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Real-world effectiveness and safety of Guselkumab for the treatment of psoriasis: a 6-month prospective study in a series of psoriatic patients

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Abstract. – OBJECTIVE: Guselkumab is a fully human monoclonal IgG1 antibody which, by selectively binding to the p19 subunit of IL-23, prevents it from binding to the IL-23 receptor on the cell surfaces. To date, no prospective data are available on the efficacy and safety of this drug in everyday clinical practice in patients with psoriasis (PSO).

MATERIALS AND METHODS: This is a longitudinal, single arm, real-world, prospective study to investigate the effect of Guselkumab on PSO and quality of life (DLQI) in 44 PSO patients. Outcomes were PASI, BSA, DLQI at 3 and 6 months.

RESULTS: The longitudinal analysis showed that PASI improved from a median value of 24.1 at baseline to 2.0 at 6-months and this was also true for BSA (from 23.0 to 2.0) and DLQI (from 24.0 to 2.5) (all $p<0.001$). At 6-months, PASI75, PASI90 and PASI100 were 95.5%, 59.1% and 16%, respectively. The PSO improvement related with the increase of DLQI (ΔPASI *vs.* ΔDLQI, r=0.77, $p<0.001$). No clinically relevant adverse events were observed.

CONCLUSIONS: This study demonstrates the effectiveness and safety of Guselkumab on PSO in real world and shows that the reduction of PSO severity due to the drug is directly related with the improvement of quality of life in this patient population.

Key Words:
Guselkumab, Psoriasis, Quality of life.

Abbreviations

IL: interleukin, FDA: food and drug administration, EMA: European Medicines Agency, DLQI: Dermatology Life Quality Index, PSO: Psoriasis, PSA: Psoriatic Arthritis, PASI: Psoriasis Area Severity Index, BSA: Body Surface Area, IQR: Interquartile range.

Introduction

Psoriasis is a chronic, immune-mediated disease affecting about 3% of the worldwide population[1]. This disease often coexists with other complications (such as psoriatic arthritis, cardiovascular impairment, overweight/obesity, anxiety/depression, and inflammatory bowel disease, etc.) which complicate the clinical management of patients[2,3] and negatively impact upon their quality of life and work efficiency[4]. Notwithstanding the use of conventional therapies such as topical medications, phototherapy, and standard systemic treatments[5], to date the prognosis of psoriasis still remains rather unsatisfactory.

Compelling evidence which has emerged so far coherently shows that the etiology of psoriasis includes a dysregulation between keratinocytes and immune cells, a mechanism which involves inflammatory cytokines[6]. On the basis of these findings, biologic and small-molecule drugs, such as tumor necrosis factor/interleukin 12/23 inhibitors, were developed and proposed as valid treatment options to stimulate skin clearance[5,7-18]. Furthermore, to date new biologics[7,19-29] with different mechanisms of action are available, and among these Guselkumab represents a very promising therapeutic option.

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Guselkumab is a fully human monoclonal IgG1 antibody which, by selectively binding to the p19 subunit of IL-23, does not allow it to bind to the IL-23 receptor on the cell surfaces. By this inhibitory mechanism, it prevents the release of inflammatory cytokines and chemokines involved in the pathway leading to the disease[30-32]. This hypothesis is corroborated by exploratory pharmacodynamic studies showing that Guselkumab reduces circulating levels of IL-17A, IL-17F and IL-22 in patients with psoriasis[33]. Guselkumab is also the first in its class to be formally approved in 2017 by FDA and EMA as a treatment option in adults with moderate-to-severe plaque psoriasis who were eligible for systemic therapy with a recommended dosage of 100 mg (administered by subcutaneous injection at 0 and 4 weeks), followed by a maintenance dose every 8 weeks thereafter[32,34-36].

In the setting of a longitudinal, single arm, prospective, observational, cohort study we investigated for the first time the real-world effect of Guselkumab on psoriasis severity and quality of life (assessed by Dermatology Life Quality Index- DLQI) in a series of patients with psoriasis.

