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Original Article

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Comparative Efficacy of Ustekinumab and Guselkumab in Improving Itch in Severe Psoriasis Patients

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ABSTRACT

Background: Biologics effectively improve psoriatic skin lesions, but their impact on itch relief remains unclear.
Objective: To evaluate itch improvement in severe psoriasis patients treated with ustekinumab or guselkumab.
Methods: This retrospective study analyzed patients with severe psoriasis who completed initial efficacy evaluations after treatment with either biologic. Itch severity was assessed using numerical rating scale (NRS), visual analog scale, and verbal rating scale. NRS improvement was evaluated after three injections.
Results: Among 108 patients (74 on ustekinumab, 34 on guselkumab), 77 (71.3%) had moderate-to-severe itch (NRS ≥4) at baseline. Of these, 63 (81.8%) achieved an NRS improvement of ≥4 points. Ustekinumab showed greater itch relief compared to guselkumab in NRS (p=0.033). On the other hand, guselkumab showed more reduction for psoriatic skin lesions than ustekinumab in the Psoriasis Area and Severity Index (p=0.040). In the moderate-to-severe itch group, patients with large plaques experienced significantly greater improvement in NRS than those with small plaques (p=0.012).
Conclusion: While guselkumab is generally preferred for psoriatic skin lesions, ustekinumab may provide superior itch relief.

Keywords: Guselkumab; Pruritus; Psoriasis; Ustekinumab

INTRODUCTION

Pruritus, commonly known as itching, is often overlooked as a significant symptom of psoriasis despite its high prevalence, affecting 60%–90% of patients (itch visual analog scale [VAS, 0–10] score: 5.2–6.4)[1]. Unlike visible skin lesions, psoriatic itch is invisible and frequently underestimated. However, pruritus can profoundly impact patients' quality of life, limiting social and economic activities[2]. Its development involves numerous mediators[3], and although the link between psoriatic lesion severity and itch intensity is unclear, the Koebner phenomenon may play a central role in perpetuating the itch–scratch cycle[4]. Severe itch, when uncontrolled, can lead to scratching, new lesions, and disease exacerbation[2,4].

Biologics have revolutionized the treatment of severe psoriasis[5,6]. Their efficacy is typically assessed using the Psoriasis Area and Severity Index (PASI), often without evaluating itch improvement. Importantly, a reduction in PASI scores does not always correlate with itch relief[2]. Psoriatic itch can occur in lesion-free areas, and patients with prolonged disease may experience chronic

pruritus[2]. Further research is required to better understand the relationship between psoriasis and pruritus and to optimize management strategies.

This study aimed to evaluate itch improvement in patients with severe psoriasis treated with ustekinumab or guselkumab.

MATERIALS AND METHODS

Patients

We retrospectively analyzed data from 108 patients with severe psoriasis treated with either ustekinumab or guselkumab between January 2013 and July 2022 at our institution. Patients who completed first efficacy evaluations after three additional injections were included. The evaluation time point was set at 28 weeks for both ustekinumab and guselkumab. The study was approved by the Institutional Review Board of Kyungpook National University Hospital (KNUH 2022-02-019).

Data collection and analysis

Baseline data included sex, age at biologic initiation, height, weight, medical history, psoriatic lesion locations (scalp, face, nails, acral), psoriasis type (small or large plaque), and disease duration. Psoriasis severity was assessed using the PASI and body surface area (BSA). Itch intensity over the past 24 hours was evaluated using three scales: VAS (0–100: no pruritus to worst possible pruritus), numerical rating scale (NRS, 0–10: no pruritus to most severe pruritus), verbal rating scale (VRS, 0–4: no pruritus to very severe pruritus).

Patients were grouped by initial NRS scores: non-itch (0), mild itch (1–3), and moderate-to-severe itch (≥4). Moderate-to-severe cases were further classified into those with or without itch improvement after treatment. Improvement was defined as an NRS decrease of ≥4 points. **Fig. 1** provides a study flowchart. Differences in demographic characteristics, PASI scores, and BSA values were analyzed between groups.

