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ORIGINAL RESEARCH

Comparative Effectiveness of Adalimumab versus Secukinumab for the Treatment of Psoriatic Arthritis: A Matching-Adjusted Indirect Comparison

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ABSTRACT

Introduction: The Phase III FUTURE I and II trials demonstrated the clinical efficacy of secukinumab in active psoriatic arthritis (PsA). In the absence of head-to-head trials, this study compared the clinical efficacy and cost effectiveness of adalimumab 40 mg versus secukinumab 150 and 300 mg for the treatment of active PsA.

Methods: A matching-adjusted indirect comparison was conducted using individual patient data from the ADEPT trial of adalimumab and published data from FUTURE I and II. To adjust for the cross-trial differences, individual patients in ADEPT were re-weighted so that the mean baseline characteristics (including age, weight, gender, race, baseline methotrexate use, psoriasis ≥3% body surface area, baseline PASI score, presence of dactylitis and enthesitis, and HAQ-DI) matched those in the FUTURE trials. Response rates relative to placebo and incremental costs per responder (CPR) over 24 weeks for ACR 20/50/70 and PASI 75/90 were compared between adalimumab and secukinumab 150 and 300 mg from the German social health insurance (SHI) perspective.

Results: After matching, mean baseline characteristics were balanced across the ADEPT and the FUTURE I and II populations. The mean differences between adalimumab and secukinumab 150 mg in relative ACR 20/50/70 and PASI 75/90 response rates were 9.5, 3.0, 6.0, 13.1, and 6.7%, respectively ($p > 0.05$ for all comparisons). Post-match relative ACR 20/50/70 and PASI 75 to placebo were also higher with adalimumab compared to secukinumab 300 mg. Adalimumab had lower incremental costs per responder over 24 weeks for all outcomes compared with secukinumab 150 and 300 mg.

Conclusions: In the absence of direct comparisons between adalimumab and secukinumab, this study provides valuable and reliable evidence for physicians and payers. After adjusting for cross-trial differences in baseline characteristics, adalimumab was associated with higher relative ACR and PASI rates and lower incremental CPRs compared with secukinumab 150 mg or 300 mg at week 24 among patients with active PsA.

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INTRODUCTION

Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory condition associated with psoriasis that affects musculoskeletal structures. The prevalence of PsA is 0.3–1.0% in the general population and around 10–40% of psoriasis patients will develop PsA in their lifetime [1–5]. Disease severity varies amongst individuals and can range from mild swelling and inflammation to joint incapacitation. PsA can lead to significant joint damage and disability, reduced quality of life, as well as decreased life expectancy [1]. Patients with PsA have an increased prevalence of cardiovascular disease, metabolic syndrome, obesity, type 2 diabetes mellitus, hypertension, and a 60% increased risk of mortality compared to the general population [6–8].

The overarching goal of PsA treatment is to optimize quality of life through reducing or reversing signs and symptoms and inhibiting the progression of joint damage [9, 10]. Traditional pharmacological therapies including non-steroidal anti-inflammatory drugs (NSAIDs), steroids, and conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) have demonstrated efficacy in controlling joint symptoms and are commonly used in the clinical management of active PsA [11]. However, treatment for PsA has evolved considerably with the development of small molecule agents in the past decade. Currently available therapeutic options with small-molecule agents include tumor necrosis factor inhibitors (TNFi; including adalimumab, etanercept, infliximab, golimumab, and certolizumab), a phosphodiesterase-4 inhibitor (apremilast), an interleukin (IL)-12/23 inhibitor (ustekinumab), and an IL-17 inhibitor (secukinumab). Randomized controlled trials (RCTs) of these agents have demonstrated substantial clinical responses in skin and joint manifestations as well as improvement in quality of life [12–22].

According to the European League Against Rheumatism (EULAR) 2015 treatment guidelines, csDMARDs are recommended as the initial treatment for PsA patients [10]. TNF, phosphodiesterase-4, IL-12/23, and IL-17 inhibitors are considered for patients with inadequate response to csDMARDs. Specifically, TNFi are recommended as the first option for biologic DMARDs (bDMARDs) after failure of csDMARDs; IL-17 or IL-23 inhibitors may be considered in patients who have failed or for whom TNFi are inappropriate; a phosphodiesterase-4 inhibitor can be considered when bDMARDs are inappropriate [10]. Though csDMARDs are recommended as first-line treatment in most instances, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) guideline recommends that special consideration on early escalation of therapy be given to patients with poor prognostic factors [9].