Table I. Main demographic and clinical characteristics of the study sample.

	N = 44
Age (years)	52 ± 15
Males (%)	52%
Smoking habit (%)	Never smokers: 41.9% Current smokers: 53.5% Past smokers: 4.7%
Height (cm)	167 ± 9
Weight (kg)	79.9 ± 18.0
BMI (kg/m^2)	28.5 ± 5.3
Familiarity (%)	70.5%
Patients with PSA (%)	9%
Bio-naive patients (%)	32%
Atopic dermatitis (%)	2.3%
Severe psoriasis (%)	6.8%
Lupus-like reaction (%)	2.3%
Paradoxal psoriasiform reaction after secukinumab (%)	2.3%
Pustular psoriasis (%)	2.3%
Hypertension (%)	40.9%
Diabetes mellitus (%)	20.5%
Dyslipidemia (%)	45.5%
Inflammatory bowel disease (%)	2.3%

Data are expressed as mean and standard deviation or as percent frequency, as appropriate.

Patients and Methods

Patients

The study sample was composed of 22 patients with PSO followed-up in outpatient clinics of Grande Ospedale Metropolitano "Bianchi Melacrino Morelli" di Reggio Calabria Italy and 22 from Messina, Italy. The main demographic and clinical characteristics of patients are given in Table I. The study was in conformity with the ethical guidelines of our institutions and with the Declaration of Helsinki and informed consent was obtained from each participant.

Drug Administration/Dose

According to the FDA and EMA indication, all enrolled patients were treated with a dosage of 100 mg (administered by subcutaneous injection at 0 and 4 weeks) of Guselkumab, followed by a maintenance dose every 8 weeks thereafter.

Inclusion/Exclusion Criteria

Data from both male and female patients, aged ≥18 years, with moderate-to-severe plaque psoriasis, who were systemic-treatment naïve or who had failed at least one systemic therapy or relapsed immediately after achieving significant improvement or had contraindications for standard systemic therapies, were considered for this study. For effectiveness analysis data from only those patients who have completed 24 weeks of therapy with Guselkumab were considered.

Outcomes Assessment

The severity of PSO was assessed by the Psoriasis Area and Severity Index (PASI). The PASI is a measure of the average redness, thickness, and scaling of the lesions (each graded on a 0-4 scale), weighted by the area of involvement. The percentage of body surface area (BSA) involved was also measured in categories of 0%, 1-3%, 4-9%, 10-20%, 21-29%, 30-50%, and 51-100%. Quality of life was assessed by Dermatology Life Quality Index (DLQI). These outcomes were collected in all patients, at baseline, 3 months and 6 months. As outcome variables we also considered PASI 75, PASI 90 and PASI 100.

Safety Assessment

Safety assessment was done by analyzing all the AEs reported by the patients during treatment. The primary safety endpoint was the percentage of patients experiencing ≥1 AEs during 24 weeks of treatment.

Statistical Analysis

In Table I, data were summarized as mean and standard deviation or as percent frequency, as appropriate. The evolution over time of PSO (in terms of PASI and BSA), as well as of quality of life (by DLQI), was investigated by plotting the median and the interquartile range (IQR) of these variables at each point in time (that is, at baseline, at 3rd and 6th month). Within-patient comparison across time was performed by the Friedman test. The correlation between two variables considered simultaneously was investigated by the Pearson Product Moment Correlation Coefficient (r) and *p*-value. At baseline, the association between PASI and BSA with DLQI was investigated by adjusting for the potential confounding effect of age and gender. In these analyses, data were expressed as partial correlation coefficient (partial r) and *p*-value. A *p*-value <0.05 was considered statistically significant. Data analysis was performed by a standard statistical package (SPSS for Windows, Version 22, Chicago, IL, USA).

