Original paper

Efficacy of guselkumab compared with adalimumab for psoriasis: a meta-analysis of randomized controlled studies

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Abstract

Introduction: The efficacy of guselkumab versus adalimumab for psoriasis remains controversial.
Aim: We conducted a systematic review and meta-analysis to explore the influence of guselkumab versus adalimumab on treatment efficacy for psoriasis.
Material and methods: We have searched PubMed, Embase, Web of Science, EBSCO, and Cochrane library databases for randomized controlled trials (RCTs) published until March 2021 and assessing the efficacy and safety of guselkumab versus adalimumab for psoriasis. This meta-analysis was performed using the random-effects model.
Results: Three RCTs were included in the meta-analysis. Overall, compared with adalimumab for psoriasis, guselkumab was associated with improved PASI 100 (OR = 2.18; 95% CI: 1.47 to 3.23; $p = 0.0001$), PASI 90 (OR = 2.63; 95% CI: 2.11 to 3.27; $p < 0.00001$), PASI 75 (OR = 3.10; 95% CI: 2.35 to 4.08; $p < 0.00001$) and PGA 0/1 (OR = 2.04; 95% CI: 1.26 to 3.31; $p = 0.004$), as well as decreased DLQI (SMD = –0.24; 95% CI: –0.34 to –0.13; $p < 0.00001$). In addition, guselkumab resulted in higher DLQI score 0/1 (OR = 1.88; 95% CI: 1.51 to 2.33; $p < 0.00001$) than adalimumab.
Conclusions: Guselkumab showed better efficacy than adalimumab for psoriasis.

Key words: guselkumab, adalimumab, psoriasis, efficacy, randomized controlled trials.

Introduction

Psoriasis is known as a chronic immune-mediated inflammatory disease, and its treatment is still a big challenge despite the development of therapeutic options [1–5]. These patients often desire complete skin clearance and improved long-term efficacy [6–8]. Selectively blocking the interleukin (IL)-23 or IL-17 pathways has become an important approach to treat psoriasis [9–11].

Previous findings confirmed that selective inhibition of IL-23 facilitated clinical response and molecular improvements in the skin [12–14]. Guselkumab, a fully human IgG1 lambda monoclonal antibody, can bind IL-23 and block binding and signalling through its receptor. Guselkumab was injected subcutaneously with 100 mg once every 8 weeks. Phase I and phase II revealed high levels of efficacy [9, 14]. Adalimumab, an anti-tumor necrosis factor α (TNF-α) therapy, has been widely used for the treatment of moderate-to-severe plaque psoriasis [15–18].

Recently, several studies have compared the efficacy of guselkumab with adalimumab for psoriasis, but their results show some inconsistency [9, 19, 20].

Aim

This meta-analysis of RCTs aims to assess the efficacy of guselkumab versus adalimumab for psoriasis.

Material and methods

This systematic review and meta-analysis were performed based on the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement and Cochrane Handbook for Systematic Reviews of Interventions [21, 22]. No ethical approval and patient

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consent were required because all analyses were based on previously published studies.

Literature search and selection criteria

We have systematically searched several databases including PubMed, Embase, Web of Science, EBSCO, and the Cochrane library for RCTs published from inception to March 2021 with the following keywords: "guselkumab", and "adalimumab", and "psoriasis". The reference lists of retrieved studies and relevant reviews were also handsearched and the above process was performed repeatedly in order to include additional eligible studies.

The inclusion criteria were presented as follows: (1) study design is RCT, (2) patients are diagnosed as psoriasis, and (3) intervention treatments are guselkumab versus adalimumab.

Data extraction and outcome measures

Some baseline information was extracted from the original studies, and they included the first author, number of patients, age, body mass index (BMI), duration of psoriasis and detailed methods in two groups. Data were extracted independently by two investigators, and discrepancies were resolved by consensus. We have contacted the corresponding author to obtain the data when necessary.

The primary outcomes were 100% or greater improvement from baseline in Psoriasis Area and Severity Index (PASI 100), PASI 90, PASI 75. Secondary outcomes included physician Global Assessment (PGA) 0/1, change in Dermatology Life Quality Index score (DLQI), and DLQI score 0/1.

