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ORIGINAL ARTICLE

Efficacy and safety of secukinumab in active rheumatoid arthritis with an inadequate response to tumor necrosis factor inhibitors: a meta-analysis of phase III randomized controlled trials

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Abstract

Objectives To address the efficacy and safety of secukinumab in comparison with placebo in active rheumatoid arthritis (RA) patients who had an inadequate response to tumor necrosis factor (TNF) inhibitors.

Methods Databases of PubMed, Embase, and Web of Science were searched to identify the relevant randomized controlled trials (RCTs). Risk ratio (RR) and 95% confidence interval (95% CI) were calculated with the Mantel–Haenszel random effects method. Statistical heterogeneity was assessed using the Cochran Q and I^2 tests.

Results A total of 1292 patients from three phase III RCT studies were included. Compared with placebo, secukinumab 150 mg was superior at 24 weeks in terms of ACR20 with RR (1.66, 95% CI 1.33, 2.08; $P < 0.0001$; $I^2 = 0\%$), ACR50 (1.88, 95% CI 1.29, 2.72; $P = 0.0009$; $I^2 = 0\%$), and ACR70 (2.15, 95% CI 1.15, 4.02; $P = 0.02$; $I^2 = 0\%$). Consistent effects were also observed in pooled group of 150 mg and 75 mg secukinumab. For secukinumab 75 mg alone, ACR20 response rate was significantly higher compared with placebo (RR 1.62, 95% CI 1.29, 2.03; $P < 0.00001$; $I^2 = 0\%$). Although ACR50 and ACR70 response rates showed a favorable trend to be higher, no statistical difference was observed (RR 1.68, 95% CI 0.99, 2.85, $P = 0.05$, $I^2 = 47\%$; RR 1.81, 95% CI 0.78, 4.21, $P = 0.17$, $I^2 = 34\%$, respectively). Compared with the placebo group, there was no increased risk of adverse effects (AEs) and serious AEs at 16 weeks in the pooled secukinumab group.

Conclusions In active RA patients with an inadequate response to TNF inhibitors, secukinumab may be a therapeutic option. Secukinumab 150 mg showed significantly better clinical efficacy with no increased risk of AEs and serious AEs compared with placebo.

Trial registration Clinical Trials.gov identifier: NCT01770379, NCT01350804, NCT01377012

Key Points

- *Secukinumab 150 mg showed significantly better clinical efficacy in active RA patients with an inadequate response to TNF inhibitors.*
- *No increased risk of AEs and serious AEs in secukinumab group compared with placebo.*

Keywords Efficacy and safety · Rheumatoid arthritis · Secukinumab · Tumor necrosis factor inhibitors

Yanrong Huang and Yong Fan contributed equally to this work.

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Introduction

Rheumatoid arthritis (RA) is an autoimmune inflammatory disease, characterized by symmetrical synovial inflammation and subsequent joint destruction [1]. Several medications have been currently available for the treatment of RA, including conventional synthetic disease-modifying antirheumatic drugs (DMARDs), biological DMARDs, and JAK inhibitors as well as glucocorticoids. Though tumor necrosis factor (TNF) inhibitors and JAK inhibitors are recommended for the RA patients with insufficient efficacy and/or toxicity with

conventional synthetic DMARDs, joint inflammation and progression of bone damage remain difficult to be controlled in some patients [2, 3]. Thus, there is unmet need of investigating other therapeutic options.

Interleukin-17 (IL-17) has been considered as a vital pro-inflammatory cytokine involved in both chronic inflammation and joint damage in RA [4–6]. Researchers have found that IL-17 levels were significantly elevated in peripheral blood and synovial fluid as well as synovium tissue of RA patients [7–11], which are more importantly, positively correlated with RA disease severity [12]. Inhibiting the IL-17/IL-17R signal pathway, such as blockade or deficiency of IL-17R or neutralization of IL-17 with anti-IL-17 antibodies, decreased the inflammation and joint damage of murine collagen-induced arthritis as well as adjuvant-induced arthritis [13–16]. Further studies in various stages of different arthritis models had confirmed the pivotal contribution of IL-17 in the pathogenesis of arthritis.

Secukinumab is a novel selectively human IgG1 monoclonal antibody that directly binds and neutralizes IL-17A. It has been confirmed effective for treating psoriatic arthritis (PsA), moderate-to-severe psoriasis, and ankylosing spondylitis [17]. Findings from a proof of concept trial and phase II dose-finding trials suggested that secukinumab may provide benefit for RA patients [18–20]. Several randomized controlled trials (RCTs) tried to evaluate the efficacy and safety of secukinumab in RA patients with DMARD naive or inadequate to at least one DMARD agent or intolerance to TNF inhibitors. There are three phase III RCTs discussing the patients who have an inadequate response to TNF inhibitors, and the sample size of each RCT was relatively limited [21–23]. Thus, we set out to perform a systematic review and meta-analysis of phase III RCTs, particularly focusing on the efficacy (American College of Rheumatology 20%/50%/70% (ACR20/50/70) improvement criteria response rate) and safety of secukinumab in active RA patients with an inadequate response to or intolerance of TNF inhibitors.

Methods

Study identification

Databases of PubMed, Embase, and Web of Science (updated to September 30, 2018) were used to identify and select the relevant articles with the search terms “secukinumab” and “rheumatoid arthritis” for all publications without language restriction by two independent authors (HYR and FY). Additional records were procured by a hand-search of the references of primitive literature, and reviews were also identified so as to not miss eligible studies. In addition, the US National Institutes of Health ongoing trials register (www.clinincaltrials.gov) and abstract list of meetings were searched for additional related studies. For the published articles by the overlapping authors, with same data, we only included the most lately and completed study.

Study selection

The eligible studies of our meta-analysis met the following inclusion criteria as a result of discussion by two authors (HYR and FY): (1) efficacy and safety evaluation of secukinumab in adult RA patients; (2) patients with active RA who have an inadequate response to TNF inhibitors, as defined in each trial; (3) phase III RCT; (4) sufficient data about ACR20/50/70, adverse events (AEs) and serious AEs were available to calculate the risk ratio (RR) with 95% confidence interval (CI). The following were exclusion criteria: (1) observational or non-randomized studies, (2) reviews or case reports, and (3) duplicated studies.

