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META-ANALYSIS

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Efficacy and safety of benralizumab in eosinophilic granulomatosis with polyangiitis: A meta-analysis of eight studies

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Abstract

Objective: Eosinophilic granulomatous polyangiitis (EGPA) is a rare autoimmune disease characterized by multisystemic inflammation, with eosinophils playing a central role in its pathogenesis. Traditional management relies heavily on corticosteroids and immunosuppressants, which are associated with significant side effects. The emergence of biologic agents, such as benralizumab, offers targeted therapeutic options by inhibiting the interleukin-5 receptor α, thereby reducing eosinophilic inflammation.

Methods: This systematic review and meta-analysis comprehensively evaluate the efficacy and safety of benralizumab in EGPA patients, focusing on its ability to reduce oral corticosteroid (OCS) use, facilitate remission and spare immunosuppressants. We searched MEDLINE, LILACS and ISI Web of Science databases for relevant studies up to July 2024.

Results: Eight studies, including both randomized controlled trials (RCTs) and observational studies, were included in the meta-analysis, involving a total of 396 EGPA patients. The pooled analysis demonstrated a significant reduction in OCS dose, with an overall estimated effect of −8.25 mg/day (95% CI, −9.39 to −7.10). Complete remission was achieved in 56.8% of patients, and immunosuppressants were reduced or discontinued in 28.1% of cases. Adverse events (AEs) were reported in 21.9% of patients, with only one discontinuation due to an AE.

Conclusion: These findings provide robust evidence supporting the use of benralizumab as an effective and well-tolerated treatment option for EGPA, significantly reducing OCS requirements and offering promising remission rates. Future research should focus on larger, multicentre RCTs to confirm these findings and further elucidate the long-term benefits and safety profile of benralizumab in EGPA.

KEYWORDS
anti-IL5r, benralizumab, EGPA, meta-analysis

1 | INTRODUCTION

Eosinophilic granulomatous polyangiitis (EGPA) is a rare, multisystemic, immune-mediated inflammatory disease, classified as a small-vessel necrotizing vasculitis belonging to the antineutrophil cytoplasm antibody (ANCA)-associated vasculitis group. It is classically considered a Th2-driven disease, in which the increased expression of eosinophilic specific mediators such as interleukin-5 (IL-5) is responsible for enhanced eosinopoiesis, eosinophil maturation, activation and prolonged survival.[1]

Classically, EGPA is characterized by history or presence of asthma, a blood eosinophil level equal to or greater than 10% or an absolute eosinophil blood count (EBC) of more than 1000 cells per cubic millimetre, and the presence of two or more typical criteria such as histopathological evidence of eosinophilic vasculitis, neuropathy, pulmonary infiltrates, sinonasal abnormality, cardiomyopathy, glomerulonephritis, alveolar haemorrhage, palpable purpura or ANCA positivity.[1] The disease progresses through three sequential phases: late-onset asthma, blood and tissue eosinophilia, and, finally, vasculitis based on clinical observations.[2]

Standard therapy relies on systemic corticosteroids in combination with immunosuppressants for severe and/or refractory diseases,[3] but since the central role of eosinophils in EGPA indicates that both extravascular and intravascular eosinophils can induce tissue damage through degranulation independent of ANCA-associated vasculitis,[4] the recent development of biologic agents offered new therapeutic options for this disease. Mepolizumab (MEPO) is a humanized monoclonal anti-IL-5 antibody, while benralizumab (BENRA), approved since 2017 for severe eosinophilic asthma, is a humanized monoclonal that binds to the alpha subunit of the human interleukin 5 receptor (IL-5Rα) with high affinity and specificity. Both act to reduce EBC levels with beneficial effects in severe eosinophilic asthma, and other hypereosinophilic disorders, including eosinophilic esophagitis, chronic rhinosinusitis with nasal polyposis and finally EGPA.[5,6]

To date, only two randomized controlled trial (RCT) on EGPA has been conducted. The first is the MIRRA study which showed that a dosage of 300 mg of MEPO every 4 weeks resulted in significant remission rates, including systemic corticosteroid reduction, compared to placebo.[7] The second one by Wechsler et al. demonstrated the non-inferiority of BENRA to MEPO in EGPA patients.[8] This evidence was obtained from a relatively small sample (70 cases under BENRA vs. 70 cases under MEPO treatment) as EGPA is a rare disease. However, several observational studies about the use of BENRA in EGPA have been conducted. These studies vary in sample size, follow-up duration and patient demographics. Their results may complement and expand data from the and increase the generalizability of the results.

