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DERMATOLOGIC THERAPY WILEY

CORRESPONDENCE

# Reply to "Switch from ustekinumab to guselkumab in patients with psoriasis in real clinical practice using the "minimal disease activity" parameter"

Dear Editor,

We read with interest the paper "Switch from ustekinumab to guselkumab in patients with psoriasis in real clinical practice using the "minimal disease activity" parameter" recently published by Magdaleno-Tapial et al. in this journal.[1]

The Authors report the results of a multicenter retrospective study on 32 patients with moderate-to-severe psoriasis switched from ustekinumab to guselkumab, after failure in achieving minimal disease activity[2] within 52 weeks of therapy with the former.

Herein, we report our real-life experience with a similarly sized, single-center retrospective cohort, consisting of 30 patients with moderate-to-severe psoriasis switching from ustekinumab to guselkumab.

The switch was proposed to patients meeting the following inclusion criteria: significant residual Psoriasis Area and Severity Index (PASI) (i.e., failed PASI75), patient-reported dissatisfaction or residual disease in sensitive areas (e.g., face, scalp, palms, soles, and genitals) despite weight-appropriate treatment with ustekinumab for at least 6 months. Need for dose intensification or escalation to dosing every 8 weeks was considered as an adjunctive inclusion criterion.

Patients' characteristics, including demographics, comorbidities, previous treatments, and clinical features are summarized in Table 1. At the baseline, a slight male sex preference (M:F = 3.9:1 vs. 1.5:1), greater representation of cardiovascular comorbidities (7/30 [23.3%] vs. 3/32 [9.3%]) and history of previous treatment with IL-17 inhibitors (4/30 [13.3%] vs. 0) were noted in our cohort. Twenty-nine, 25, and 22 patients reached weeks 12, 24, and 52 of therapy, respectively, counting from the time of switching. Although mean PASI at the time of switching was similar across the two studies (6.45 vs. 7.4), the proportion of patients achieving PASI <1 was lower than that reported by Magdaleno-Tapial et al. both at week 12 (45% vs. 82%), at week 24 (56% vs. 87%) and at week 52 (50% vs. 100%). Nevertheless, the therapeutic target of PASI 75 was achieved by 55% of patients at week 12, by 72% of patients at week 24 and by 82% of patients at week 52; whereas the PASI 90 target was reached by 38% of patients at week 12, by 40% of patients at week 24 and by 45% at week 52 (Figure 1). PASI75 and PASI90 responses, relative to the time of switching, were in line with those obtained in the phase III NAVIGATE trial[3] and real-life studies[4,5] (Table 2), and no switch-related adverse events were reported in our study.

Unsurprisingly, those that achieved a PASI90 response at 52 weeks had lower PASI scores at time of switching than those that

**TABLE 1** Demographics and clinical features of reported patients

| | *n* (%) |
|---|---|
| Gender | |
| Male | 23 (77%) |
| Female | 7 (23%) |
| Age (years), mean ± SD | 53 ± 14 |
| Body mass index, mean ± SD | 27.56 ± 4.72 |
| Comorbidities | |
| Overweight | 16 (53%) |
| Obesity | 5 (16%) |
| Dyslipidemia | 4 (13%) |
| Arterial hypertension | 6 (20%) |
| Diabetes mellitus type 2 | 4 (13%) |
| Psoriatic arthropathy | 1 (3%) |
| Hepatopathy | 4 (13%) |
| Previous conventional systemic treatments | |
| Cyclosporine A | 18 (60%) |
| Methotrexate | 17 (57%) |
| Acitretin | 16 (53%) |
| Narrow band Ultraviolet B Phototherapy | 4 (13%) |
| Photochemotherapy | 3 (10%) |
| Dimethyl fumarate | 1 (3%) |
| Apremilast | 1 (3%) |
| Previous biologic treatments | |
| Ustekinumab only | 15 (50%) |
| Anti-TNF | 12 (40%) |
| Anti-LFA1 | 3 (10%) |
| Anti-IL17 | 4 (13%) |
| Two biologics | 4 (13%) |
| Three biologics | 8 (27%) |
| Four biologics | 3 (10%) |
| Mean duration of ustekinumab treatment (months), mean ± SD | 50.4 ± 32.8 |

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did not (median: 5.1 [interquartile range, IQR: 3.3–7.9] vs. 8 [IQR: 5.6–9.7], $p = 0.04$, Mann–Whitney $U$ test, two-sided). Presence of a relevant burden in terms of comorbidities (i.e., at least two comorbid conditions among arterial hypertension, overweight/obesity, diabetes mellitus type 2, dyslipidemia, cardiovascular disease and psoriatic arthritis) was associated with failure in achieving PASI90 at 52 weeks ($p = 0.007$, chi-square test, two-sided). Moreover, failure in achieving PASI90 at 52 weeks was also associated with previous treatment with ustekinumab 90 mg ($p = 0.035$, chi-square test, two-sided), as an indirect confirmation of the presence of comorbid overweight/obesity in this group. Curiously, the proportion of overweight/obese patients was comparable across the two studies, however, as stated, cardiovascular comorbidities were more represented in our cohort, possibly highlighting the synergistic, detrimental effect of comorbid conditions.