Evidence on the comparative effectiveness of one of the most commonly used TNFi, adalimumab, versus the recently approved secukinumab, plays an important role in clinical and healthcare economic decision-making [23]. In the absence of head-to-head trials that compare adalimumab and secukinumab, indirect comparisons can provide valuable information in terms of comparative clinical efficacy and cost-effectiveness [24]. Previous network meta-analyses (NMA) between adalimumab and secukinumab for the treatment of active PsA found these two treatments to be comparable in terms of American College of Rheumatology (ACR) 20 and PsA response criteria (PsARC) [25, 26]. NMA is a well-accepted indirect comparison technique which utilizes aggregate data from trial publications. However, it can be subject to heterogeneity of patient populations across trials. Matching-indirect comparison (MAIC) is a statistical method that uses individual patient data (IPD) of at least one trial to achieve balanced baseline characteristics across trial populations and compares efficacy among the balanced populations. Three studies have used MAIC to compare the clinical efficacy and costs per responder of adalimumab and secukinumab for the treatment active PsA [27–29]. These studies reported higher or comparable

ACR rates and lower costs per responder for secukinumab vs. adalimumab. However, none of these studies were anchored on the placebo arm. The anchor-based approach preserves the within-trial randomization of RCTs and provides additional adjustment for cross-trial differences. Recent guidance from the Decision Support Unit (DSU) of the Health and Care Excellence (NICE) states that when connected evidence with a common comparator is available, only anchored forms of population adjustment should be used [24, 30].

The current study conducted an anchor-based MAIC to balance the cross-trial differences in baseline characteristics between the adalimumab trial and the aggregated secukinumab trials and compared the clinical and economic effectiveness of adalimumab versus secukinumab relative to placebo for the treatment of active PsA.

METHODS

Data

Phase III RCTs with adalimumab and secukinumab in patients with PsA were identified through a targeted literature search. Trials that met the following criteria were included in the analysis: (1) recruited adult patients with moderate-to-severe PsA; (2) included treatment of adalimumab or secukinumab; and (3) reported clinical outcomes including ACR and Psoriasis Area and Severity Index (PASI) response rates. The ADEPT pivotal trial for adalimumab and the FUTURE I and FUTURE II pivotal trials for secukinumab were included in the study because of similar trial designs and common primary outcomes [12, 17, 22, 31, 32]. All three trials (1) recruited adult patients with moderate-to-severe PsA defined by $\geq$3 swollen joints and $\geq$3 tender or painful joints; (2) allowed patients to be on concomitant methotrexate during the trial period; (3) included patients with inadequate responses to or intolerance to NSAIDs; (4) required a wash-out period for psoriasis treatment such as topical, photo, and systemic therapies. Common primary outcomes included ACR 20/50/70 responses, and PASI 75/90 responses for patients with $\geq$3% body surface area involvement. The primary endpoint was at week 24 for all three RCTs. Non-responder imputation was used for placebo patients who received rescue treatment before the primary endpoint. Although the loading phase of FUTURE I was scheduled at week 0 and 2 and was slightly different from the EMA-approved dosage, it was included in the current analysis given its nature as a pivotal trial. A sensitivity analysis comparing ADEPT and FUTURE II (alone) was conducted.

There were a number of differences in trial design between these trials. The FUTURE I and FUTURE II trials further restricted the duration of disease to be at least 6 months and excluded patients with potent opioid analgesic use. The ADEPT trial allowed for a maximum dose of methotrexate use at 30 mg per week while the FUTURE I and FUTURE II trials capped the maximum dose at 25 mg per week. All patients in the ADEPT trial were TNFi naïve, while approximately 30% of patients in FUTURE I and FUTURE II were TNFi experienced and could have received up to three prior anti-TNF agents.

IPD was available for the ADEPT trial. Aggregate baseline characteristics and outcomes were available from the publications of the FUTURE I and FUTURE II trials. With the advantage of IPD of ADEPT, the above-mentioned difference in trial design was resolved to the extent possible by excluding patients from ADEPT who did not meet the inclusion and exclusion criteria of FUTURE I and FUTURE II. Specifically, patients in ADEPT with disease duration of less than 6 months, or potent opioid analgesic use, or a maximum methotrexate dose over 25 mg per week were excluded from this study. To account for the population difference regarding prior TNFi treatment, a sensitivity analysis comparing ADEPT and the TNFi-naïve population in FUTURE II was conducted (FUTURE I was not included in the sensitivity analysis because baseline characteristics for TNFi-naïve patients from this trial were not reported) [33]. This article is based on previously conducted studies, and does not involve any new studies of human or animal subjects performed by any of the authors.