Here, we combined by meta-analysis data from all the observational individual studies of BENRA for EGPA published to date plus the "benralizumab arm" of the Wechsler et al. study to assess the magnitude of benefit across different populations and to explain possible heterogeneity in results.

2 | METHODS

2.1 | Search strategy and selection criteria

We undertook and reported this systematic review and meta-analysis following with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

The study protocol is registered at PROSPERO (CRD42023494191). From inception (no backward time limit) to 10th July 2024, we searched MEDLINE, LILACS and the ISI Web of Science databases for published studies assessing the effectiveness and safety of BENRA in patients suffering from EGPA. A full list of the search terms is available in Figure 1 in the appendix. Studies were included in the meta-analysis if: (1) they included patients with EGPA; (2) included patients who were prescribed BENRA for EGPA; (3) assessed the relevant outcome measures of the treatment effect that is oral corticosteroids (OCS) and safety, regardless of whether these were the primary endpoints. Studies were excluded if they did not report the required information. There was no language or date restriction. We checked all reference lists and articles citing included studies and recent reviews for any additional relevant studies.

2.2 | Data collection process

We screened titles and abstracts, reviewed full texts, extracted data and assessed the risk of bias/study quality independently in duplicate (FS, AGS), using a standardized pre-piloted form.[9] We resolved disagreements by consensus adjudication or discussion with a third reviewer (RR).

We collected characteristics of studies, setting, eligibility criteria, population studied, intervention and outcomes.

2.3 | Outcomes

The effect of BENRA was assessed through a comparison of outcomes before starting BENRA treatment (time of BENRA initiation screening visit before initiation) and at