Statistical analysis

Categorical variables (e.g., sex, lesion location, psoriasis type, medical history) were compared using χ^2 tests. Continuous variables (e.g., age, body mass index [BMI], psoriasis duration, PASI, BSA, VAS, NRS, VRS) were analyzed using Student's t-test or one-way analysis of variance at a significance level of 0.05.

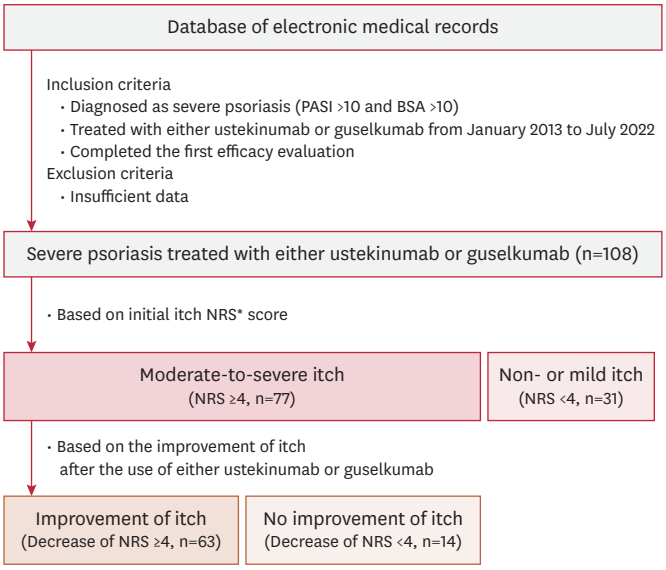

Fig. 1. Flowchart of this study.
PASI: Psoriasis Area and Severity Index, BSA: body surface area, NRS: numerical rating scale.
*NRS: self-rated degree of itch, from 0 (no pruritus) to 10 (most-severe pruritus imaginable).

RESULTS

Patient demographics and characteristics

Table 1 summarizes data for 108 patients (69 males, 39 females) with a mean age of 44.3 years and mean psoriasis duration of 17.0 years. BMI distribution was 0.9% underweight, 51.9% normal weight, 37.0% overweight, and 10.2% obese. Psoriasis types included 38.9% small-plaque and 61.1% large-plaque psoriasis. Mean VAS, NRS, and VRS scores were 59.2, 5.9, and 2.5, respectively.

Among patients, 3 reported no itch, 28 had mild itch, and 77 had moderate-to-severe itch (NRS ≥4). Average NRS scores were 1.4±0.9 for the non/mild itch group and 7.7±1.8 for the moderate-to-severe group. Of the moderate-to-severe group, 81.8% (63/77) showed itch improvement, while 18.2% (14/77) did not. In the moderate-to-severe itch group, large-plaque psoriasis was significantly associated with itch improvement (p=0.012).

PASI and itch intensity changes

Table 2 shows that 104 (96.3%) patients achieved PASI 75 after biologic treatment, where 4 (3.7%) patients are in the non/mild itch group. In the non/mild itch group, average NRS scores changed minimally (1.4 to 1.1). In the moderate-to-severe itch group with improvement, NRS scores significantly decreased (8.0 to 1.4), whereas in the group without improvement, NRS scores changed modestly (6.1 to 4.6).

Biologic distribution and itch improvement

This study included two biologic treatments: ustekinumab and guselkumab. Of the 108 patients, 74 (68.5%) received ustekinumab, and 34 (31.5%) received guselkumab. **Fig. 2** illustrates the distribution of biologics by itch severity and improvement.

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Table 1. Patients' demographic and clinical features