Data extraction and outcome measurement

Data extraction was done by two authors (HYR and FY) from the identified studies in duplicate using a common extraction form; we also invited a third reviewer (ZZL) to seek opinion for the disagreements. We extracted the first author’s name, year of publication, number of patients, age, ethnicity, study design, name of the drug with dosing route and frequency, efficacy, and AEs. We extracted data from all secukinumab and placebo groups from each trial to calculate the final mean and SD for baseline characteristics. There were five outcome indicators to evaluate the efficacy and safety. The American College of Rheumatology (ACR) 20%, 50%, and 70% response rates at week 24 were the efficacy outcomes. ACR response criteria are widely used to assess and establish the improvement in tender or swollen joint counts along with improvement in three of the following five parameters: acute phase reactant, patient assessment, physician assessment, pain scale, and disability/functional questionnaire. Achieving ACR20/50/70 means patients achieved at least 20/50/70% improvement in tender or swollen joint counts, as well as 20/50/70% improvement in three of the other five parameters. Meanwhile, AEs and serious AEs at week 16 were safety outcomes.

Quality assessment

The quality of the included RCTs was assessed in accordance with the Cochrane quality assessment tool based on seven domains including sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, incomplete outcome data, selective outcome reporting, and baseline imbalance. “Low risk,” “high risk,” or “unclear” was scored for included trials. The quality of the studies was

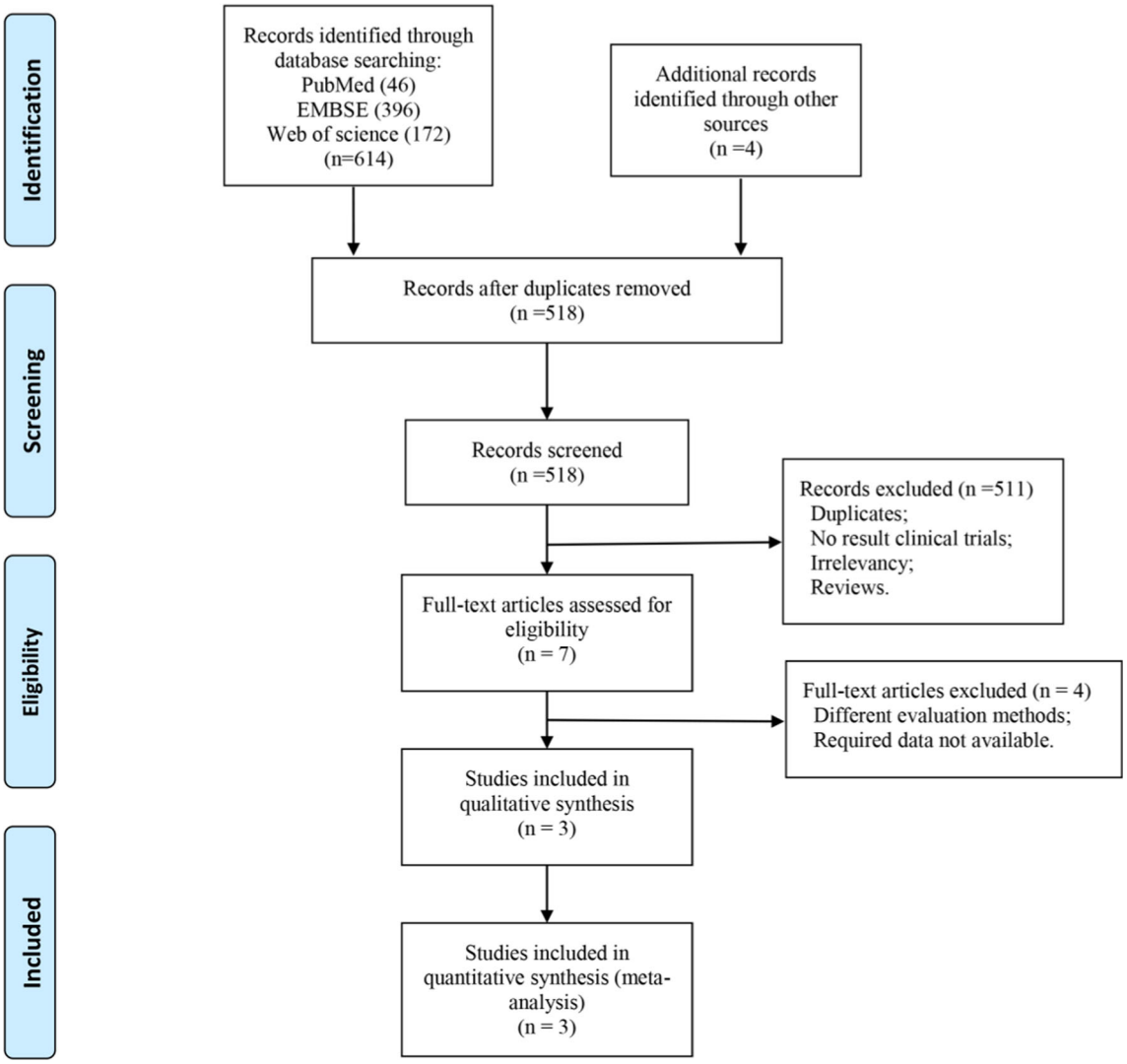

Fig. 1 Study flow chart of the article identification, inclusion, and exclusion

evaluated by two reviewers independently (HYR and FY), and we also tried to contact with authors of those included RCTs in order to obtain more information to do a more comprehensive analysis. Moreover, we invited a third reviewer (ZZL) to seek opinion of the disagreements for further evaluating the risk of bias of individual studies.

Statistical analyses

We reviewed the meta-analysis using the Mantel–Haenszel random effects model under Review Manager (RevMan5.3, Cochrane Collaboration, Nordic Cochrane Center, Copenhagen, Denmark) for statistical analyses based on the basis of the heterogeneity. Dichotomous variables (ACR20/50/70, AEs, and serious AEs) were pooled as RR with 95% CI which are shown in forest plots. Statistical significance is defined as P value < 0.05. Study heterogeneity was evaluated by Cochran's Q and I^2 index (low heterogeneity ($I^2 < 25\%$), moderate heterogeneity (I^2 26–50%), or high heterogeneity ($I^2 > 50\%$). We used funnel plots to assess the potential publication bias and sensitivity analyses were evaluated by comparing random effects model and fix effects model.