Statistical Methods

The current study used MAIC to compare efficacy of adalimumab and secukinumab in treating moderate-to-severely active PsA in the absence of head-to-head trials. The MAIC methodology adjusts for cross-trial differences by matching the baseline characteristics using IPD from the trial(s) of one treatment and aggregate data for trial(s) of the other treatment. The outcomes of interest were then compared between balanced trial populations. This approach has been applied by a number of studies and has been acknowledged by health technology assessment authorities including NICE [30, 34–39]. The steps to conduct MAIC are described below in detail.

Selection of Baseline Characteristics

All baseline characteristics that were known to be prognosis factors or effect modifiers of the efficacy outcomes based on medical experts' opinion and were reported in the ADEPT trial and the FUTURE I and FUTURE II trials were used for matching. Matched baseline characteristics included age, weight, gender, race, baseline methotrexate use, presence of psoriasis with $\geq$3% body surface area involvement, proportion of psoriatic patients with PASI score $>$ 10, presence of dactylitis, presence of enthesitis, and baseline HAQ-DI score.

Matching of Baseline Characteristics

A total of three matches were conducted: (1) adalimumab patients from the ADEPT trial were re-weighted to match the baseline characteristics of the pooled secukinumab 150 mg arm from the FUTURE I and FUTURE II trials; (2) adalimumab patients were re-weighted again to match the baseline characteristics of the secukinumab 300 mg arm from FUTURE II trial; (3) placebo patients from the ADEPT trial were also re-weighted to match the pooled placebo patients from the FUTURE I and FUTURE II trials. For each match, patients in the ADEPT trial were assigned weights such that weighted baseline characteristics of the ADEPT trial matched exactly to those reported in the FUTURE I and FUTURE II trials. The weight, which represented a patient's odds of being enrolled in ADEPT vs. FUTURE I and FUTURE II, was calculated using a logistic regression model adjusting for all available baseline characteristics. Baseline characteristics between ADEPT and FUTURE I and FUTURE II before matching were compared using Wilcoxon rank-sum test for continuous variables and Chi-square test for categorical variables.

Comparison of Outcomes After Matching

After matching, ACR 20/50/70 relative to placebo at the primary endpoint of week 24 were compared between adalimumab and secukinumab 150 and 300 mg separately. PASI 75/90 relative to placebo were also assessed among those with $\geq$3% body surface area involvement by psoriasis. Weighted *t* tests were used to compare the outcomes after matching. Numbers needed to treat (NNTs) were defined as the number of patients that need to be treated in order to achieve one additional responder compared to placebo and was calculated as the reciprocal of the response rate difference between the biologic treatment and placebo for both adalimumab and secukinumab.

Incremental Cost Per Responder Analysis

Incremental cost per responder (CPR) over the 24-week trial period was calculated for each outcome from the German social health insurance (SHI) perspective. Incremental CPR was calculated as the product of NNT and drug costs over the trial period and represents the additional cost to achieve one additional responder compared with placebo. Drug costs over the trial period were calculated by multiplying the unit drug acquisition cost (2015 German pharmacy selling price [40]) and the EMA-approved dosing schedule over 24 weeks (adalimumab 40 mg every other week, secukinumab 150 or 300 mg with initial dosing at weeks 0, 1, 2, and 3 followed by monthly maintenance dosing from week 4) [41, 42].

RESULTS

Sample Size

A total of 134 patients from the adalimumab arm and 147 patients from the placebo arm in the ADEPT trial were included in the MAIC. 32 patients (17 in the adalimumab arm and 15 in the placebo arm) were excluded from analysis due to missing values at baseline or differences in study designs between ADEPT and FUTURE I and FUTURE II. In the pooled FUTURE I and FUTURE II trials, 302 patients from secukinumab 150 mg, 100 from secukinumab 300 mg, and 300 from the placebo arms were included in the analysis.

Baseline Characteristics

Before matching, significant differences in some baseline characteristics were observed between the patient populations of ADEPT and the pooled FUTURE I and FUTURE II trials. Compared to secukinumab 150 mg-treated patients, adalimumab-treated patients in ADEPT included a higher proportion of Caucasians (97 vs. 83%, $p < 0.001$), less severity of psoriasis (≥3% body surface area: 44 vs. 55%, $p = 0.035$; among those, baseline PASI score >10: 24 vs. 57%, $p < 0.001$), and less enthesitis (35 vs. 63%, $p < 0.001$) (Table 1). Significant differences in baseline PASI scores (adalimumab vs. secukinumab: 24 vs. 49%; $p < 0.001$) and presence of enthesitis (35 vs. 56%; $p = 0.001$) were also observed between the secukinumab 300 mg and adalimumab arms (Table 2). Separate matches were conducted for adalimumab and secukinumab 150 mg, adalimumab and secukinumab 300 mg, and placebo arms of the ADEPT and the pooled FUTURE I and FUTURE II trials. After matching, all baseline characteristics were exactly balanced between treatment arms (all $p = 1.000$) (Tables 1, 2).