Results

The study sample comprised 44 patients with PSO, in 4 cases (9%) associated with PSA. Their mean age was 52 years, 52.3% were males, 20.5% were diabetics, 45.5% had hypertension, 45.5% had dyslipidemia and only a minority (2.3%) were affected by inflammatory bowel disease. The body mass index was 28.5 kg/m^2 on average. Of note, 32% of individuals were bio naïve. The remaining patients' characteristics are given in Table I. Previous treatments who underwent patients are given in the **Supplementary Table**.

The median values (and IQR) of PASI, BSA and DLQI at baseline were 24.1 (12.8-30.2), 23.0 (15.2-32.0) and 24.0 (18.5-26.0), respectively, and were strongly and significantly interrelated between them (PASI *vs.* DLQI, r=0.76, *p*<0.001; BSA *vs.* DLQI, r=0.59, *p*<0.001) implying that patients with more severe disease had also a more deranged quality of life at study inception. Of note, these associations held true also after data adjustment for the potential confounding effect of age and gender (PASI *vs.* DLQI, partial r=0.78, *p*<0.001; BSA *vs.* DLQI, partial r=0.60, *p*<0.001).

Evolution of PASI, BSA and DLQI Over Time

The evolution of PASI, BSA and DLQI over time is shown in Figure 1. The analysis showed a rapid and marked decrease in the severity of PSO, as well as a concomitant increase of quality of life (the lower the DLQI, the higher the quality of life), during treatment with Guselkumab. PASI reduced from a median value of 24.1 at baseline to 2.0 at 6 months (*p*<0.001) and this was also true for BSA (from 23.0 to 2.0, *p*<0.001) and DLQI (from 24.0 to 2.5, *p*<0.001) (Figure 1). PASI 75, PASI 90 and PASI 100 across time are reported in Figure 2. At 6 months PASI 75, PASI 90 and PASI 100 were 95.5%, 59.1% and 16%, respectively (Figure 2). Of note, the improvement of the disease severity across time (as assessed by PASI and BSA) was paralleled by a marked increase of quality of life (Figure 3) and again these relationships held true also after data adjustment for age and gender (DPASI *vs.* DDLQI, r=0.78, *p*<0.001;D BSA *vs.* D DLQI, r=0.58, *p*<0.001). No adverse events were registered throughout the follow-up period.

Discussion

This is the very first prospective real-world study with a 6 month follow-up period demon-

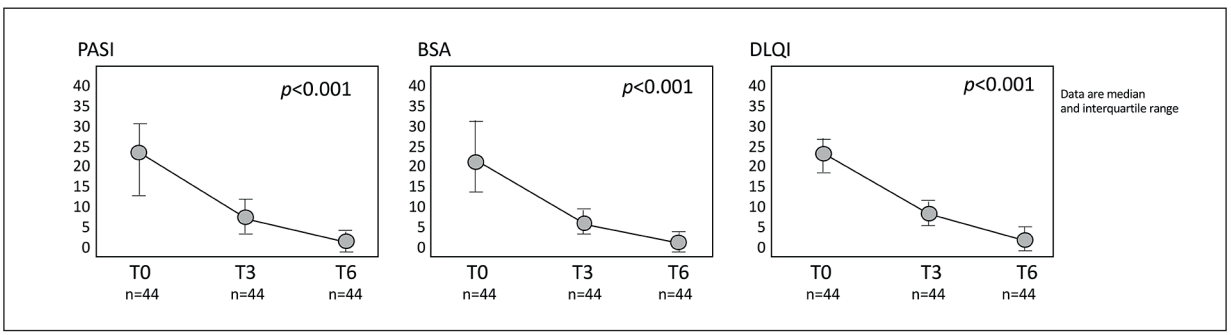

Figure 1. Evolution of PASI, BSA and DLQI of patients across the follow-up period. Data are median and interquartile range.