Results

Publication selection and characteristics of eligible articles in the meta-analysis

The details of search program in this study are shown in Fig. 1. Totally, 614 articles were retrieved from PubMed, Embase, and Web of Science. After browsing the titles and abstracts, 607 publications were removed due to no result clinical trials of secukinumab or duplicated articles. Seven articles were taken to a full-text review for more detailed evaluation, of which, three were further excluded because of the missing

Table 1 Characteristics of individual studies included in the network meta-analysis

First author	ClinicalTrials.gov identifier	Age (yesrs)	Sample	Inclusion criteria	Ethnicity	Study design	Study centers	Treatment regimen
Edokoupilová (2018) [21]	NCT01770379 (REASSUR-E 2)	54.2 ± 11.3	242	Aged > 18 years with an RA diagnosis fulfilling ACR2010 revised criteria > 3 months before screening and active disease, defined by ≥ 6/68 tender joints and ≥ 6/66 swollen joints, and who were positive for either anti-CCP antibodies or RF, in combination with either hsCRP ≥ 10 mg/L or ESR ≥ 28 mm/h.	Caucasian 64.9%, Asian 22.7%, Black 4.1%, Native American 1.7%, Other 6.2%, Unknown 0.4%	Randomized, double-blind, double-dummy, placebo-controlled, multicenter, parallel-group study	69 centers in 15 countries	Secukinumab 150 mg or 75 mg or placebo[a]
Francisco J. Blanco (2017) [23]	NCT01350804 (NURTURE 1)	55.4 ± 11.9	413		Caucasian 73.8%, Asian 1.2%, Black 3.4%, Other 21.5%	Double-blind, double-dummy, randomized, parallel-group, active comparator and placebo-controlled study	121 centers in 15 countries	Secukinumab 150 mg or 75 mg or placebo[b]
Hasan Tahir (2017) [22]	NCT01377012 (REASSUR-E)	52.9 ± 11.8	637		Caucasian 39.9%, Asian 34.1%, Black 4.6%, Native American 16.3%, Other 0.5%, Unknown 0.2%	Double-blind, randomized, parallel-group, placebo-controlled	139 centers in 15 countries	Secukinumab 150 mg or 75 mg or placebo[c]

[a] Subcutaneous secukinumab 150 mg, secukinumab 75 mg, or placebo at baseline, weeks 1, 2, 3, and 4, and then every 4 weeks

[b] Intravenous secukinumab at a dose of 10 mg/kg (at baseline and weeks 2 and 4) followed by subcutaneous secukinumab at a dose of either 150 mg or 75 mg every 4 weeks or, alternatively, or placebo on the same dosing schedule

[c] Intravenous secukinumab 10 mg/kg (baseline, weeks 2 and 4) followed by subcutaneous secukinumab 150 mg or 75 mg every 4 weeks (starting from week 8) or placebo at the same dosing schedule

RA, rheumatoid arthritis; *ACR*, American College of Rheumatology; *anti-CCP antibodies*, anti-cyclic citrullinated peptide antibodies; *RF*, rheumatoid factor; *hsCRP*, high-sensitivity C-reactive protein; *ESR*, erythrocyte sedimentation rate; *sc*, subcutaneous

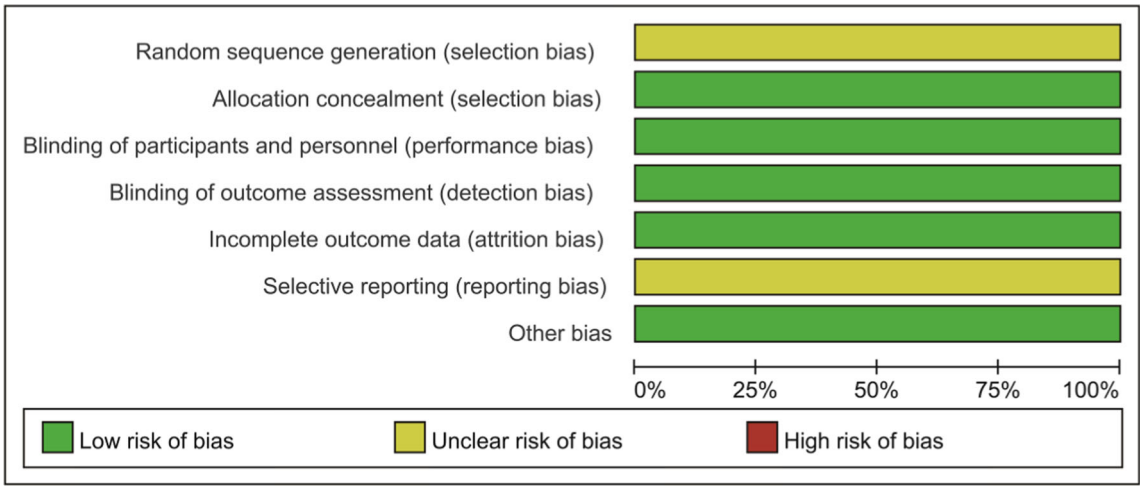

Fig. 2 Risk of bias graph exhibiting the review of the authors' judgments about each risk of bias item, presented as percentages across all included studies

required data [18, 19, 24]. Moreover, two of three studies were non-fulfillment of our inclusion criteria (the patients with active RA who had an inadequate response to TNF inhibitors). The population of these two studies was DMARD naive or inadequately responded to at least one conventional synthetic DMARD [18, 19]. For the third study, we indeed tried several times to contact the author via email; however, no reply was received. Moreover, we noticed that there were only 29 patients (randomly located in five groups) who insufficiently responded TNF inhibitor in the study [24]. The last study, which focused on fatigue, physical function, and health-related quality of life, instead of clinical efficacy and safety