Indirect Comparison

Before matching, adalimumab patients had a numerically higher relative efficacy to placebo compared to secukinumab 150 mg in ACR 20/50/70 and PASI 75/90 responses. After matching, adalimumab continued to demonstrate a higher relative efficacy vs. placebo in all of the above outcomes compared with secukinumab 150 mg. The mean difference in relative efficacy of adalimumab versus secukinumab 150 mg in ACR20/50/70 was 9.5% ($p = 0.176$), 3.0% ($p = 0.656$), and 6.0% ($p = 0.259$), respectively (Fig. 1). Among patients with active psoriasis, the post-matching relative efficacy of PASI 75/90 responses were numerically higher in adalimumab-treated compared with secukinumab 150 mg treated patients with a mean difference of 13.1% ($p = 0.058$) and 6.7% ($p = 0.317$) (Fig. 1).

Compared with patients treated with secukinumab 300 mg, patients receiving adalimumab had a higher relative efficacy to placebo in all outcomes with the exception of PASI 90 before matching. After matching, adalimumab demonstrated a numerally higher relative efficacy in ACR 20 (mean difference: 5.3%, $p = 0.507$), ACR 50 (6.2%, $p = 0.381$), ACR 70 (6.0%, $p = 0.312$), and PASI 75 (7.3%, $p = 0.411$) responses, and a numerically lower relative efficacy in PASI 90 (−4.3%, $p = 0.636$) (Fig. 2). No statistically significant differences were observed in skin (PASI) or joint (ACR) outcomes at week 24 between adalimumab with secukinumab 150 or 300 mg.

Cost Per Responder

The unit cost per dose for adalimumab 40 mg, secukinumab 150 mg, and secukinumab 300 mg were 822, 938, and 1877€ (based on the cost of secukinumab two-pen package) respectively, and the number of doses over 24 weeks were 12 for adalimumab 40 mg and nine for secukinumab 150 and 300 mg.

The incremental CPR of adalimumab relative to placebo was considerably lower for all skin and joint outcomes compared with secukinumab 150 mg over 24 weeks. The difference in the incremental CPR of adalimumab and secukinumab was 2227, 1685, and 5964€ for ACR 20, ACR 50, and ACR 70, respectively (Fig. 3). For patients with active psoriasis, difference in incremental CPR for PASI 75 and PASI

Table 1 Baseline characteristics of ADEPT vs. FUTURE I and II (secukinumab 150 mg)

Baseline characteristics	ADEPT before matching		ADEPT after matching		FUTURE I/II		*P* value before matching	
	Adalimumab 40 mg (*N* = 134) [A]	Placebo (*N* = 147) [B]	Adalimumab 40 mg (ESS = 49) [C]	Placebo (ESS = 79) [D]	Secukinumab 150 mg (*N* = 302) [E]	Placebo (*N* = 300) [F]	Treatment [A] vs. [E]	Placebo [B] vs. [F]
Demographics								
Age (years) (mean)	48.7	49.2	48.6	49.0	48.6	49.0	–[a]	–[a]
Weight (kg) (mean)	85.4	85.7	86.5	82.0	86.5	82.0	–[a]	–[a]
Female (%)	43.3	44.2	50.0	55.0	50.0	55.0	0.195	0.032*
White (%)	97.0	93.9	83.4	82.6	83.4	82.6	<0.001*	0.001*
Disease characteristics								
Methotrexate use at baseline (%)	51.5	49.0	54.6	58.3	54.6	58.3	0.544	0.062
Psoriasis (≥3% body surface area), (%)	44.0	45.6	55.0	50.7	55.0	50.7	0.035*	0.311
PASI score >10 (%)	23.7	28.4	56.6	56.6	56.6	56.6	<0.001*	<0.001*
Presence of dactylitis (%)	42.5	36.7	45.0	47.7	45.0	47.7	0.627	0.029*
Presence of enthesitis (%)	35.1	37.4	62.9	60.6	62.9	60.6	<0.001*	<0.001*
HAQ-DI (mean)	0.9	1.0	1.2	1.2	1.2	1.2	–[a]	–[a]

* *P* value <0.05

ESS effective sample size, *SD* standard deviation

[a] SDs were not available for age, weight and HAQ-DI in FUTURE I and FUTURE II publications at the time of the analysis, therefore statistical comparisons before matching could not be conducted for these characteristics

Table 2 Baseline characteristics of ADEPT vs. FUTURE I and II (secukinumab 300 mg)