Demographic variables and psoriatic measures	Non- or mild itch (n=31)	Moderate-to-severe itch (n=77)		Total (n=108)
		Improvement (n=63)	No improvement (n=14)	
Age	50.7±12.8	41.6±12.8	42.4±12.3	44.3±13.2
Male	15 (48.4)	46 (73.0)	8 (57.1)	69 (63.9)
Duration of psoriasis (yr)	18.3±12.5	15.7±9.8	19.5±13.6	17.0±11.1
Body mass index (kg/m^2)				
Underweight (<18.5)	0 (0.0)	1 (1.6)	0 (0.0)	1 (0.9)
Healthy weight (18.5–24.9)	17 (54.8)	33 (52.4)	6 (42.9)	56 (51.9)
Overweight (25.0–29.9)	11 (35.5)	22 (35.0)	7 (50.0)	40 (37.0)
Obesity (≥30)	3 (9.7)	7 (11.0)	1 (7.1)	11 (10.2)
Location of psoriatic skin lesions				
Scalp	9 (29.0)	37 (58.7)	10 (71.4)	56 (51.9)
Face	7 (22.6)	27 (42.9)	6 (42.9)	40 (37.0)
Nail	18 (58.1)	35 (55.6)	8 (57.1)	61 (56.5)
Acral	18 (58.1)	38 (60.3)	8 (57.1)	64 (59.3)
Type of psoriasis				
Small plaque	16 (51.6)	18 (28.6)	8 (57.1)	42 (38.9)
Large plaque	15 (48.4)	45 (71.4)	6 (42.9)	66 (61.1)
Medical history				
Diabetes mellitus	0 (0.0)	3 (4.8)	0 (0.0)	3 (2.8)
Hypertension	4 (12.9)	8 (12.7)	3 (21.4)	15 (13.9)
PASI score (0–72)	18.0±8.7	20.4±10.0	15.8±5.0	19.1±9.2
BSA (%)	26.1±16.7	29.7±16.0	22.6±13.0	27.7±16.0
Itch measurement				
VAS (0–100)	14.5±9.6	80.5±17.3	62.1±17.6	59.2±32.9
NRS (0–10)	1.4±0.9	8.0±1.8	6.1±1.5	5.9±3.3
VRS (0–4)	1.0±0.4	3.2±0.8	2.4±0.8	2.5±1.2

Values are presented as mean ± standard deviation or number (%).
PASI: Psoriasis Area and Severity Index, BSA: body surface area, VAS: visual analog scale, NRS: numerical rating scale, VRS: verbal rating scale.

Table 2. Changes in the PASI score, BSA, and itch intensity after biologic use

Psoriatic measures	Non- or mild itch (NRS <4, n=31)		Moderate-to-severe itch (NRS ≥4, n=77)			
			Improvement (n=63)		No improvement (n=14)	
	Baseline	Week 28	Baseline	Week 28	Baseline	Week 28
PASI score	18.0±8.7	1.2±1.7	20.4±10.0	1.7±2.4	15.8±5.0	2.4±6.7
BSA (%)	26.1±16.7	3.0±4.7	29.7±16.1	3.3±4.8	22.6±13.0	4.5±11.9
Itch						
VAS (0–100)	14.5±9.6	10.3±16.0	80.5±17.3	14.0±13.9	62.1±17.6	39.3±23.0
NRS (0–10)	1.4±0.9	1.1±1.6	8.0±1.8	1.4±1.4	6.1±1.5	4.6±2.3
VRS (0–4)	1.0±0.4	0.5±0.5	3.2±0.8	0.8±0.7	2.4±0.8	1.6±0.9

Values are presented as mean ± standard deviation.
PASI: Psoriasis Area and Severity Index, BSA: body surface area, NRS: numerical rating scale, VAS: visual analog scale, VRS: verbal rating scale.

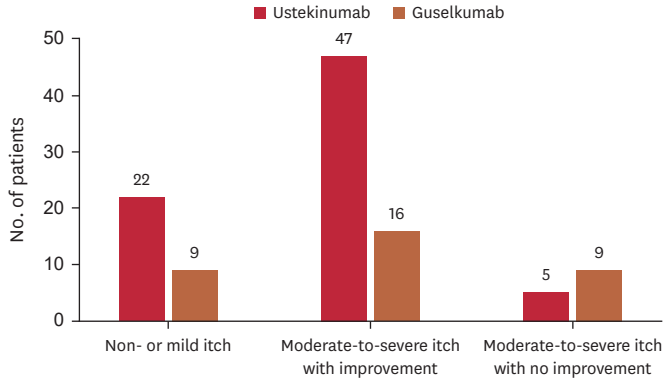

Fig. 2. Number of patients treated with ustekinumab or guselkumab according to initial itch intensity and itch improvement.