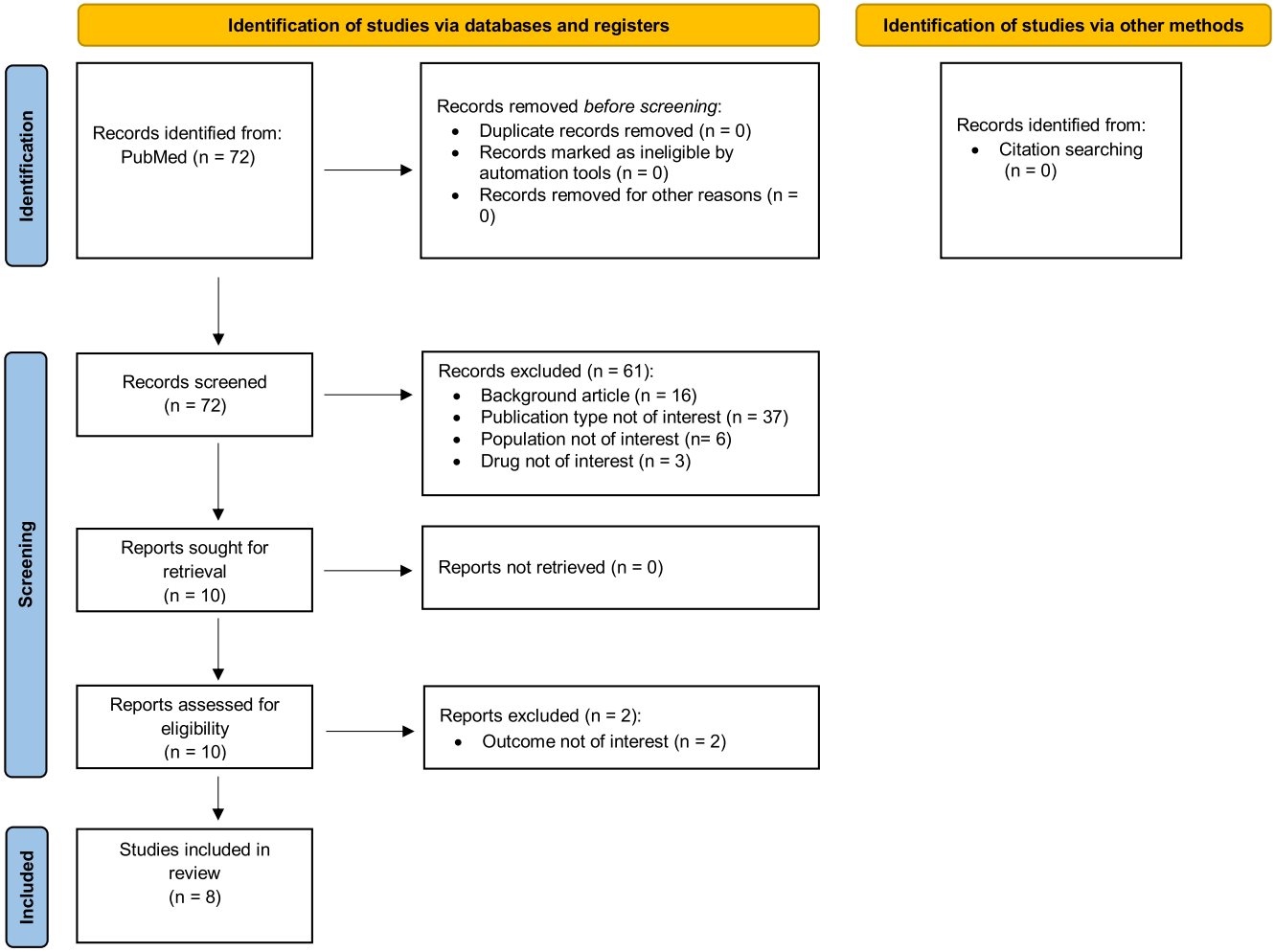

FIGURE 1 Flow diagram of research screening. #1 benralizumab OR anti-IL5r [Ti; Ab]—#2 EGPA [Ti; Ab] OR eosinophilic granulomatosis with polyangiitis [Ti; Ab]—#1 AND #2.

the end of the study observation period. For meta-analysis we utilized only the data from the "benralizumab arm" for the Wechsler et al. study.[8]

We considered the following critical outcomes: (1) decrease in OCS dose (mean OCS dose) expressed in mg of prednisone equivalent; (2) safety (type and number of treatment-related adverse events, AEs). We also assessed the effect of BENRA on immunosuppressants sparing and achieving remission. Patients failing to meet the established follow-up duration will be excluded from the meta-analysis. To enhance the analytical rigour, we will prioritize the follow-up period that captures the largest patient cohort in each study.

2.4 | Data analysis and risk of bias assessment

We pooled summary measures using DerSimonian and Laird random-effects, estimating heterogeneity using the Mantel–Haenszel model.[10] We combined continuous outcomes across studies (mean OCS dose) using unstandardized mean difference (MD).

We used GRADEpro GDT (available from gradepro.org) to create the summary of finding tables, and meta-analyses and statistical analyses were performed using both ProMeta 3.0 and RevMAN software.