Baseline characteristics	ADEPT before matching		ADEPT after matching		FUTURE I/II		*P* value before matching	
	Adalimumab 40 mg ($N = 134$) [A]	Placebo ($N = 147$) [B]	Adalimumab 40 mg (ESS = 76) [C]	Placebo (ESS = 79) [D]	Secukinumab 300 mg ($N = 100$) [E]	Placebo ($N = 300$) [F]	Treatment [A] vs. [E]	Placebo [B] vs. [F]
Demographics								
Age (years) (mean)	48.7	49.2	46.9	49.0	46.9	49.0	–[a]	–[a]
Weight (kg) (mean)	85.4	85.7	85.4	82.0	85.4	82.0	–[a]	–[a]
Female (%)	43.3	44.2	49.0	55.0	49.0	55.0	0.385	0.032*
White (%)	97.0	93.9	96.0	82.6	96.0	82.6	0.673	0.001*
Disease characteristics								
Methotrexate use at baseline (%)	51.5	49.0	44.0	58.3	44.0	58.3	0.257	0.062
Psoriasis (≥3% body surface area) (%)	44.0	45.6	41.0	50.7	41.0	50.7	0.643	0.311
PASI score > 10 (%)	23.7	28.4	48.8	56.6	48.8	56.6	<0.001*	<0.001*
Presence of dactylitis (%)	42.5	36.7	46.0	47.7	46.0	47.7	0.598	0.029*
Presence of enthesitis (%)	35.1	37.4	56.0	60.6	56.0	60.6	0.001*	<0.001*
HAQ-DI (mean)	0.9	1.0	1.3	1.2	1.3	1.2	–[a]	–[a]

ESS effective sample size, *SD* standard deviation

* *P* value <0.05

[a] SDs were not available for age, weight and HAQ-DI in FUTURE I and FUTURE II publications at the time of the analysis, therefore statistical comparisons before matching could not be conducted for these characteristics

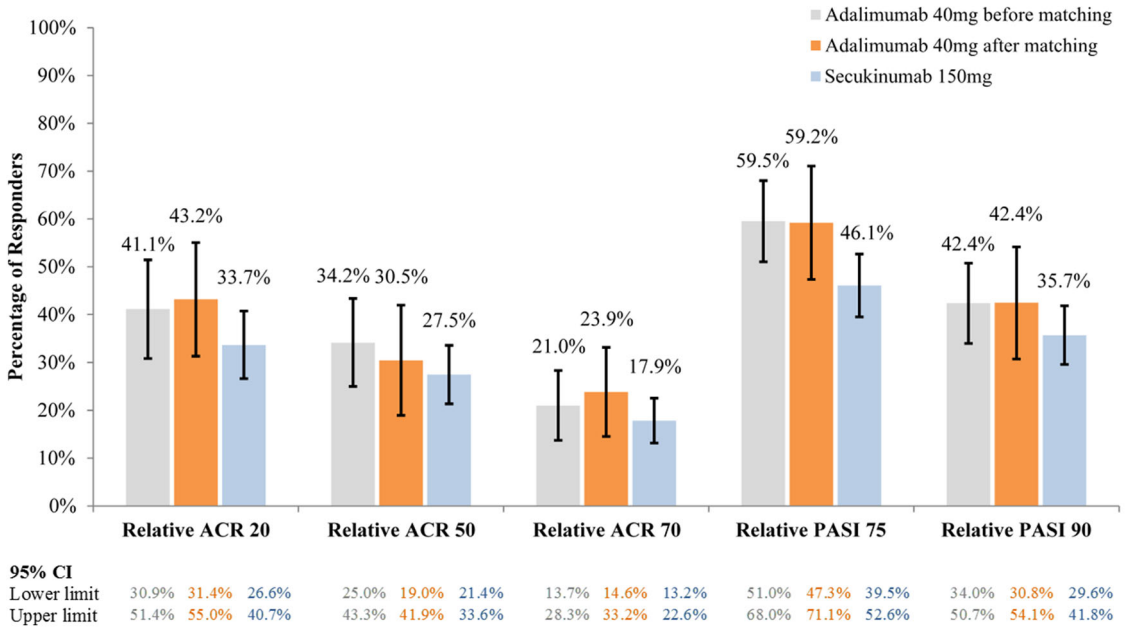

Fig. 1 Relative ACR 20, ACR 50, ACR 70, PASI 75, and PASI 90 of adalimumab vs. secukinumab 150 mg