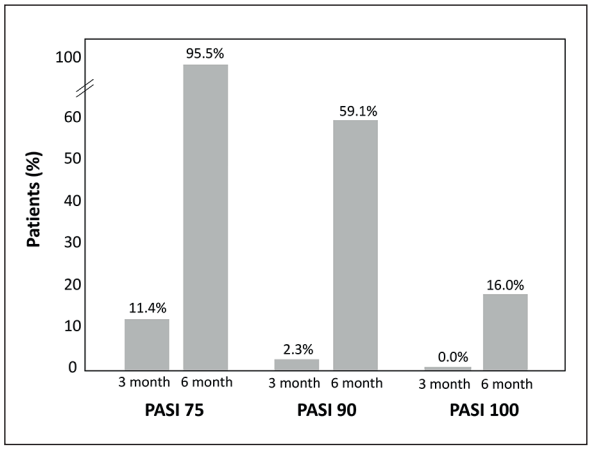

Figure 2. Evolution of PASI 75, PASI 90 and PASI 100 of patients across the follow-up period. Data percent frequencies.

strating that Guselkumab is effective and safe in routine clinical practice of patients with psoriasis and that the reduction of the disease severity due to this drug is closely related to the improvement of quality of life in the same patients' cohort. Of note, at 6 months PASI 75, PASI 90 and PASI 100 were 95.5%, 59.1% and 16%, respectively.

In the Calabria and Sicily regions, Gulsekumab has been available for the treatment of psoriasis since June 2019. Thus, to date, information on the efficacy and safety of Guselkumab in real-world clinical practice is still limited[37-39], whereas data from clinical trials and open extension over a 4-year follow-up period are now available[40]. Once efficacy of a given drug has been successfully demonstrated in an experimental setting, real world studies are requested to provide scientific evidence that the same drug also works in routine clinical practice. For this reason, real-world studies are considered as complementary to randomized controlled clinical trials. The need for real-world analyses on the effectiveness and safety of Guselkumab is mainly due to the fact that patients with psoriasis treated in every day clinical practice may differ from those enrolled in clinical trials because of the stringent inclusion/exclusion criteria adopted in this type of studies. In fact, in the real world, the clinical background of patients (such as comorbidities), as well as the adoption of multiple therapies, may influence the biologic treatment choice and the course of the disease as well. To address these issues, we conducted a prospective, observational, cohort study in a series of 44 patients to assess the effectiveness and safety of Guselkumab in patients with psoriasis attending a real world setting in the Reggio Calabria and Messina dermatology wards. Our results substantially confirm findings from phase 3 clinical trials VOYAGE 1 and 2[21-22]. In particular, PASI 75 at 6 months was 91.2% and 89.1% in the VOYAGE 1 and VOYAGE 2 trials respectively, and the magnitude of such effects did not materially differ from that observed in our study (PASI 75: 95.5%). PASI 90 and PASI 100 were both higher in the VOYAGE 1 (80.2% and 44.4%, respectively) and VOYAGE 2 trials (75.2% and 44.2%, respectively) than those we found in our real-world study (59.1% and 16%). Such differences may depend on the inclusion/exclusion criteria of our study with respect to