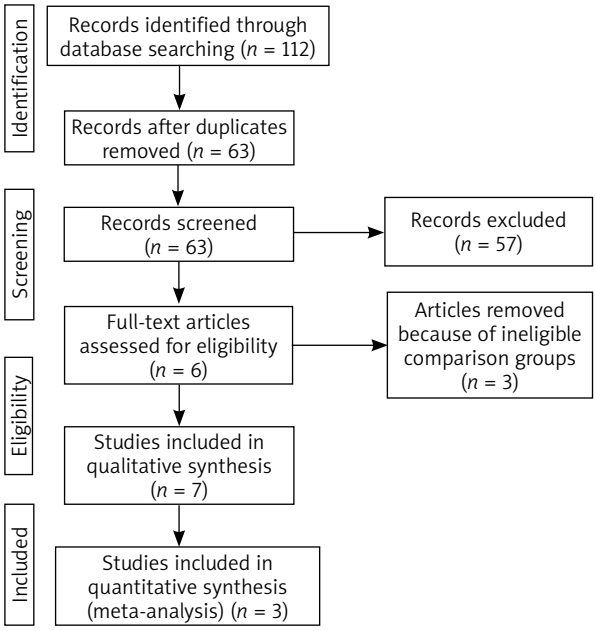

Figure 1. Flow diagram of the study searching and selection process

Quality assessment in individual studies

The methodological quality of each RCT was assessed by the Jadad Scale which consists of three evaluation elements: randomization (0–2 points), blinding (0–2 points), dropouts and withdrawals (0–1 points) [23]. One point would be allocated to each element if they have been conducted and mentioned appropriately in the original article. The score of Jadad Scale varies from 0 to 5 points. An article with Jadad score ≤ 2 is considered to be of low quality. The study is thought to be of high quality if Jadad score ≥ 3 [24].

Statistical analysis

We assessed the odd ratio (OR) with 95% confidence interval (CI) for dichotomous outcomes (PASI 100, PASI 90, PASI 75, PGA 0/1, and DLQI score 0/1) and standard mean difference (SMD) with 95% CI for continuous outcomes (change in DLQI). Heterogeneity was evaluated using the I^2 statistic, and $I^2 > 50\%$ indicated significant heterogeneity [25]. The random-effects model was used for all meta-analyses. We searched for potential sources of heterogeneity for significant heterogeneity. Sensitivity analysis was performed to detect the influence of a single study on the overall estimate via omitting one study in turn or performing the subgroup analysis. Owing to the limited number (< 10) of included studies, publication bias was not assessed. Results were considered as statistically significant for $p < 0.05$. All statistical analyses were performed using Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK).

Results

Literature search, study characteristics and quality assessment

Figure 1 showed the detail flowchart of the search and selection results. 112 potentially relevant articles were identified initially. Finally, three RCTs were included in the meta-analysis [9, 19, 20].

The baseline characteristics of three included RCTs were shown in Table 1. These studies were published between 2015 and 2017, and the total sample size was 1658. Among the included RCTs, guselkumab was administered at a dose of 100 mg weeks 0 and 4, then every 8 week or 200 mg at weeks 0 and 4 and every 12 weeks thereafter. Adalimumab was taken at the dose of 80 mg week 0, then 40 mg week 1, and every 2 weeks. Among three included RCTs, all three studies reported each outcomes [9, 19, 20]. Jadad scores of the three included studies varied from 4 to 5, and all three studies have high quality based on the quality assessment.

Primary outcomes: PASI 100, PASI 90 and PASI 75

The random-effects model was used for the analysis of primary outcomes. The results found that compared to adalimumab for psoriasis, guselkumab was associated with improved PASI 100 (OR = 2.18; 95% CI: 1.47 to 3.23; $p = 0.0001$) with significant heterogeneity among the studies ($I^2 = 51\%$, heterogeneity $p = 0.0001$, Figure 2), PASI 90 (OR = 2.63; 95% CI: 2.11 to 3.27; $p < 0.00001$) with no heterogeneity among the studies ($I^2 = 0\%$, heterogeneity $p = 0.57$, Figure 3) and PASI 75 (OR = 3.10; 95% CI: 2.35 to 4.08; $p < 0.00001$) with no heterogeneity among the studies ($I^2 = 0\%$, heterogeneity $p = 0.37$, Figure 4).