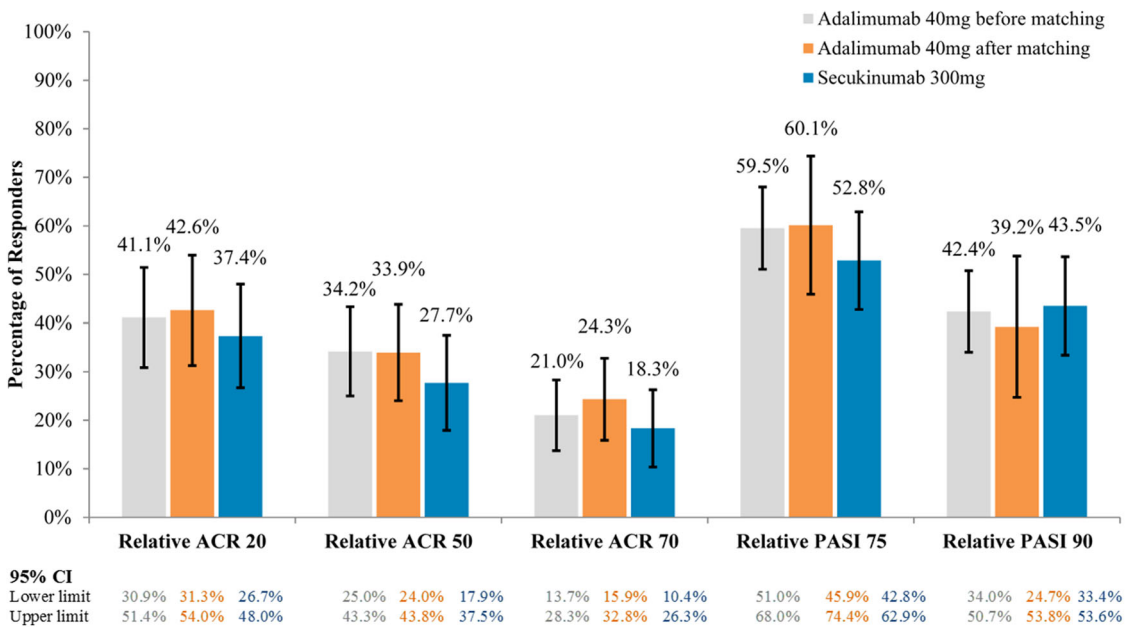

Fig. 2 Relative ACR 20, ACR 50, ACR 70, PASI 75, and PASI 90 of adalimumab vs. secukinumab 300 mg

90 was 1664 and 403€, comparing adalimumab with secukinumab 150 mg (Fig. 3). Cost effectiveness was also observed for adalimumab compared with secukinumab 300 mg in all outcomes over 24 weeks (incremental CPR difference: 22,067€ for ACR 20; 31,898€ for ACR 50; 51,602€ for ACR 70; 15,565€ for PASI 75; 13,672€ for PASI 90) (Fig. 4).