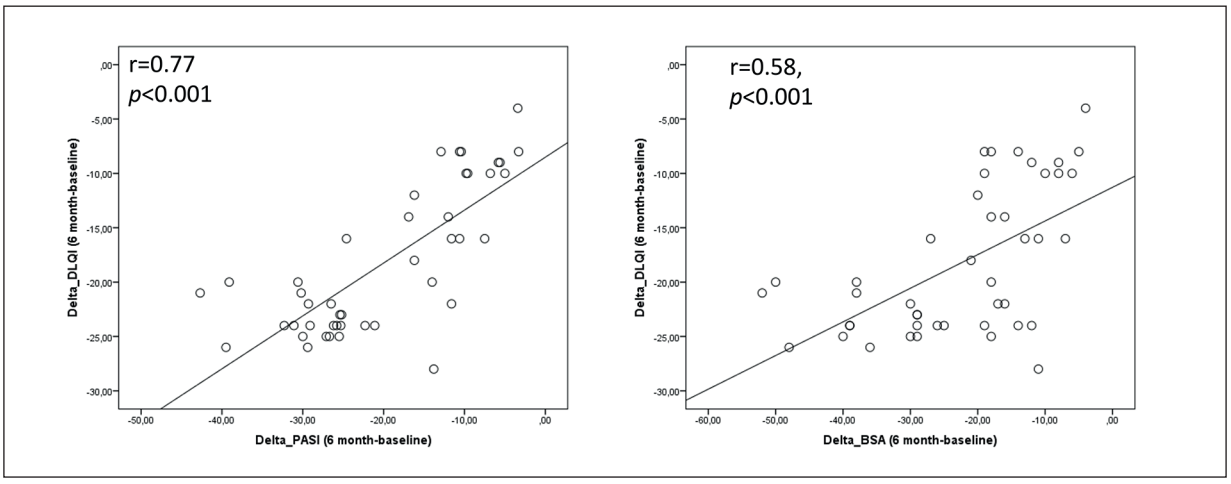

Figure 3. Interrelationships between changes of PASI and BSA with concomitant changes of DLQI. Data are Pearson correlation coefficient and *p*-values.

those contemplated in the VOYAGE 1 and VOYAGE 2 trials. For example, the mean PASI (24.1 *vs.* 21.8) and age (52.0 *vs.* 43.5) were higher and the proportion of males (52.0% *vs.* 69.8%) was lower in our study than in the VOYAGE 2 trial and similar differences were also found in respect to VOYAGE 1 trial.

Another interesting finding which emerged in our study is that DLQI improved in close parallelism with the reduction of psoriasis severity due to Guselkumab. Indeed, we found that changes in DLQI over a 6-month period were strongly related to those of PASI ($r=0.77$, $p<0.001$) and the strength of such a relationship indicates that 59% of the improvement of quality of life (i.e., $0.77^2=0.59$ or 59%) is attributable to the improvement of PASI. In our study, the improvement of DLQI at 6 months *vs.* baseline (-18.2±6.7) was higher than that observed in VOYAGE 1 (-11.6±7.6) and VOYAGE 2 (-11.9±6.7) trials. Such differences may depend on the fact that the quality of life of patients was more impaired in our study (median: 24, interquartile range: 18.5-26.0; mean ± standard deviation: 22.4±5.4) than in those of VOYAGE 1 (14.0±7.5) and VOYAGE 2 (14.7±6.9) trials. Given the fact that the lower the quality of life at enrollment, the higher the margin of improvement due to the drug, differences in DLQI at baseline in part explains the higher magnitude of the effect of Guselkumab which emerged in our real world study compared to that reported in VOYAGE 1 and VOYAGE 2 trials.

Our results are in line with those of Fougerousse et al[41] showing the effectiveness and tolerance of Guselkumab for psoriasis under real-life conditions over a 16-week follow period. However, the novelty of our study is that our study remains the first one describing the effectiveness and safety of Guselkumab by using a prospective (rather than a retrospective) study design and over a longer time period (6 months).

Another specific aim of our study was to assess the safety of Guselkumab in routine clinical practice. In our patients' cohort, the drug has shown a good tolerability profile and no side effects were reported by patients. The absence of relevant adverse effects of the drug which emerged in our study may depend on the relatively low sample size (n=44) and/or reduced follow-up period (up to 6 months). Thus, the safety profile of Guselkumab in the real world needs to be further investigated in larger studies with a longer period of follow-up.