Sensitivity analysis

There was significant heterogeneity for PASI 100. However, some heterogeneity was still seen when performing sensitivity analysis by omitting one study in each turn.

Secondary outcomes

In comparison with adalimumab for psoriasis, guselkumab resulted in the obvious increase in substantially improved PGA 0/1 (OR = 2.04; 95% CI: 1.26 to 3.31; $p = 0.004$; Figure 5), decreased DLQI (SMD = –0.24; 95% CI: –0.34 to –0.13; $p < 0.00001$; Figure 6) and higher DLQI score 0/1 (OR = 1.88; 95% CI: 1.51 to 2.33; $p < 0.00001$; Figure 7).

Discussion

Guselkumab was documented to be highly effective in treating a broad moderate-to-severe psoriasis population [20]. VOYAGE 2 revealed that guselkumab was superior to placebo at the week-16 coprimary endpoints (IGA 0/1 and PASI 90), and was also superior to adalimumab in terms of IGA 0/1, PASI 75/PASI 90 [19]. Guselkumab had the potential in treating difficult regional psoriasis, including scalp, nails, and hands/feet, which was evidenced by improvements in the patient-reported outcomes evaluated in VOYAGE 1 [20].

Our meta-analysis confirmed that guselkumab was able to produce better treatment efficacy than adalimumab for psoriasis, which was supported by the improvement in PASI 100, PASI 90, PASI 75, PGA 0/1 and DLQI score 0/1. In addition, significant improvements in health-related quality of life (Medical Outcomes Study 36-Item Short Form) were reported in VOYAGE 2 after guselkumab treatment, which was superior to both placebo and adalimumab [19].

Guselkumab was effective in treating adalimumab nonresponders (not achieving PASI 90). After 20 weeks of guselkumab treatment, two thirds of the 112 adalimumab nonresponders who switched to guselkumab were reported to achieve PASI 90 [19]. The mechanisms

Table 1. Characteristics of included studies

No.	Author	Guselkumab group						Adalimumab group						Jada scores
		Number	Age [years]	Female (*n*)	BMI [kg/m^2]	Duration of psoriasis [years]	Methods	Number	Age [years]	Female (*n*)	BMI [kg/m^2]	Duration of psoriasis [years]	Methods	
1	Reich 2017	496	43.7 ±12.2	147	29.6 ±6.5	17.9 ±12.0	Guselkumab 100 mg weeks 0 and 4, then every 8 weeks	248	43.2 ±11.9	78	29.6 ±6.6	17.6 ±11.7	Adalimumab 80 mg week 0, then 40 mg week 1, and every 2 weeks through week 23	5
2	Blauvelt 2017	329	43.9 ±12.74	89	29.7 ±6.22	17.9 ±12.27	Guselkumab 100 mg weeks 0 and 4, then every 8 weeks	334	42.9 ±12.58	85	29.8 ±6.48	17.0 ±11.27	Adalimumab 80 mg week 0, 40 mg week 1, then 40 mg every 2 weeks through week 47	5
3	Gordon 2015	208	44.0, median	59	–	18.5 ±12.17	Guselkumab (5 mg at weeks 0 and 4 and every 12 weeks thereafter, 15 mg every 8 weeks, 50 mg at weeks 0 and 4 and every 12 weeks thereafter, 100 mg every 8 weeks, or 200 mg at weeks 0 and 4 and every 12 weeks thereafter) through week 40	43	50.0	13	–	19.3 ±12.79	Adalimumab 80 mg week 0, 40 mg week 1, then 40 mg every 2 weeks	4