In the ustekinumab group, 52 patients (70.3%) initially had moderate-to-severe itch. Of these, 47 patients (90.4%) experienced itch improvement, while 5 (9.6%) showed no improvement. In the guselkumab group, 25 patients (73.5%) had moderate-to-severe itch at the start. Of these, 16 patients (64.0%) showed improvement, and 9 (36.0%) did not.

Notably, the improvement in itch intensity (NRS) was significantly greater in the ustekinumab group (mean change, 4.6) compared to the guselkumab group (mean change, 3.1) (p=0.033). On the other hand, guselkumab showed more reduction for psoriatic skin lesions than ustekinumab in PASI (p=0.040). If the moderate-to-severe itch group is considered, the improvement in itch intensity (NRS) was much greater than in ustekinumab

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Table 3. Characteristics of patients without improvement in moderate-to-severe itch intensity

Demographic variables and psoriatic measure	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12	Case 13	Case 14
Sex	M	F	M	F	M	M	M	F	F	M	F	M	F	M
Age (yr)	60	16	28	41	46	59	45	39	48	42	27	43	55	45
Duration of psoriasis (yr)	50	8	17.3	33.8	10.3	31.2	2.3	14	18	7.9	25	10.8	35	10
Height (cm)	168	165	172	164	187	170	176	160	164	167	163	176	158	181
Weight (kg)	74	52	110	70	100	67	78	60	65	74	52	80	63	80
Body mass index (kg/m^2)	26.2	19.1	37.2	26.3	28.6	23.2	25.2	23.4	24.2	26.5	19.6	25.8	25.2	24.4
Location of psoriatic skin lesions (scalp, face, nail, acral)	Nail, Acral	Scalp	Scalp, Face, Nail, Acral	Scalp, Face	Scalp, Nail, Acral	Scalp, Nail	Nail, Acral	Scalp, Acral	Scalp, Face, Nail, Acral	Scalp, Face, Nail, Acral	None	Scalp, Face, Acral	None	Scalp, Face, Nail
Type of psoriasis (small plaque, large plaque)	Small	Large	Large	Small	Small	Large	Large	Large	Large	Small	Small	Small	Small	Small
Medical history	-	-	-	HTN	-	-	-	-	-	HTN	-	HTN	-	-
Type of biologics	Us	Us	Us	Us	Us	Gu	Gu	Gu	Gu	Gu	Gu	Gu	Gu	Gu
At baseline														
PASI score (0–72)	10.5	11.6	22.5	16.9	21.6	10.4	15.9	14.3	21.4	16.6	11.4	24.4	12.6	10.5
BSA (%)	18	10	44	22	34	11	16	14	29	24	14	52	18	10
Itch measurement														
VAS (0–100)	80	70	90	50	30	50	70	50	90	70	70	50	50	50
NRS (0–10)	8	7	8	5	4	5	7	6	9	6	6	5	5	5
VRS (0–4)	3	3	3	2	1	2	2	2	4	3	3	2	2	2
At week 28														
PASI score (0–72)	0.8	0.9	2.2	0.9	0.8	0	0.4	3.5	0	0	0	0.4	0	0
BSA (%)	1	1.5	4	2	2	0	1	10	0	0	0	1	0	0
Itch measurement														
VAS (0–100)	50	40	70	10	20	80	70	20	60	30	40	20	20	20
NRS (0–10)	5	4	8	2	2	8	7	3	8	4	5	3	2	3
VRS (0–4)	1	1	3	1	1	2	2	2	4	1	1	2	1	2

M: male, F: female, HTN: hypertension, Us: ustekinumab, Gu: guselkumab, PASI: Psoriasis Area and Severity Index, BSA: body surface area, VAS: visual analog scale, NRS: numerical rating scale, VRS: verbal rating scale.

(mean change, 6.3; standard deviation [SD], 2.2) compared to the guselkumab group (mean change, 4.3; SD, 2.9) (p=0.001).