We used the Quality Appraisal of Case Series Studies Checklist developed by the Institute of Health Economics (IHE) (available from http://www.ihe.ca/research-programs/rmd/cssqac/cssqac-about) for longitudinal studies with responses as "yes", "unclear/partial" or "no". We classified studies as being of acceptable quality (low to moderate risk of bias) if ≥70% "yes" responses.[11] Publication bias was assessed quantitatively by funnel plots, Egger's linear regression test, fail-safe calculation and trim-and-fill analysis.[12,13]

The quality of evidence was evaluated using the GRADE approach.[14] GRADE defines high certainty evidence when confidence that the true effect lies close to that of the estimate of the effect is very high; moderate certainty evidence when confidence in the effect estimate

is moderate (i.e. the true effect is likely to be close to the estimate, but there is a possibility that it is substantially different); low certainty evidence when the confidence in the effect estimate is limited (i.e. the true effect might be substantially different from the estimate of the effect); and very low certainty when confidence in the effect estimate is very low (i.e. the true effect is likely to be substantially different from the estimate of effect).

Meta-regression was also used to predict the size of the outcome variable according to the values of one or more explanatory variables such as: (1) age; (2) study length/duration; (3) Birmingham Vasculitis Activity Score (BVAS) at baseline[15]; (4) EBC at baseline; (5) sample size of studies.

Clinical and methodologic hypotheses motivated the selection of characteristics defining subgroups/explanatory variables: (1) study design (prospective vs. retrospective studies); (2) study type (unicentre vs. multicentre studies).

We in turn excluded each study to ensure that no single study would be solely responsible for the significance of any result (influential analysis) and tested between-study heterogeneity using χ^2 and quantified using I^2 statistic.[16]

3 | RESULTS

3.1 | Study selection

Our bibliographic searches yielded a total of 72 records. After the initial screening and triage process, 10 studies were assessed for eligibility, and ultimately, 8 articles met the inclusion criteria and were included in the meta-analysis (Figure 1).[8,17–23]

3.2 | Quality assessment and risk of bias

The overall quality for all outcomes was deemed acceptable (low risk of bias) in most studies. All eight studies reported ≥70% "yes" responses according to the critical appraisal tool adopted (Table S1). Therefore, the overall certainty of the evidence for the effective outcome was judged to be moderate for OCS (Table S2).

3.3 | Studies' and patients' characteristics

Table 1 provides a summary of the eight qualifying studies.

Two studies provided separated data by subgroups. Specifically, Cottu et al.[19] classified patients by the previous administration of MEPO: (1) "without prior mepolizumab" (Cottu-WOM) and (2) "With prior mepolizumab" (Cottu-WM); Mümmler et al.[22] analysed separately patients receiving BENRA in different stage of disease: (1) "Group A Maintenance therapy phase" (Mümmler-A) and (2) "Group B Induction therapy phase" (Mümmler-B).

There was only one double-blind-placebo-controlled study (Wechsler et al).[8] Five studies were retrospective, three studies were prospective. There were four multicentre studies.

The duration of treatment varied across the studies, ranging from 21 to 96 weeks, with a mean duration of 45 weeks. The baseline patient population included 396 individuals (216 females, 56.2%), with a mean age of 51.3 years old (SD ± 15.5), of whom 355 completed the studies. The sample size of the studies varied greatly, ranging from 5 to 121 patients. Moreover, 207 above 396 patients (52.3%), were previously treated with other monoclonal antibodies (mAb), such as MEPO (189 cases), omalizumab (8 cases) and reslizumab[10]; in particular, two studies and the "without prior mepolizumab" arm of Cottu et al. study, were not treated with mAb. The EBC mean at baseline was 510 cells (SD ± 502). In seven out eight studies, BENRA was administered subcutaneously with a dose of 30 mg once a month for 3 months, then 30 mg every 2 months; while in Wechsler et al. study patients received BENRA 30 mg once a month.

Furthermore, patient's characteristics are shown in Table 2. BVAS at baseline was available in seven of out eight studies with a mean score of 4.3. ANCA positivity was present in 74 cases (18.7%). As concerns clinical manifestations, 92 patients (23.8%) had cardiac involvement, 132 cases (34.2%) presented neurologic manifestations, 21 (5.4%) had renal involvement, 68 patients (17.6%) had skin eruptions, 291 patients (91.5%) had sinonasal involvement and 215 patients (55.7%) had pulmonary involvement.