Study or subgroup	Guselkumab group Events	Total	Adalimumab group Events	Total	Weight (%)	Odds ratio IV, random, 95% CI
Blauvelt 2017	123	329	57	334	43.1	2.90 [2.02, 4.17]
Gordon 2015	12	42	11	43	13.6	1.16 [0.45, 3.03]
Reich 2017	169	496	51	248	43.3	2.00 [1.39, 2.86]
Total (95% CI)		**867**		**625**	**100.0**	**2.18 [1.47, 3.23]**
Total events	304		119			

Heterogeneity: $\tau^2 = 0.06$; $\chi^2 = 4.12$, d$f = 2$ ($p = 0.13$); $I^2 = 51\%$
Test for overall effect: $Z = 3.87$ ($p = 0.0001$)

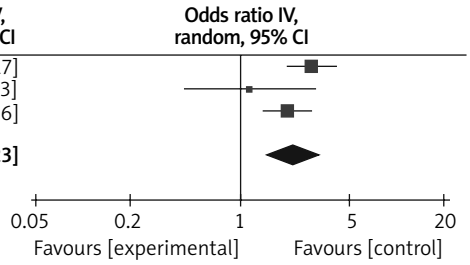

Figure 2. Forest plot for the meta-analysis of PASI 100

Study or subgroup	Guselkumab group Events	Total	Adalimumab group Events	Total	Weight (%)	Odds ratio IV, random, 95% CI
Blauvelt 2017	241	329	166	334	45.3	2.77 [2.00, 3.84]
Gordon 2015	24	42	19	43	6.5	1.68 [0.71, 3.97]
Reich 2017	347	496	116	248	48.2	2.65 [1.93, 3.63]
Total (95% CI)		**867**		**625**	**100.0**	**2.63 [2.11, 3.27]**
Total events	612		301			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.14$, d$f = 2$ ($p = 0.57$); $I^2 = 0\%$
Test for overall effect: $Z = 8.66$ ($p < 0.00001$)

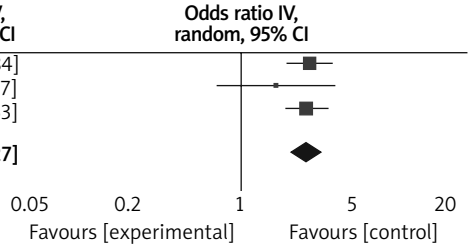

Figure 3. Forest plot for the meta-analysis of PASI 90

Study or subgroup	Guselkumab group Events	Total	Adalimumab group Events	Total	Weight (%)	Odds ratio IV, random, 95% CI
Blauvelt 2017	300	329	244	334	37.3	3.82 [2.43, 5.99]
Gordon 2015	34	42	30	43	7.5	1.84 [0.67, 5.05]
Reich 2017	428	496	170	248	55.3	2.89 [1.99, 4.18]
Total (95% CI)		**867**		**625**	**100.0**	**3.10 [2.35, 4.08]**
Total events	762		444			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.98$, d$f = 2$ ($p = 0.37$); $I^2 = 0\%$
Test for overall effect: $Z = 8.04$ ($p < 0.00001$)

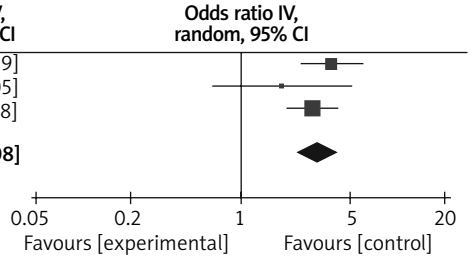

Figure 4. Forest plot for the meta-analysis of PASI 75

Study or subgroup	Guselkumab group Events	Total	Adalimumab group Events	Total	Weight (%)	Odds ratio IV, random, 95% CI
Blauvelt 2017	66	90	53	95	44.9	2.18 [1.17, 4.04]
Gordon 2015	35	42	25	43	20.1	3.60 [1.31, 9.91]
Reich 2017	88	114	40	56	35.1	1.35 [0.65, 2.80]
Total (95% CI)		**246**		**194**	**100.0**	**2.04 [1.26, 3.31]**
Total events	189		118			