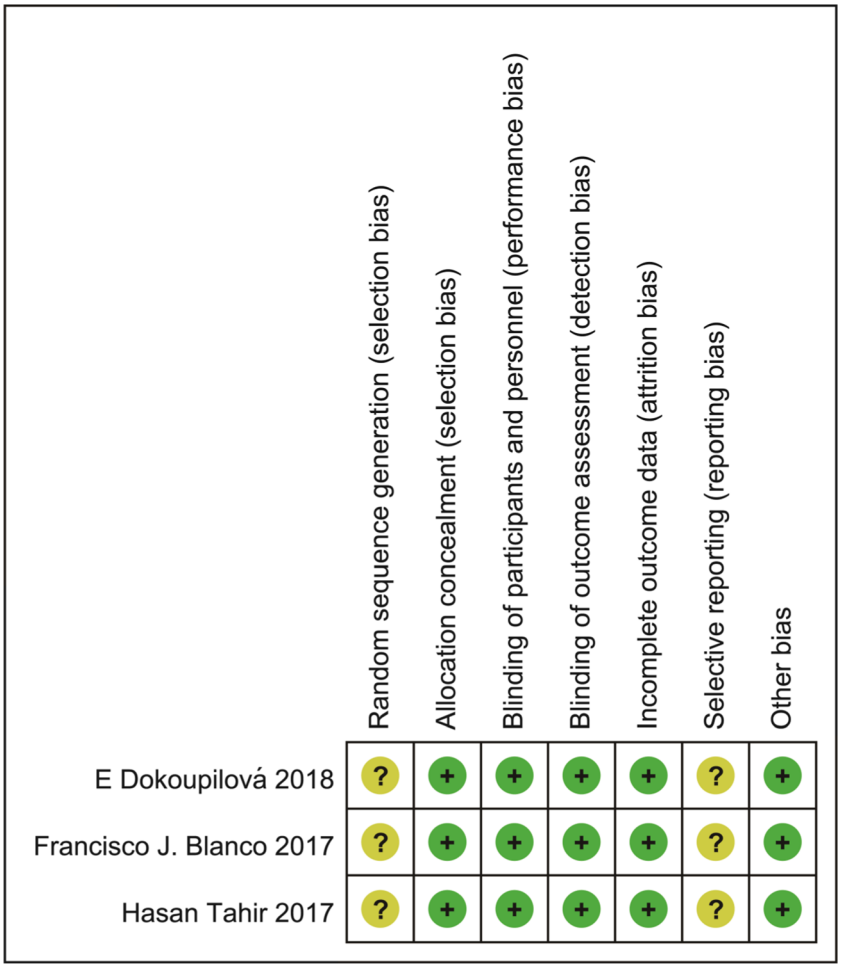

Fig. 3 Risk of bias summary revealing the review of the authors' judgment about each risk of bias item for included RCTs

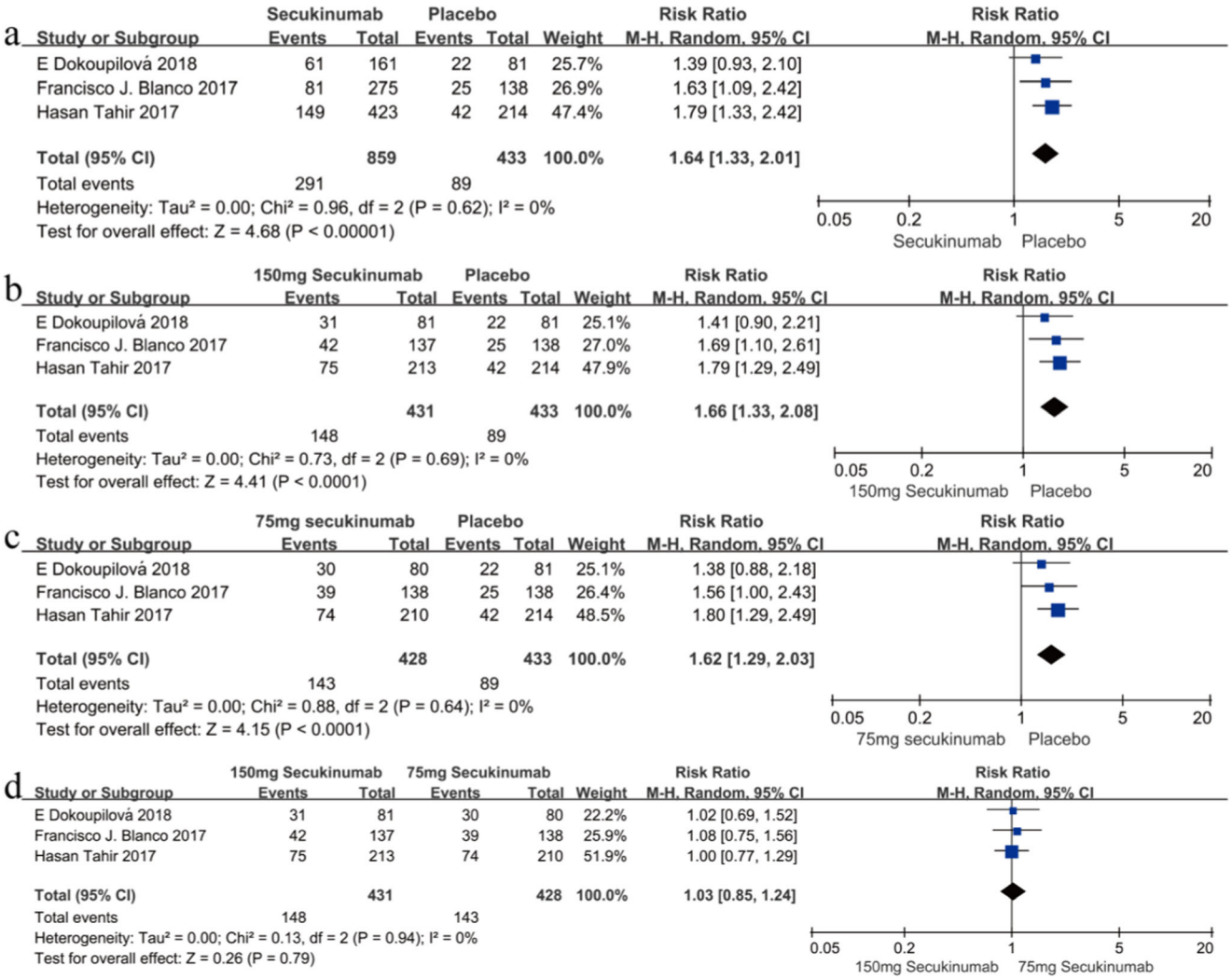

Fig. 4 Meta-analysis of secukinumab versus placebo on ACR20 response rate. **a** Pooled 150/75 mg secukinumab group versus placebo group. **b** 150 mg secukinumab group versus placebo group. **c** 75 mg secukinumab group versus placebo group. **d** 150 mg secukinumab group versus 75 mg secukinumab group. CI: confidence interval; df: degree of freedom

of secukinumab in RA patients, was also removed [25]. Finally, three RCTs met the eligibility criteria and were selected for our systematic analysis [21–23]. All these three pivotal trials (NURTURE 1, REASSURE 2, and REASSURE) were multicenter, double-blind, and placebo-controlled trials with efficacy and safety data of two different secukinumab doses (75 mg and 150 mg) versus placebo. Particularly, NURTURE 1 was designed by double-dummy protocol with abatacept as the active-controlled arm [23].

In this meta-analysis, three RCTs included 859 patients in secukinumab arm and 433 patients in placebo arm (Clinical Trials.gov identifier: NCT01770379, NCT01350804, NCT01377012). All the trials were conducted in patients with active RA who had an inadequate response to TNF inhibitors. And all the patients were allowed to have one conventional synthetic DMARDs (mostly methotrexate) with stable dosage for at least 4 weeks before randomization. The efficacy data regarding ACR20, 50, and 70 at 24 weeks, as well as AEs and serious AEs at 16 weeks were available in the included articles. Patients assigned to placebo were re-randomized to secukinumab 75 mg or 150 mg if the ACR20 response at week 16 was < 20% improvement from baseline, while ACR20 responders in the placebo group at week 16 were re-randomized to secukinumab 75 mg or 150 mg starting at week 24. The standardized summary table of studies included in the meta-analysis is listed in Table 1.