3.4 | OCS sparing

The overall estimated effect (ES) for OCS consumption across all studies was −8.47 (95% CI, −9.86 to −7.09), indicating a significant reduction in the use of OCS in EGPA patients treated with BENRA. A moderate degree of heterogeneity was observed among the results of individual studies [heterogeneity: $\tau^2 = 2.11$, $\chi^2 = 19.25$, df = 9 ($p = 0.02$), $I^2 = 53\%$; test for overall effect: $Z = 12.02$ ($p < 0.00001$); Figure 2]. The fail-safe number was 873 and Egger's test yielded a p-value of 0.035, indicating the probability of publication bias (trimmed study = 0). After careful consideration, the study by Mümmler-B was excluded from the meta-analysis due to its outlier status, as it significantly deviated from the overall trend observed in the remaining studies. As a result, the overall ES for OCS sparing across all studies was −8.25 (95% CI, −9.39 to −7.10). Notably, heterogeneity

TABLE 1 Studies' characteristics.

Study, year	Study type	Study duration (weeks)	Patients at baseline, *n*	Age, mean (SD)	Female, *n* (%)	Previous therapy with other mAb, *n* (%)	Patients who completed the study, *n*	EBC at baseline, mean (SD)	Benralizumab dose administered subcutaneously
Guntur, 2020	P; SC	24	10	47 (10)	5 (50)	0 (0)	10	350 (311)	30 mg every month for 3 months. Then, 30 mg every 2 months
Padoan, 2020	P; SC	24	5	43.6 (23.1)	4 (80)	3 (60)	5	1064 (945)	30 mg every month for 3 months. Then, 30 mg every 2 months
Cottu-WOM, 2023	R; MC	21	37	51.4 (18.7)	16 (43.2)	0 (0)	37	805 (575)	30 mg every month for 3 months. Then, 30 mg every 2 months
Cottu-WM, 2023	R; MC	21	31	50.4 (19.5)	16 (51.6)	31 (100)	31	88 (113)	30 mg every month for 3 months. Then, 30 mg every 2 months
Nolasco, 2023	R; MC	96	26	50.3 (11.5)	14 (53.8)	1 (3.8)	26	1078 (1015)	30 mg every month for 3 months. Then, 30 mg every 2 months
Bettiol, 2023	R; MC	48	121	53.5 (13.5)	64 (53)	40 (33)	85	560 (645)	30 mg every month for 3 months. Then, 30 mg every 2 months
Mümmler-A, 2024	R; SC	48	17	58 (18)	12 (71)	8 (47)	15	197 (251)	30 mg every month for 3 months. Then, 30 mg every 2 months
Mümmler-B, 2024	R; SC	48	9	55 (14)	4 (44)	1 (11)	7	412 (717)	30 mg every month for 3 months. Then, 30 mg every 2 months
Nanzer, 2024	R; SC	48	70	49.4 (14.3)	36 (51.6)	24 (34)	70	235 (227)	30 mg every month for 3 months. Then, 30 mg every 2 months
Wechsler, 2024	P; MC	48	70	54 (12)	45 (64)	0 (0)	69	306 (225)	30 mg every month
Total		**45**	**396**	**51.3 (15.5)**	**216 (56.2)**	**207 (52.3)**	**355**	**510 (502)**	

Abbreviations: EBC, eosinophils blood count; mAb, monoclonal antibody; MC, multicentre; P, prospective; R, retrospective; SC, single centre; SD, standard deviation.

TABLE 2 Patient's characteristics.