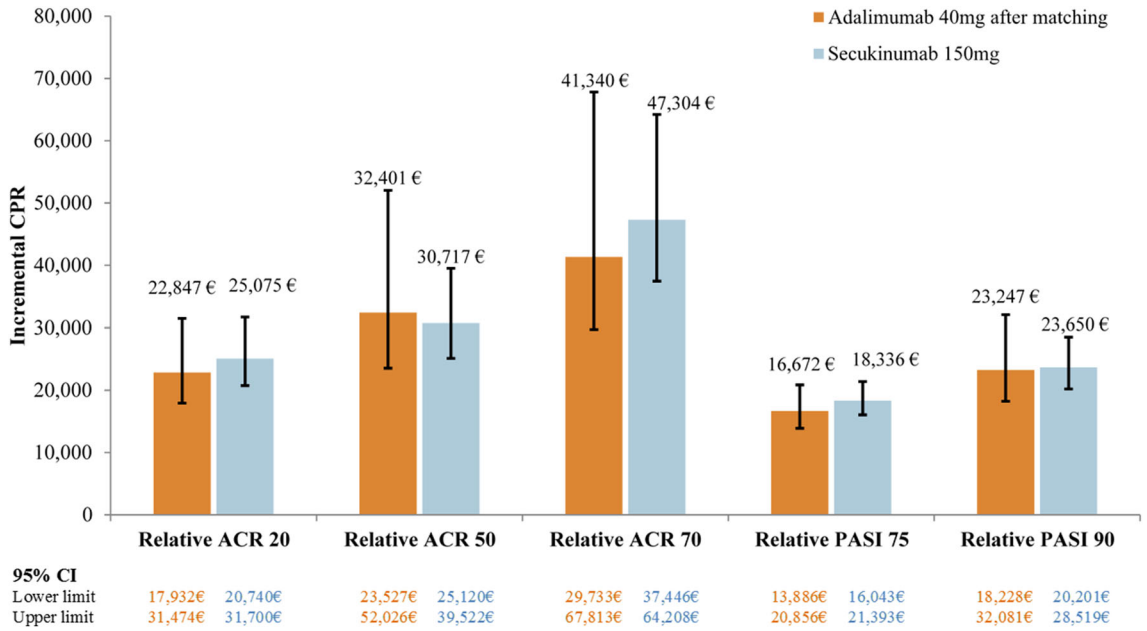

Fig. 3 Incremental CPR for ACR 20, ACR 50, ACR 70, PASI 75, and PASI 90 of adalimumab vs. secukinumab 150 mg after matching

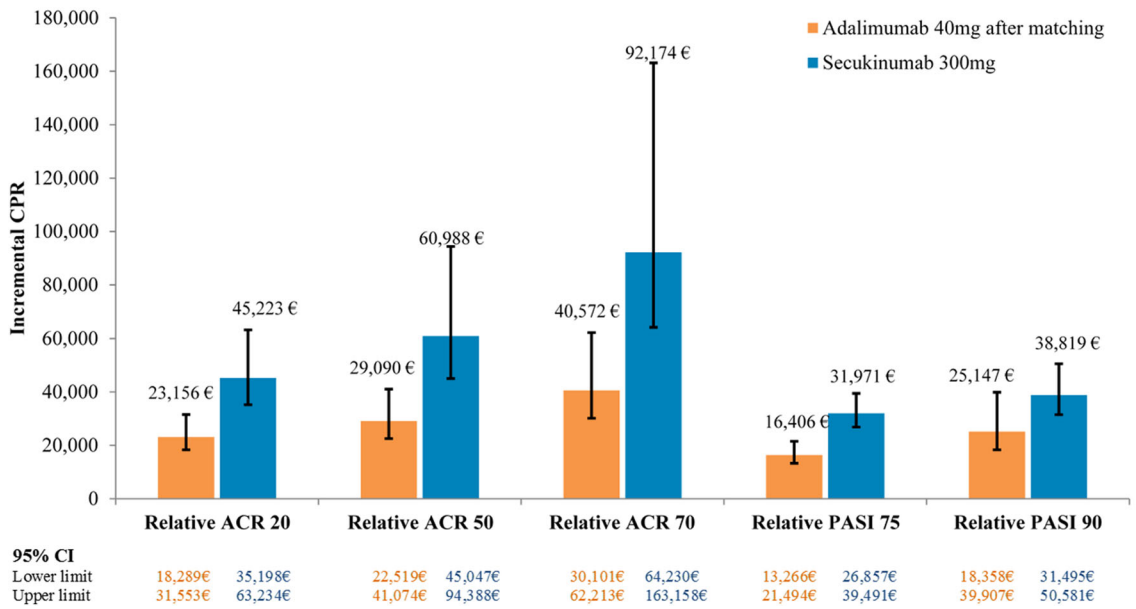

Fig. 4 Incremental CPR for ACR 20, ACR 50, ACR 70, PASI 75, and PASI 90 of adalimumab vs. secukinumab 300 mg after matching

DISCUSSION

The current study compared the clinical efficacy and economic effectiveness of adalimumab and secukinumab in the treatment of moderate-to-severely active PsA. Adalimumab is one of the most commonly used TNFi since it was approved by FDA in 2004 and by EMA in 2006 for PsA. TNFi are recommended by the EULAR and GRAPPA guidelines as the first biologic treatments to be considered for PsA patients with inadequate responses to NSAIDs and csDMARDs [42]. Secukinumab is the newest biologic agent approved by FDA and EMA for PsA in 2015 and is currently recommended for patients for whom TNFi are inappropriate [10]. As both adalimumab and secukinumab have demonstrated clinical benefits for patients with moderate-to-severe PsA in RCTs [12, 31, 32], it is of interest to understand the comparative effectiveness of these two therapies. As there have been no published head-to-head trials between adalimumab and secukinumab at the time of the current analysis (one head-to-head trial [NCT02745080] is currently being conducted and is estimated to be completed in November 2019), an indirect comparison is necessary [43]. However, a naïve side-by-side comparison across different trials is not recommended as it ignores differences in study designs and imbalances in patient populations.

The current study found that adalimumab had numerically higher response rates and was more cost effective than secukinumab 150 and 300 mg for most joint and skin outcomes. The findings of the current study are consistent with a previous NMA study in PsA, where comparable ACR 20 and PASI 75 response rates between adalimumab, secukinumab 150 mg, and secukinumab 300 mg were reported both for all patients and for the subgroups with comorbid psoriasis and biologic-naïve patients [25]. PsARC rates, which were assessed in another NMA study, were reported comparable between secukinumab and adalimumab as well [26].