Bias assessment and sensitivity analysis

The Cochrane quality assessment tool was used for evaluating risk of bias in each study which indicated five of seven items low risk of bias. Unfortunately, random sequence generation and selective reporting incomplete outcome data were unclear in the three RCTs (Figs. 2 and 3). Overall, the statistical heterogeneity of all the outcomes assessed by the I^2 test ranged

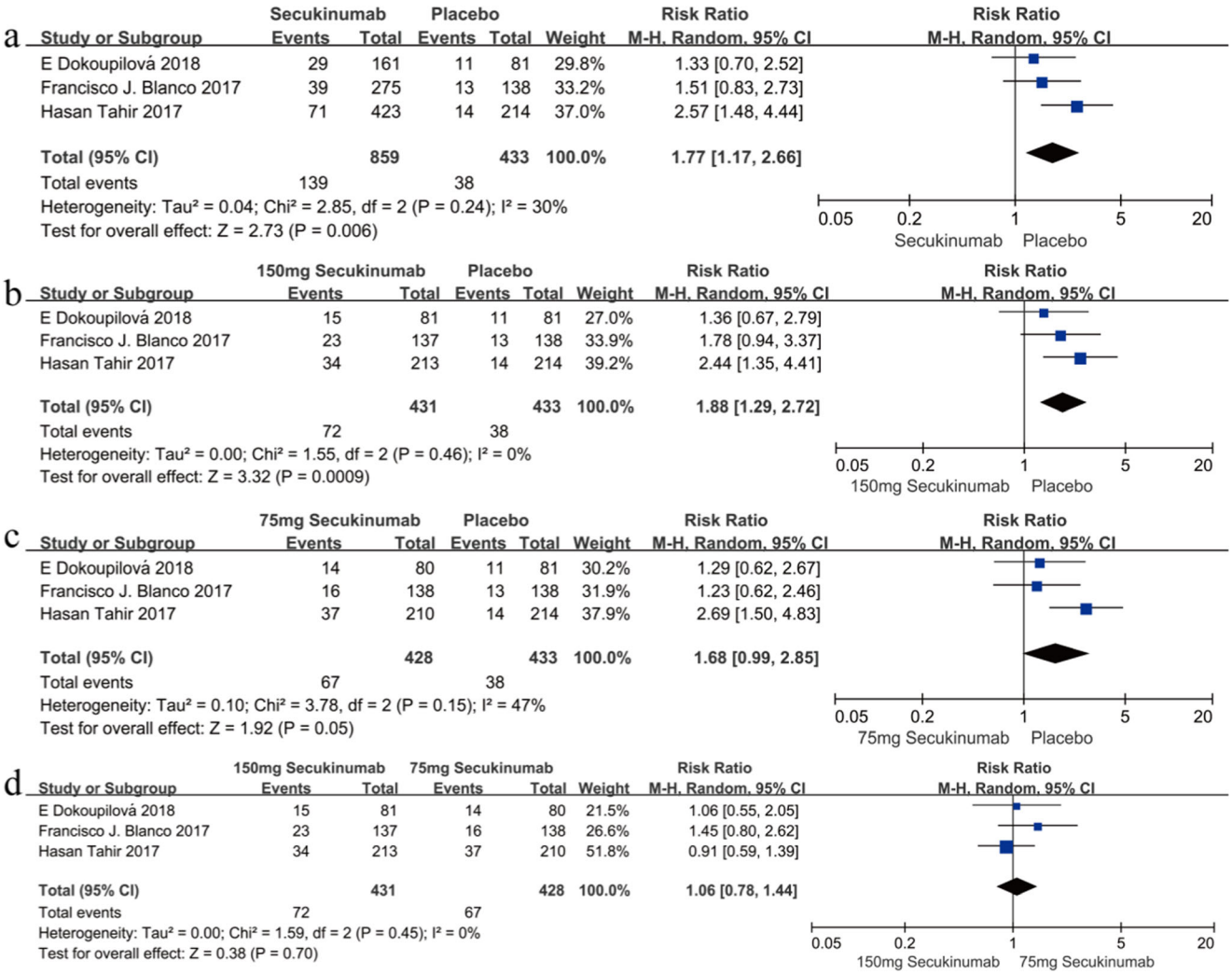

Fig. 5 Meta-analysis of secukinumab versus placebo on ACR50 response rate. **a**: Pooled 150/75 mg secukinumab group versus placebo group; **b**: 150 mg secukinumab group versus placebo group; **c**: 75 mg secukinumab group versus placebo group; **d**: 150 mg secukinumab group versus 75 mg secukinumab group. CI: confidence interval; df: degree of freedom

from 0 to 76%. For the Mantel–Haenszel random effects method, funnel plot analysis showed no evidence of publication bias in all comparisons (supplementary material Fig. 1). In addition, random and fixed effect models performed the same interpretation, indicating that no evidence of model selection may significantly affect our meta-analysis results (Supplementary Material Tables 1, 2).

Clinical efficacy of secukinumab at 24 weeks

ACR20, 50, and 70 at 24 weeks were considered the primary efficacy outcomes in this meta-analysis. Secukinumab was more effective as the estimated RRs of 150 mg, 75 mg, and pooled 150 mg/75 mg secukinumab versus placebo in terms of ACR20 response were 1.66 (95% CI 1.33, 2.08; $P < 0.0001$; $I^2 = 0\%$), 1.62 (95% CI 1.29, 2.03; $P < 0.0001$; $I^2 = 0\%$), and 1.64 (95% CI 1.33, 2.01; $P < 0.00001$; $I^2 = 0\%$) respectively (Fig. 4a–c). Nevertheless, the RR of 150 mg versus 75 mg secukinumab in ACR20 was 1.03 (95% CI 0.85, 1.24; $P = 0.79$; $I^2 = 0\%$) (Fig. 4d), showing insignificant difference between the two dosages.