Study, year	Patients at baseline, *n*	BVAS	ANCA positivity, *n* (%)	Cardiac involvement, *n* (%)	Neurologic involvement, *n* (%)	Renal involvement, *n* (%)	Skin involvement, *n* (%)	Sinonasal involvement, *n* (%)	Pulmonary involvement, *n* (%)
Guntur, 2020	10	10 (n.a.)	3 (30)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Padoan, 2020	5	3.6 (1)	1 (20)	0 (0)	1 (20)	0 (0)	0 (0)	5 (100)	3 (60)
Cottu-WOM, 2023	37	3.3 (1.5)	9 (24.3)	5 (13.6)	0 (0)	0 (0)	0 (0)	n.a.	3 (8.1)
Cottu-WM, 2023	31	2.7 (1.6)	3 (9.7)	0 (0)	1 (3.3)	0 (0)	0 (0)	n.a.	2 (6.7)
Nolasco, 2023	26	6.7 (4.7)	7 (26.9)	5 (19.2)	7 (26.9)	2 (7.7)	4 (15.4)	23 (88.5)	15 (57.7)
Bettiol, 2023	121	4.4 (4.5)	23 (21)	32 (26)	54 (45)	10 (8)	42 (35)	111 (92)	88 (73)
Mümmler-A, 2024	17	n.a.	2 (12)	7 (41)	6 (35)	0 (0)	3 (18)	16 (94)	14 (82)
Mümmler-B, 2024	9	n.a.	0 (0)	6 (67)	2 (22)	1 (11)	0 (0)	8 (89)	9 (100)
Nanzer, 2024	70	1.9 (2)	19 (27)	20 (28.6)	23 (32.9)	4 (5.7)	12 (17.1)	65 (92.9)	32 (45.7)
Wechsler, 2024	70	2.3 (3.5)	7 (10)	17 (24)	38 (54)	4 (6)	7 (10)	63 (90)	49 (70)
Total	**396**	**4.3**	**74 (18.7)**	**92 (23.8)** *	**132 (34.2)** *	**21 (5.4)** *	**68 (17.6)** *	**291 (91.5)** *	**215 (55.7)** *

Abbreviation: n.a., not available.

*Studies with no reported data are not in included in calculation.