Heterogeneity: $\tau^2 = 0.04$; $\chi^2 = 2.47$, d$f = 2$ ($p = 0.29$); $I^2 = 19\%$
Test for overall effect: $Z = 2.89$ ($p = 0.004$)

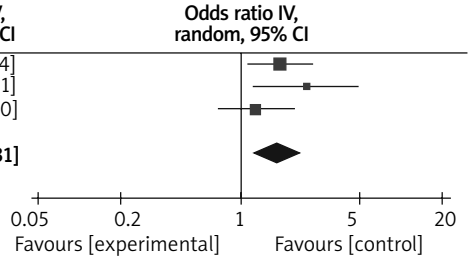

Figure 5. Forest plot for the meta-analysis of PGA 0/1

Study or subgroup	Guselkumab group Mean	SD	Total	Adalimumab group Mean	SD	Total	Weight (%)	Std. mean difference IV, random, 95% CI
Blauvelt 2017	–11.2	7.24	322	–9.3	7.8	328	46.5	–0.25 [–0.41, –0.10]
Gordon 2015	–11.4	6.83	42	–10.1	9	43	6.1	–0.16 [–0.59, 0.26]
Reich 2017	–11.3	6.8	496	–9.7	6.8	248	47.4	–0.24 [–0.39, –0.08]
Total (95% CI)			**860**			**619**	**100.0**	**–0.24 [–0.34, –0.13]**

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.16$, d$f = 2$ ($p = 0.92$); $I^2 = 0\%$
Test for overall effect: $Z = 4.44$ ($p < 0.00001$)

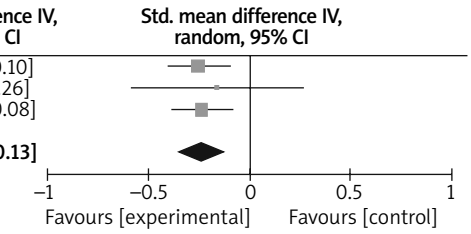

Figure 6. Forest plot for the meta-analysis of change in DLQI

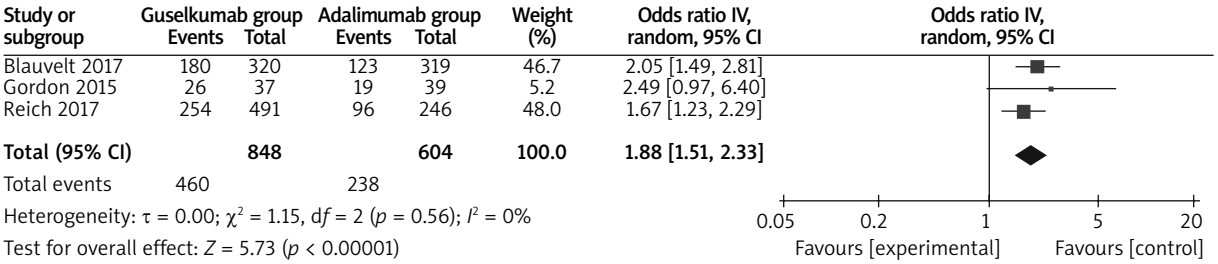

Figure 7. Forest plot for the meta-analysis of DLQI score 0/1

mediating the broader efficacy of guselkumab is elusive in psoriasis. TNF-α and IL-17A 29 are important effector cytokines to primarily act on keratinocytes [26, 27]. IL-23 is the overarching master cytokine for psoriasis through activating T cells and inducing the production of IL-17 and IL-22 which are implicated in psoriasis pathogenesis [28, 29]. Therefore, guselkumab could provide higher efficacy and durable responses via targeting the IL-23 pathway [20].

The safety profile of guselkumab was confirmed in VOYAGE 1 and VOYAGE 2 [19, 20]. Several limitations exist here. Firstly, our analysis was based on only three RCTs, and more RCTs with a larger sample size should be conducted to explore this issue. Next, different doses and methods of guselkumab were included, which may account for the significant heterogeneity. Finally, ideal methods for guselkumab remain elusive.

Conclusions

Guselkumab is superior to adalimumab for the treatment of psoriasis.

Conflict of interest

The authors declare no conflict of interest.

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