In terms of ACR50 response, the estimated RRs of 150 mg, 75 mg, and pooled 150 mg/75 mg secukinumab versus placebo were 1.88 (95% CI 1.29, 2.72; $P = 0.0009$; $I^2 = 0\%$), 1.68 (95% CI 0.99, 2.85; $P = 0.05$; $I^2 = 47\%$), and 1.77 (95% CI 1.17, 2.66; $P = 0.006$; $I^2 = 30\%$) respectively (Fig. 5a–c). Compared with the placebo group, both the 150 mg and pooled 150 mg/75 mg secukinumab groups showed higher ACR70 response rates with RR 2.15 (95% CI 1.15, 4.02; $P = 0.02$; $I^2 = 0\%$) and 2.03 (95% CI 1.14, 3.60; $P = 0.02$; $I^2 = 0\%$) (Fig. 6a, b), whereas the 75 mg secukinumab group did not show a significantly increased ACR70 response (RR 1.81, 95% CI 0.78, 4.21; $P = 0.17$; $I^2 = 34\%$) (Fig. 6c). The 150 mg secukinumab was not dramatically superior to the 75 mg secukinumab in ACR50/ACR70 response (Figs. 5d, 6d). Patients received secukinumab 150 mg as well as

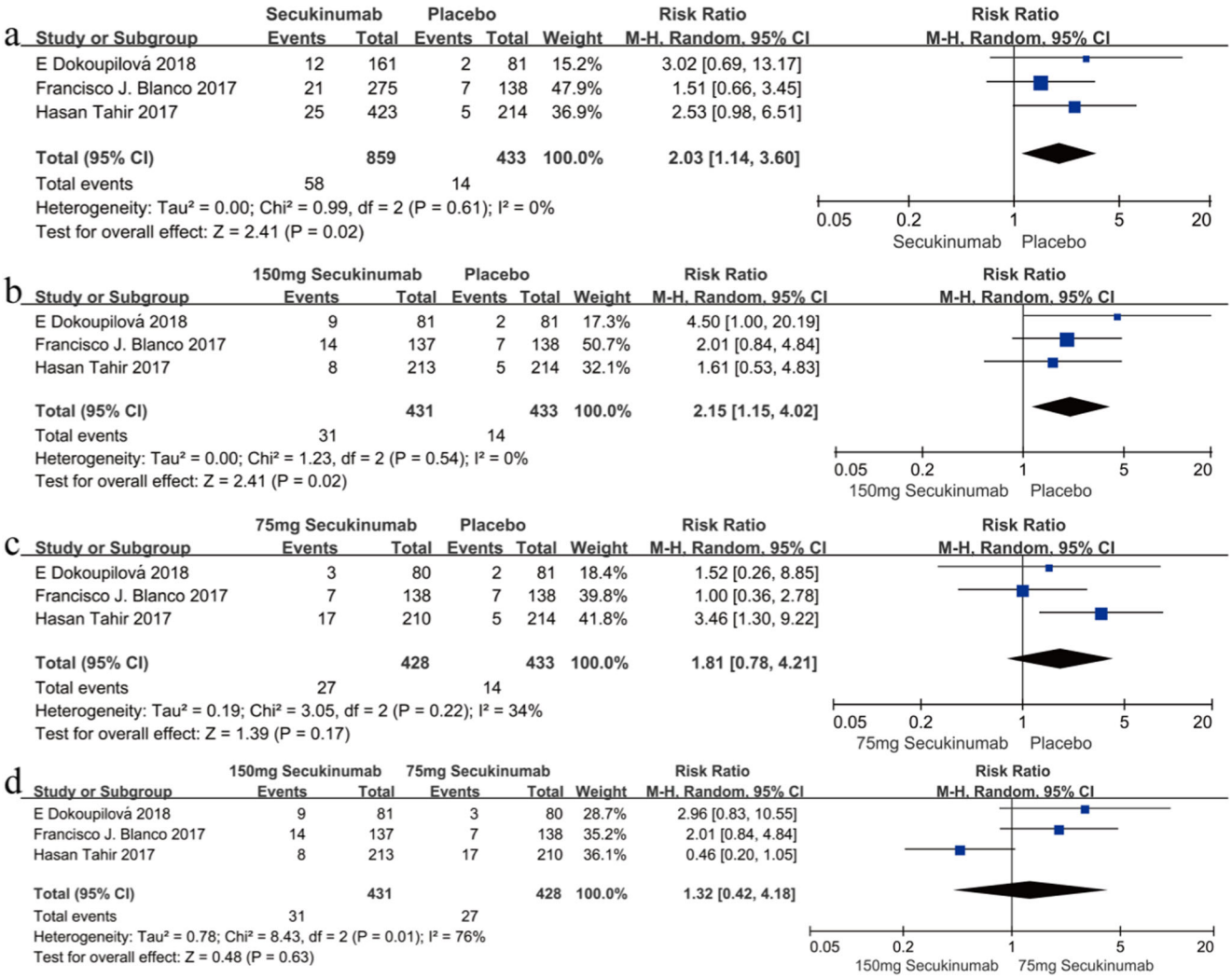

Fig. 6 Meta-analysis of secukinumab versus placebo on ACR70 response rate. **a** Pooled 150/75 mg secukinumab group versus placebo group. **b** 150 mg secukinumab group versus placebo group. **c** 75 mg secukinumab group versus placebo group. **d** 150 mg secukinumab group versus 75 mg secukinumab group. CI: confidence interval; df: degree of freedom

150 mg/75 mg showed significantly better ACR20, 50, and 70 response than placebo, and only a trend of efficacy was demonstrated in patients who received 75 mg secukinumab.

Safety in the secukinumab therapy and placebo arms

AEs and serious AEs at 16 weeks were considered the safety outcomes in this meta-analysis. The most frequent AEs reported were infections, nasopharyngitis, upper respiratory tract infection, arthralgia, and hypertension. No significant difference was found between the secukinumab group and placebo group in both AEs and serious AEs with overall RR 1.13 (95% CI, 0.94, 1.37; $P = 0.18$) and 1.19 (95% CI, 0.59, 2.39; $P = 0.63$), respectively (Figs. 7 and 8).

Taken together, these findings suggested that secukinumab (especially 150 mg) was effective and well tolerated in active RA patients with an inadequate response to, or intolerance of, TNF inhibitors.

Discussion

Treat-to-target strategy has dramatically improved the outcomes of RA patients. But the DMARDs currently available are not sufficient for patients to achieve the target; therefore, more clinical studies are ongoing to investigate the possibility of novel agents for the treatment of RA [26, 27]. Recently, secukinumab, an IL-17A inhibitor, was recommended by the US Food and Drug Administration and the Committee for Medicinal Products for Human Use of the European Medical Agency as a new treatment option for psoriasis and ankylosing spondylitis. In addition, effectiveness of secukinumab in RA patients has been shown in some clinical trials in the aspect of achieving ACR response and deceasing disease activity score [18, 24, 28]. Patient-reported outcomes were also found to be dramatically improved along with the improvement of other clinical endpoints. Moreover, the improvement of patient-