Conclusions

Although this study has the limitation of a relatively short follow-up period and low sample size, it provides promising data supporting the efficacy and safety of Guselkumab in a real-world context. Nonetheless, future studies evaluating the long-term efficacy and safety of Guselkumab are warranted to confirm its usefulness in a chronic disease like psoriasis.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Gudjonsson JE, Elder JT. Psoriasis: epidemiology. Clin Dermatol 2007; 25: 535-546.
2) Kaushik SB, Lebwohl MG. Psoriasis: which therapy for which patient: psoriasis comorbidities and preferred systemic agents. J Am Acad Dermatol 2019; 80: 27-40.
3) Lebwohl MG, Bachelez H, Barker J, Girolomoni G, Kavanaugh A, Langley RG, Paul CF, Puig L, Reich K, van de Kerkhof PC. Patient perspectives in the management of psoriasis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey. J Am Acad Dermatol 2014; 70: 871-881.
4) Bhosle MJ, Kulkarni A, Feldman SR, Balkrishnan R. Quality of life in patients with psoriasis. Health Qual Life Outcomes 2006; 4: 35.
5) Menter A, Gottlieb A, Feldman SR, Van Voorhees AS, Leonardi CL, Gordon KB, Lebwohl M, Koo JYM, Elmets CA, Korman NJ, Beutner KR, Bhushan R. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 1. overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol 2008; 58: 826-850.
6) Eberle FC, Brück J, Holstein J, Hirahara K, Ghoreschi K. Recent advances in understanding psoriasis. F1000Res 2016; 5: 770.
7) Rendon A, Schäkel K. Psoriasis pathogenesis and treatment. Int J Mol Sci 2019; 23; 20. pii: E1475.
8) Menter A, Tyring SK, Gordon K, Kimball AB, Leonardi CL, Langley RG, Strober BE, Kaul M, Gu Y, Okun M, Papp K. Adalimumab therapy for moderate to severe psoriasis: a randomized, controlled phase III trial. J Am Acad Dermatol 2008; 58: 106-115.
9) Gordon KB, Langley RG, Leonardi C, Toth D, Menter MA, Kang S, Heffernan M, Miller B, Hamlin R, Lim L, Zhong J, Hoffman R, Okun MM. Clinical response to adalimumab treatment in patients with

moderate to severe psoriasis: double-blind, randomized controlled trial and open-label extension study. J Am Acad Dermatol 2006; 55: 598-606.