Characteristics of patients without itch improvement

Table 3 details the 14 patients without itch improvement. Baseline PASI scores (>10; range, 10.4–24.4) indicated severe psoriasis, and initial NRS scores (4–9) reflected moderate-to-severe itch. Despite PASI reductions exceeding 75% (92.3% in 13 patients exceeded and 6 [43%] patients achieved complete clearance), itch-related VAS, NRS, and VRS scores remained unchanged (mean change, 22.9, 1.6, and 0.8, respectively).

DISCUSSION

Itch is a key symptom of inflammatory skin diseases like atopic dermatitis (AD) and psoriasis, with significant psychosocial impacts, including reduced quality of life, poor sleep, and fatigue from nocturnal scratching[7,8]. Approximately 60%–90% of psoriasis patients experience pruritus[1], yet it remains underrecognized, even with the advent of biologics[9].

Psoriatic itch plays a role in disease progression through the itch–scratch cycle, where scratching worsens plaques or triggers new lesions via the Koebner phenomenon[10]. Although traditionally considered less severe than AD-related itch, recent meta-analyses show comparable baseline itch intensity between moderate-to-severe psoriasis and AD, emphasizing its underestimated impact on patients' lives[11].

In this study, severe psoriasis patients (BSA >10, PASI >10) were categorized by itch severity (NRS, 0, 1–3, ≥4). Most patients (71.3%) had moderate-to-severe itch, with an average NRS score of 7.7 in this group, significantly higher than previous studies. This may reflect the high disease severity in our cohort, though itch intensity does not always correlate with PASI scores, warranting further research into this relationship.

The clinical factor influencing the improvement in moderate-to-severe itch, specifically plaque type (small vs. large), suggests that itch may depend more on psoriasis type than on severity. Biologics targeting the interleukin (IL)-23/17 pathway have transformed psoriasis treatment, with IL-23 being crucial for Th17 cell maintenance[12,13]. Ustekinumab (IL-12/23 inhibitor) and guselkumab (IL-23 inhibitor) have demonstrated efficacy, though

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their roles in itch remain unclear.

In this study, 63 of 77 patients (81.8%) with moderate-to-severe itch improved following treatment, with 90.4% of ustekinumab-treated patients showing improvement compared to 64.0% for guselkumab. Despite guselkumab's superior efficacy in clearing skin lesions, ustekinumab was more effective in relieving itch, possibly due to its dual blockade of IL-12/23. IL-12 could play a crucial role in psoriatic itch by influencing both inflammatory and neurogenic pathways. It promotes interferon-γ secretion, which enhances skin inflammation and increases the expression of nerve growth factors that sensitize peripheral nerves, leading to heightened itch perception (pruriception)[14-16]. Additionally, IL-12 contributes to keratinocyte hyperproliferation, impairing the skin barrier and increasing exposure to external irritants and transepidermal water loss, which exacerbate itch[17]. These findings suggest IL-12/23 inhibition may better address psoriatic pruritus, though larger studies are needed to confirm this.

Notably, 18.2% of patients with moderate-to-severe itch reported persistent pruritus despite lesion improvement, highlighting the multifactorial nature of psoriatic itch. Current biologics targeting single cytokine pathways may fall short, and alternative therapies like Janus kinase inhibitors, which block multiple itch mediators, could offer solutions for refractory cases.

The study has several limitations. First, the small sample size of only 108 patients limits the ability to conduct comprehensive subgroup analyses, particularly for those without itch improvement, which reduces the generalizability of the findings. Additionally, the study was conducted at a single institution, meaning the results may not reflect the broader diversity of patient populations or clinical settings. The follow-up period was relatively short with evaluations at 28 weeks potentially missing long-term trends in itch improvement or relapse. Moreover, factors such as comorbid conditions, concurrent medications, and lifestyle influences on itch improvement were not thoroughly analyzed. Finally, while the study compared ustekinumab and guselkumab, it did not include other biologics commonly used in psoriasis treatment, thus limiting the conclusions drawn regarding itch management across different treatments.

In conclusion, while guselkumab excels in treating skin lesions, ustekinumab appears more effective for itch relief. As treatments for skin symptoms advance, addressing pruritus as a significant, quality-of-life-affecting symptom becomes increasingly important. Further research into psoriatic itch pathogenesis, qualitative assessment, and tailored treatments is essential.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

DATA SHARING STATEMENT

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

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