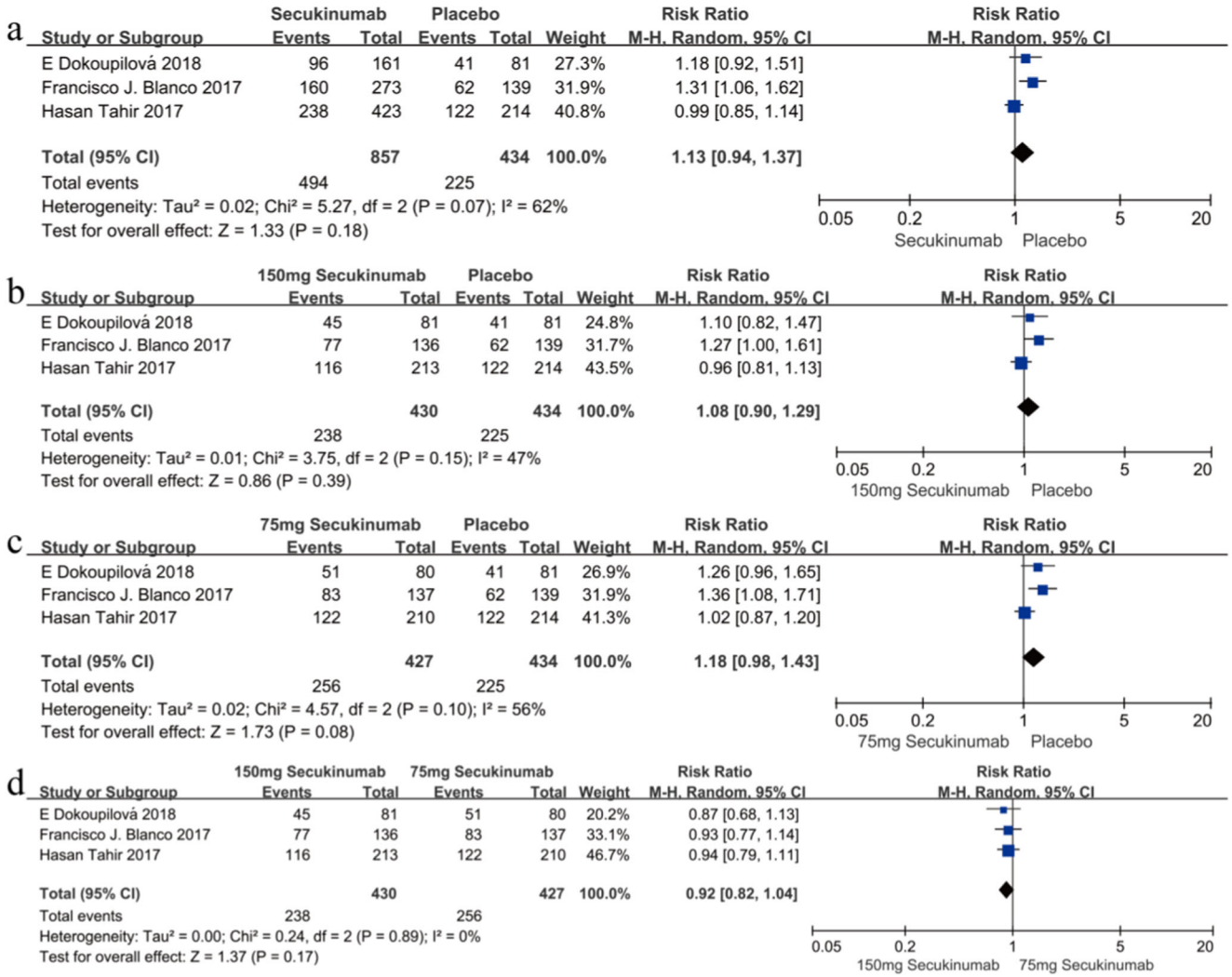

Fig. 7 Meta-analysis of adverse events at weeks 16. **a** Pooled 150/75 mg secukinumab group versus placebo group. **b** 150 mg secukinumab group versus placebo group. **c** 75 mg secukinumab group versus placebo group. **d** 150 mg secukinumab group versus 75 mg secukinumab group. CI: confidence interval; df: degree of freedom

reported outcomes was augmentative when higher clinical endpoints were achieved.

In this study, we conducted a meta-analysis to look at the efficacy and safety of secukinumab versus placebo in active RA patients who had an inadequate response to or intolerance of TNF inhibitors. Three eligible phase III RCT studies including 1292 RA patients were selected from 614 articles obtained from PubMed, Embase, and Web of Science databases by two independent authors. The ACR20/50/70 responses as well as AEs and serious AEs in this meta-analysis were assessed. Moreover, five items in seven were rated "low risk" for all included works and thus, the study design and the data of our meta-analysis were reasonable. Meanwhile, funnel plot analysis and sensitivity analysis showed no evidence of publication bias and model selection bias in our work. Generally, secukinumab 150 mg and pooled 150 mg/75 mg showed significantly higher ACR20, 50, and 70 response rates at week 24 than placebo. Although improvement in the ACR70 response rates was statistically insignificant, a trend of better efficacy with 75 mg secukinumab compared with placebo, this might be partially explained as moderate heterogeneity as well as variation in effect estimates observed in ACR70. The study from Hasan Tahir contributed to the moderate heterogeneity, which was likely to be related to ethnicity variation in patient selection (Caucasian only 39.9%). Indeed, a more possible explanation for a non-significant finding might be the nature of secukinumab itself. The current evidence is insufficient to support secukinumab as a first-line biological DMARD for the treatment of RA. But previous studies have revealed that the level of IL-17 was significantly increased in RA animal models and RA patients who had an inadequate response to TNF inhibitors. Thus, several RCTs have investigated the potential value of secukinumab as a second-line biologics in the treatment of RA. Our meta-analysis showed limited benefits of low-dose secukinumab (75 mg) in RA patients with insufficient response to TNF-α inhibitors, while secukinumab