10) Lebwohl M, Blauvelt A, Paul C, Sofen H, Węgłowska J, Piguet V, Burge D, Rolleri R, Drew J, Peterson L, Augustin M. Certolizumab pegol for the treatment of chronic plaque psoriasis: results through 48 weeks of a phase 3, multicenter, randomized, double-blind, etanercept- and placebo-controlled study (CIMPACT). J Am Acad Dermatol 2018; 79: 266-276.
11) Gottlieb AB, Blauvelt A, Thaçi D, Leonardi CL, Poulin Y, Drew J, Peterson L, Arendt C, Burge D, Reich K. Certolizumab pegol for the treatment of chronic plaque psoriasis: results through 48 weeks from 2 phase 3, multicenter, randomized, double-blinded, placebo-controlled studies (CIMPASI-1 and CIMPASI-2). J Am Acad Dermatol 2018; 79: 302-314.
12) Leonardi CL, Powers JL, Matheson RT, Goffe BS, Zitnik R, Wang A. Etanercept as monotherapy in patients with psoriasis. N Engl J Med. 2003; 349: 2014-2022.
13) Papp KA, Tyring S, Lahfa M, Prinz J, Griffiths CEM, Nakanishi AM, Zitnik R, van de Kerkhof PCM, Melvin L, Etanercept Psoriasis Study Group. A global phase III randomized controlled trial of etanercept in psoriasis: safety efficacy, and effect of dose reduction. Br J Dermatol 2005; 152: 1304-1312.
14) Paller AS, Siegfried EC, Langley RG, Gottlieb AB, Pariser D, Landells I, Hebert AA, Eichenfield LF, Patel V, Creamer K, Jahreis A; Etanercept Pediatric Psoriasis Study Group. Etanercept treatment for children and adolescents with plaque psoriasis. N Engl J Med 2008; 358: 241-251.
15) Reich K1, Nestle FO, Papp K, Ortonne JP, Evans R, Guzzo C, Li S, Dooley LT, E M Griffiths C, EXPRESS study investigators. Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: a phase III, multicentre, double-blind trial. Lancet 2005; 366: 1367-1374.
16) Gottlieb AB, Evans R, Li S, Dooley LT, Guzzo CA, Baker D, Bala M, Marano CW, Menter A. Infliximab induction therapy for patients with severe plaque-type psoriasis: a randomized, double-blind, placebo-controlled trial. J Am Acad Dermatol 2004; 51: 534-542.
17) Leonardi CL, Kimball AB, Papp KA, Yeilding N, Guzzo C, Wang Y. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). Lancet 2008; 371: 1665-1674.
18) Landells I, Marano C, Hsu MC, Li S, Zhu Y, Eichenfield LF, Hoeger PH, Menter A, Paller AS, Taieb A, Philipp S, Szapary P, Randazzo B. Ustekinumab in adolescent patients age 12–17 years with moderate-to-severe plaque psoriasis: results of the randomized phase 3 CADMUS study. J Am Acad Dermatol 2015; 73: 594-603.
19) Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths CEM, Papp K, Puig L, Nakagawa H, Spelman L, Sigurgeirsson B, Rivas E, Tsai TF, Wasel N, Tyring S, Salko T, Hampele I, Notter M, Karpov A, Helou S, Papavassilis C, ERASURE Study Group; FIXTURE Study Group. Secukinumab in plaque psoriasis--results of two phase 3 trials. N Engl J Med 2014; 371: 326-338.
20) Blauvelt A, Prinz JC, Gottlieb AB, Kingo K, Sofen H, Mulard MR, Singh V, Pathan R, Papavassilis C, Cooper S; FEATURE Study Group. Secukinumab administration by pre-filled syringe: efficacy, safety, and usability results from a randomized controlled trial in psoriasis (FEATURE). Br J Dermatol 2015; 172: 484-493.
21) Paul C, Lacour JP, Tedremets L, Kreutzer K, Jazayeri S, Adams S, Guindon C, You R, Papavassilis C; JUNCTURE study group. Efficacy, safety and usability of secukinumab administration by autoinjector/pen in psoriasis: a randomized, controlled trial (JUNCTURE). J Eur Acad Dermatol Venereol 2015; 29: 1082-1090.
22) Griffiths CE, Reich K, Lebwohl M, van de Kerkhof P, Paul C, Menter A, Cameron GS, Erickson J, Zhang L, Secrest RJ, Ball S, Braun DK, Osuntokun OO, Heffernan MP, Nickoloff BJ, Papp K; UNCOVER-2 and UNCOVER-3 investigators. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. Lancet 2015; 386: 541-551.
23) Gordon KB, Colombel JF, Hardin DS. Phase 3 trials of ixekizumab in moderate-to-severe plaque psoriasis. N Engl J Med 2016; 375: 2102.
24) Papp KA, Reich K, Paul C, Blauvelt A, Baran W, Bolduc C, Toth D, Langley RG, Cather J, Gottlieb AB, Thaçi D, Krueger JG, Russell CB, Milmont CE, Li J, Klekotka PA, Kricorian G, Nirula A. A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis. Br J Dermatol 2016; 175: 273-286.
25) Lebwohl M, Strober B, Menter A, Gordon K, Weglowska J, Puig L, Papp K, Spelman L, Toth D, Kerdel F, Armstrong AW, Stingl G, Kimball AB, Bachelez H, Wu JJ, Crowley J, Langley RG, Blicharski T, Paul C, Lacour JP, Tyring S, Kircik L, Chimenti S, Duffin KC, Bagel J, Koo J, Aras G, Li J, Song W, Milmont CE, Shi Y, Erondu N, Klekotka P, Kotzin P, Nirula A. Phase 3 studies com- paring brodalumab with ustekinumab in psoriasis. N Engl J Med 2015; 373: 1318-1328.
26) Blauvelt A, Papp KA, Griffiths CE, Randazzo B, Wasfi Y, Shen YK, Li S, Kimball AB. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. J Am Acad Dermatol 2017; 76: 405-417.

