1 and 47.4% VOYAGE 1, respectively) 10. However, PASI 90 and 100 response values obtained from this study, at weeks 16 and 24, are lower than that observed for VOYAGE 1 and VOYAGE 2 trials[10,11]. It should be noted that, in VOYAGE 1 PASI 100, the response remained relatively unchanged from

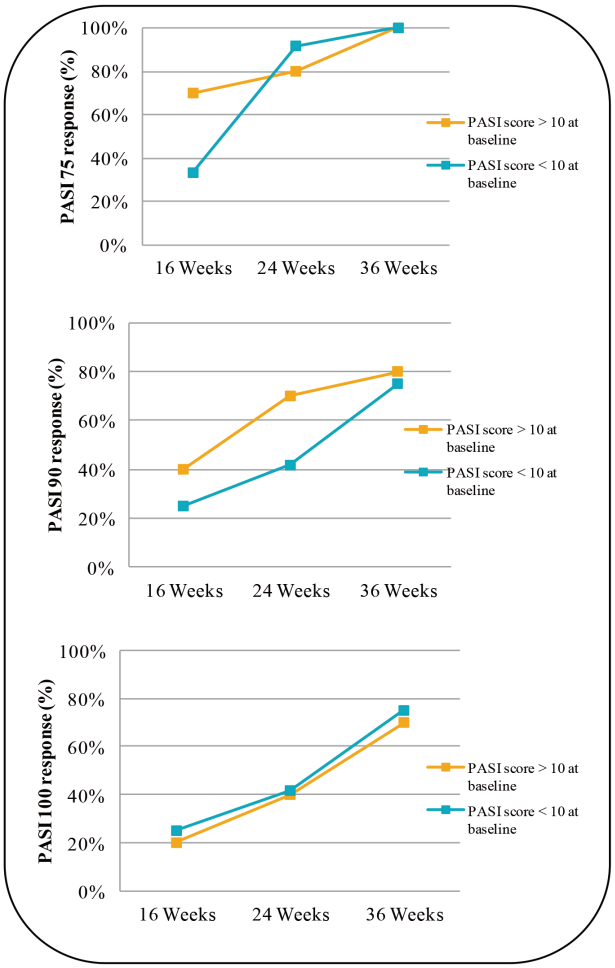

Figure 3
Patients with PASI score < 10 at baseline compared to those with PASI score >10.

week 24 to week 48 (44.4% to 47.4%), nevertheless, in this study, the PASI 100 response increases threefold from week 24 to week 36.

There are some studies that have evaluated the short-term effectiveness of guselkumab in real clinical practice[12-14]. Consistent results reported with clinical trials are even slightly higher. Galluzo M *et al.*[12] retrospectively examined a database of 52 patients with moderate-to-severe psoriasis treated with guselkumab and followed up for 1 year, and they found that the proportion of patients achieving complete remission at early as well as later time points was superior in their study compared to clinical trials. In the study performed by Fougerousse AC *et al.*[13] with 63 patients with moderate-to-severe psoriasis treated with guselkumab over a period of 16 weeks, PASI 90 response at week 16 was lower than that observed for VOYAGE 1 and VOYAGE 2; according to these authors, the differences in characteristics between patients in phase III studies and their patient population could explain these results: lower disease severity. These results are comparable to ours, considering that the 54.5% (n=12) patients had a PASI score <10 at treatment initiation with guselkumab, and the percentage of patients previously exposed to biologics was larger. Another real-life study performed in Spain by Rodriguez Fernandez-Freire L *et al.* presents results that are comparable to ours (100% of patients achieved a PASI 75 response, about 77% patients achieved PASI 90 response, and about 72% achieved PASI 100 at 36 weeks). Real-life experience using guselkumab and findings reported confirm the early, rapid and sustained effectiveness of guselkumab[10].

An important limitation of this study could be the small number of patients and the brief follow-up period. However, this drug has only recently been marketed, limiting the possibility of performing longer treatment periods[15].

Conclusion

Guselkumab shows great results in the management of moderate-to-severe psoriasis in adults, confirming its efficacy in this disease. Medium- and long-term real clinical practice will be essential, with larger sample sizes and longer follow-up periods.

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