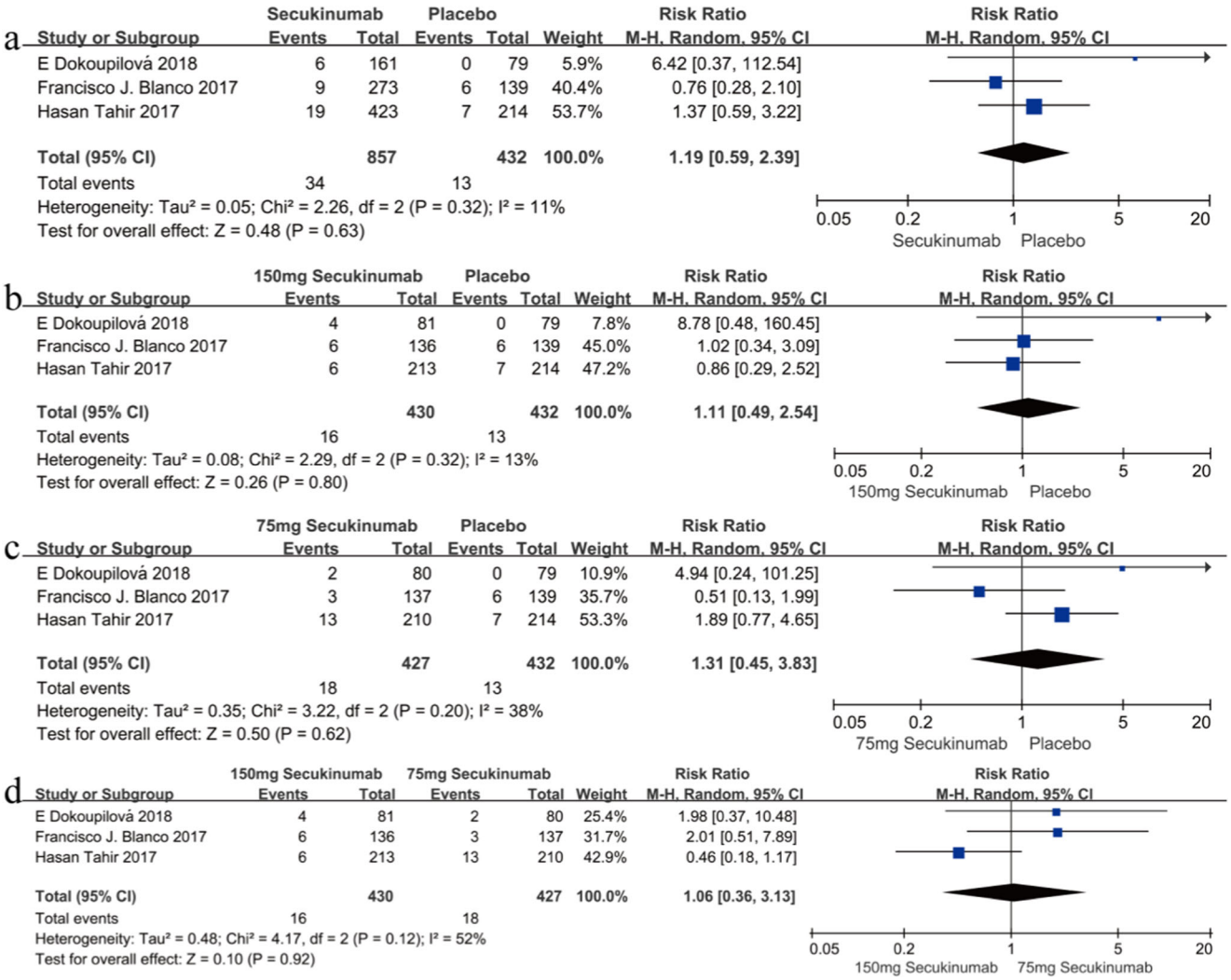

Fig. 8 Meta-analysis of serious adverse events at weeks 16. **a** Pooled 150/75 mg secukinumab group versus placebo group. **b** 150 mg secukinumab group versus placebo group. **c** 75 mg secukinumab group versus placebo group. **d** 150 mg secukinumab group versus 75 mg secukinumab group. CI: confidence interval; df: degree of freedom

150 mg did show significantly better clinical efficacy with no increased risk of AEs and serious AEs compared with placebo. This indistinctive result should be viewed with caution and needed to be further proved. Actually, it has been well established that IL-17A inhibitors were beneficial to patients with inflammatory arthritis in many clinical trials [19, 20, 24, 28, 29]. For example, a study by Burmester revealed the superior efficacy and well tolerance of secukinumab compared with placebo in biologic naive RA patients [19]. In our meta-analysis, we further showed higher efficacy of secukinumab than placebo in active RA patients who had an inadequate response to TNF inhibitors. This meta-analysis showing the superiority of 150 mg secukinumab therapy in achieving ACR20/50/70 improvement in RA patients was consistent with a previous study that 150 mg secukinumab was more effective than placebo in RA patients with inadequate response to conventional synthetic DMARDs or biologics [28]. In consideration of potential risks for more AEs caused by a high dose, most clinical trial did not include the 300 mg secukinumab group. At the same time, less effect of 75 mg secukinumab from our data indicated secukinumab 150 mg was probably the suitable dose in the treatment of RA patients. For safety profiles, secukinumab was generally well tolerated with no increased AEs and serious AEs compared with placebo through the 16 weeks.

There are several strengths of this meta-analysis. To our knowledge, this is the first meta-analysis to address the efficacy and safety of secukinumab versus placebo in active RA patients who had an inadequate response to TNF inhibitors in phase III RCTs. The total number of included 1292 patients with active RA was overwhelming compared with the patient number from each individual trial. In contrast to the individual study, we were able to present more accurate data by raising the statistical power and resolution by pooling the outcomes of individual analyses. Safety data from this meta-analysis confirmed the safety profiles of secukinumab as seen in the phase

III trials in psoriasis, PsA, and AS [30–32]. Some efficacy of secukinumab in RA was shown in several clinical studies, but the small size of these trials did not allow for definite conclusions [18–20, 28]. Our meta-analysis confirmed secukinumab (150 mg) was significantly effective in the treatment of active RA patients with an inadequate response to TNF inhibitors, while secukinumab (75 mg) showed a trend to be effective which was consistent with a previous report [33]. More importantly, the AEs and serious AEs were comparable between the secukinumab group and placebo group.

Of note, there are some limitations of our study. Firstly, we were not able to evaluate the long-term effects of secukinumab based on 24-week observation of all included clinical trials. Secondly, only three RCTs were eventually included in our meta-analysis. We assessed the ACR20, 50, and 70 responses as the efficacy outcomes and the rates of AEs and serious AEs for the safety. We were not able to comprehensively assess the efficacy and safety of secukinumab due to the limited available data. Various outcomes, such as EULAR improvement criteria, radiological progression, and patient-reported outcomes need to be addressed in the future trials. Last but not least, the protocol of the review had not been registered in the PROSPERO study. And all included studies were sponsored by Novartis Pharmaceuticals; thus, the possibility of overestimation of therapeutic effect due to sponsorship bias should be borne in mind.

Conclusions

In active RA patients with an inadequate response to TNF inhibitors, secukinumab may be a therapeutic option. Secukinumab 150 mg showed significantly better clinical efficacy with no increased risk of AEs and serious AEs compared with placebo.

Authors' contributions ZZL conceived of the work, contributed to its design and coordination, and critically revised the manuscript. HYR and FY had full access to all of the data collection, analysis, interpretation, and drafted the manuscript. LY and XWH were study investigators and contributed to the process of data collection. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Disclosures None.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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