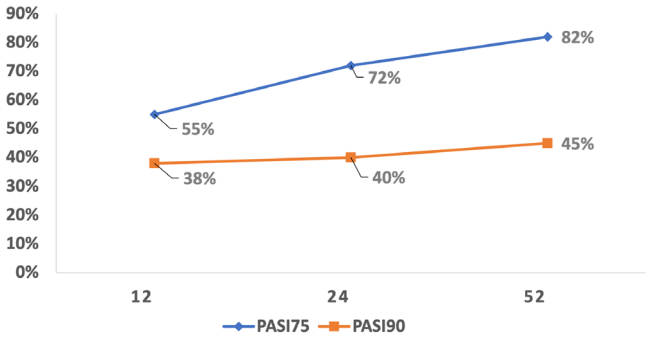


**FIGURE 1** Proportion of patients who achieved Psoriasis Area and Severity Index (PASI) 75 and PASI90 at week 12, 24, and 52.

In conclusion, we reported our real-life experience of switching from ustekinumab to guselkumab in psoriatic patients with inadequate objective and/or subjective clinical response to ustekinumab. Although this strategy leads to substantial improvements, the comorbid burden may hamper the achievement of complete clearance and should be adequately addressed for optimal patient management. Therefore, expectations should be kept realistic, especially in such cases where an unmet need in treating residual disease still exists.[6,7]

**TABLE 2** Psoriasis clinical severity was assessed by means of the Psoriasis Area and Severity Index (PASI) at week 0 (T0), 12 (T12), 24 (T24), 36 (T36), and 52 (T52) of treatment, counting from the time of switching.

| | Present study | Magdaleno-Tapial et al. | Del Alcazar et al. | Ruggiero et al. | Langley et al. |
|---|---|---|---|---|---|
| Patients (*n*) at T0 | 30 | 32 | 105 | 6 | 135 |
| Patients (*n*) at T12 | 29 | | | 6 | |
| Patients (*n*) at T24 | 25 | | 73 | | |
| Patients (*n*) at T52 | 22 | 20 | | 6 | |
| PASI at T0 (mean ± SD) | 6.45 ± 3.17 | | | 12.5 ± 4.2 | 9.8[a] |
| PASI at T12 (mean ± SD) | 2.02 ± 2.09 | 0.6 | | 2 ± 1.5 | |
| PASI at T24 (mean ± SD) | 1.71 ± 2.28 | | 1.4 ± 2.8 | | |
| PASI at T52 (mean ± SD) | 1.28 ± 1.34 | | | 0.4 ± 0.6 | |
| PASI75 at T12, *n* (%) | 16/29 (55%) | | | | |
| PASI90 at T12, *n* (%) | 11/29 (38%) | | | | 65/135 (48.1%) |
| PASI75 at T24, *n* (%) | 18/25 (72%) | | | | |
| PASI90 at T24, *n* (%) | 13/25 (52%) | | 43/73 (58.9%) | | |
| PASI90 at T36, *n* (%) | | | | | NS (51.1%)[b] |
| PASI75 at T52, *n* (%) | 18/22 (82%) | | | | |
| PASI90 at T52, *n* (%) | 10/22 (45%) | | | | |
| PASI <1 at T12, *n* (%) | 13/29 (45%) | 26/32 (82%) | | | |
| PASI <2 at T12, *n* (%) | 16/29 (55%) | | | | |
| PASI <3 at T12, *n* (%) | 20/29 (69%) | | | | |
| PASI <1 at T24, *n* (%) | 14/25 (56%) | 28/32 (85%) | | | |
| PASI <2 at T24, *n* (%) | 15/25 (60%) | | 62/73 (84.9%) | | |
| PASI <3 at T24, *n* (%) | 20/25 (80%) | | | | |
| PASI <1 at T52, *n* (%) | 11/22 (50%) | 20/20 (100%) | | | |
| PASI <2 at T52, *n* (%) | 17/22 (77%) | | | | |
| PASI <3 at T52, *n* (%) | 19/22 (86%) | | | | |

*Note*: The proportion of patients who achieved PASI <1, PASI <2 or PASI <3 at each timepoint was also reported. Responses are compared with those described in the available literature.

Abbreviation: NS, not specified.

[a]The reported numbers and mean PASI at T0 refer to the time of switching/randomization (which took place at week 16 in the NAVIGATE III trial).

[b]T36 refers to 36 weeks since the time of switching/randomization (i.e., week 52 as per reported in the NAVIGATE III trial).

## AUTHOR CONTRIBUTIONS

All authors have made substantial contribution to the work and have approved the final version of this article. Giulia Murgia and Carlo Alberto Maronese contributed to study conception and design. Giulia Murgia, Carlo Alberto Maronese, Carlo Giovanni Carrera, and Angelo Cattaneo contributed to data analysis. Giulia Murgia and Carlo Alberto Maronese reviewed the pertaining literature. Giulia Murgia, Carlo Alberto Maronese, Carlo Giovanni Carrera, Angelo Cattaneo, and Angelo Valerio Marzano edited and approved the final draft.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

## ETHICS STATEMENT

Written informed consent was obtained from the patients for publication of this report.

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