27) Reich K, Armstrong AW, Foley P, Song M, Wasfi Y, Randazzo B, Li S, Shen YK, Gordon KB. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: results from the phase III, double- blind, placebo- and active comparator-controlled VOYAGE 2 trial. J Am Acad Dermatol 2017; 76: 418-431.

28) Langley RG, Tsai TF, Flavin S, Song M, Randazzo B, Wasfi Y, Jiang J, Li S, Puig L. Efficacy and safety of guselkumab in patients with psoriasis who have an inadequate response to ustekinumab: results of the randomized, double-blind, phase III NAVIGATE trial. Br J Dermatol 2018; 178: 114-123.

29) Reich K, Papp KA, Blauvelt A, Tyring SK, Sinclair R, Thaçi D, Nograles L, Mehta A, Cichanowitz N, Li Q, Liu K, La Rosa C, Green S, Kimball AB. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (resurface 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. Lancet 2017; 390: 276-288.

30) [No Authors Listed]. Guselkumab (Tremfya) for psoriasis. JAMA 2017; 318: 237-2488.

31) Mease PJ. Inhibition of interleukin-17, interleukin-23 and the TH17 cell pathway in the treatment of psoriatic arthritis and psoriasis. Curr Opin Rheumatol. 2015; 27: 127-133

32) Markham A. Guselkumab: first Global Approval. Drugs 2017; 77: 1487-1492.

33) Megna M, Balato A, Napolitano M, Gallo L, Caso F, Costa L. Psoriatic disease treatment nowadays: unmet needs among the "jungle of biologic drugs and small molecules". Clin Rheumatol 2018; 37: 1739-1741.

34) Puig L. Guselkumab for the treatment of adults with moderate to severe plaque psoriasis. Expert Rev Clin Immunol 2019; 15: 589-597.

35) European Medicines Agency. Guselkumab (tremfya)_Summary of Product Characteristics_EMA, 2017. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/tremfya (accessed 16 October 2019).

36) FDA. TREMFYA® (guselkumab) injection, for subcutaneous use. Prescribing Information. 2017. Available at:http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/TREMFYA-pi.pdf (accessed 4 March 2019).

37) Lee EB, Reynolds KA, Pithadia DJ, Egeberg A, Wu JJ. Drug survival of guselkumab for psoriasis in a realworld setting: a single-center retrospective chart review. J Dermatolog Treat 2019; 8: 1-2.

38) Ladda M, Ighani A, Georgakopoulos J. Efficacy and safety of guselkumab in the treatment of moderate-to-severe plaque psoriasis in real-world clinical practice. 28th EADV Congress Poster n° P1612, 2019.

39) Talamonti M, D'Adamio S, Silvaggio D, Lomabardo P, Bianchi L, Galluzzo M. Guselkumab in the treatment of patients affected by moderate- severe plaque psoriasis: real-word evidence. 28th EADV Congress Poster n° P1757, 2019.

40) Griffiths CEM, Papp KA, Song M. Maintenance of response with up to 4 years of continuous guselkumab treatment: results from the Voyage 1 phase 3 trial. 39th Annual Fall Clinical Dermatology Conference October 2019 Las Vegas.

41) Fougerousse AC, Ghislain PD, Reguiai Z, Maccari F, Parier J, Bouilly Auvray D, Chaby G, Pallure V, Schmutz JL, Clément C, Jacobzone C, Begon E, Esteve E; GEM ResoPso. Effectiveness and short-term (16-week) tolerance of guselkumab for psoriasis under real-life conditions: a retrospective multicenter study. J Eur Acad Dermatol Venereol 2020; 34: e644-e646.