Compared to NMA studies that rely on aggregate data, which could be subject to imbalanced trial population, the current study has several advantages. It utilized IPD and further matched on baseline characteristics across trials to adjust for confounding factors that might affect the comparative effectiveness of the treatments. For instance, the ADEPT trial included patients with less severe psoriasis and enthesitis. Without matching these factors, comparisons of effectiveness would overlook the effect of disease severity on treatment response and generate results that are potentially biased.

Three MAIC studies, one presented at the 25th EULAR congress and two at 2016 ACR/ARHP Annual Meeting, compared clinical and cost effectiveness of secukinumab and adalimumab in PsA using IPD of the FUTURE trials and aggregated data from the ADEPT trial [27–29]. One of the studies presented at ACR/ARHP used IPD of the pooled FUTURE I and II trials and reached similar conclusion as the current study that secukinumab 150 mg and adalimumab had similar efficacy in joint outcomes at week 24. The other two studies concluded that secukinumab 300 mg had better clinical and cost effectiveness compared to adalimumab at week 48. The difference in conclusions may be attributed to the following differences in the study design. Most importantly, the current study used an anchor-based approach that accounted for the difference in placebo responses across trials and reported relative response rate to placebo, while the previous MAIC studies used an unanchored approach past week 12 [30, 39]. The anchor--based approach is recommended by the NICE DSU when connected evidence with a common comparator is available [24, 30]. Secondly, only FUTURE II was used in these two MAIC studies while this study used both FUTURE I and II. Furthermore, clinical and cost effectiveness were assessed over different time horizons (i.e., 48 weeks in the two previous MAIC studies vs. 24 weeks in the current study). Finally, our study assessed cost effectiveness from the German SHI perspective while the previous study was from the US payer perspective.

The current study has some limitations. First, though the analysis balanced cross-trial differences in study populations to the extent possible, potential residual confounding may still exist due to unobserved trial differences.

Second, all patients in ADEPT were TNFi naïve while approximately 70% of patients in FUTURE I and FUTURE II were TNFi naïve. A sensitivity analysis to compare adalimumab and secukinumab 150 mg among the TNFi-naïve population was conducted to address this limitation. In this sensitivity analysis, the relative efficacy of ACR 20, ACR 50, and ACR 70 responses of adalimumab to placebo were found to be 6.4% lower, 5.9% lower, and 0.6% higher compared to secukinumab 150 mg without statistically significant differences detected. Higher PASI response rates were observed for adalimumab with a difference of 23.8% in PASI 75 ($p = 0.037$) and a difference of 9.4% in PASI 90 ($p = 0.382$). The incremental CPR for ACR 20, ACR 50, and ACR 70 were 6186, 8491, and 4680€ higher for adalimumab compared to secukinumab 150 mg, respectively. For patients with concomitant psoriasis, incremental CPR for PASI 75 and PASI 90 were 6865 and 3349€ lower for adalimumab compared to secukinumab 150 mg. Third, when common arms were pooled for FUTURE I and FUTURE II, it was assumed that the efficacy of secukinumab intravenous administration of 10 mg/kg in FUTURE I was the same as subcutaneous injection in FUTURE II during the loading phase. Although secukinumab 300 mg is approved by EMA for PsA patients who have concomitant moderate-to-severe plaque psoriasis or who are TNFi inadequate responders [41], the current comparison between adalimumab and secukinumab 300 mg were conducted in the general PsA population since stratified baseline and outcome information was not reported for PsA patients with concomitant psoriasis in the FUTURE I and FUTURE II trials. Aside from clinical efficacies, other outcomes such as radiographic assessment and safety profiles are also important indicators of disease management in PsA. The EULAR guideline recognized radiographic damage as one of the poor prognostic factors in PsA; the GRAPPA guideline considered response to treatment inadequate when radiographic progression or structural damage occurred [9, 10]. In terms of safety profile, the GRAPPA guideline recommends taking the frequency and seriousness of adverse reactions into consideration during the choice of biologic use for PsA [9]. Therefore, future comparative effectiveness studies are encouraged to look at improvement in radiographic outcomes and safety profiles.

CONCLUSIONS

After adjusting for cross-trial differences in baseline characteristics, adalimumab was associated with numerically higher relative ACR and PASI rates and lower CPRs compared with secukinumab 150 and 300 mg at week 24 among patients with active PsA. In the absence of direct comparisons between adalimumab and secukinumab, this study provides valuable and reliable evidence for physicians and payers.

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