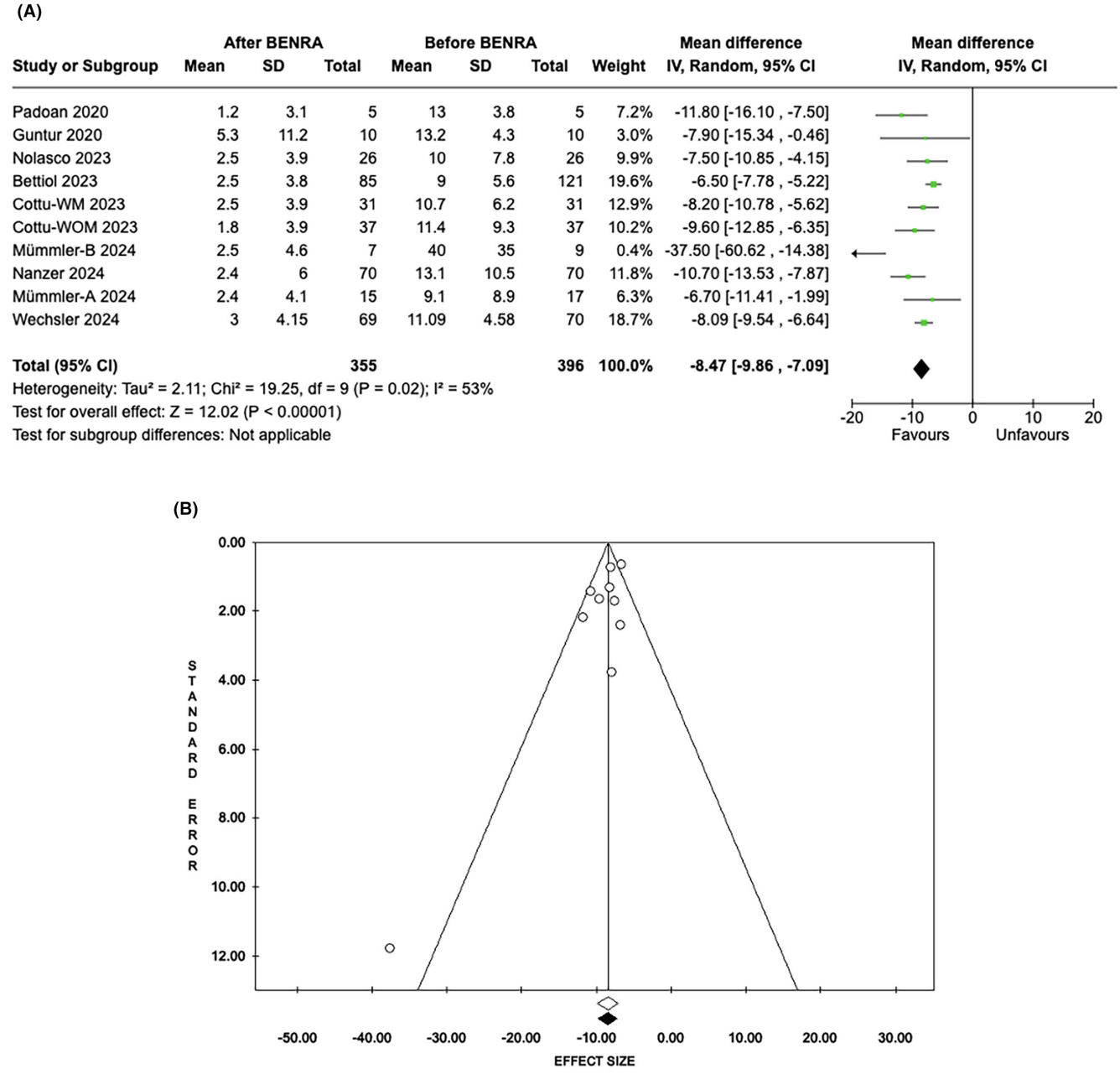

FIGURE 2 (A) Meta-analysis on benralizumab (BENRA) in EGPA patient assessing OCS sparing, reported as difference between baseline and post-treatment level. The overall estimated effect (ES) for OCS consumption across all studies was −8.47 (95% CI, −9.86 to −7.09). A moderate degree of heterogeneity was observed among the results of individual studies [heterogeneity: $\tau^2 = 2.11$, $\chi^2 = 19.25$, df = 9 ($p = 0.02$), $I^2 = 53\%$; test for overall effect: $Z = 12.02$ ($p < 0.00001$)]. (B) Funnel plot under random effect model with fail-safe number = 873, Egger's test yielded a p-value = 0.035 and trimmed study = 0, indicates the probability of publication bias.

remained moderate [Heterogeneity: $\tau^2 = 1.02$, $\chi^2 = 12.94$, df = 8 ($p = 0.11$), $I^2 = 38\%$; test for overall effect: $Z = 14.08$ ($p < 0.00001$)], however there is no significant evidence of heterogeneity between studies. The fail-safe number was 780 and Egger's test yielded a p-value of 0.154, indicating a low probability of publication bias (trimmed study = 0; Figure S1).

Furthermore, we performed the meta-regression to individualize potential sources of heterogeneity among the studies, removing the outlier study (Mümmler-B). No substantial difference in OCS sparing was seen according to study duration ($p = 0.568$; $p = 0.324$ without the outlier study), EBC at baseline ($p = 0.785$; $p = 0.781$ without the outlier study), BVAS at baseline ($p = 0.317$; data on BVAS are not available for Mümmler et al. study). Nevertheless, the meta-regression revealed a significant association between mean age of patients and the study outcome ($p = 0.022$) excluding the outlier study: the younger the patients, the greater the steroid sparing observed at the end of the study (Figure S2). Moreover, no

difference was observed between: (1) single-centre and multicentre studies; (2) prospectives and retrospective studies (Figure S3).

A total sparing of OCS (0 mg of prednisone equivalent at the end of the observation period) was reached in 195 patients (39.5%) (Table S3).

3.5 | Immunosuppressants sparing

Complete data about the use of immunosuppressive therapy were available only for four out eight studies. Patients initially treated with immunosuppressants (DMARDs) were 45.4% of the total. At the end of the observation period, they were suspended in 28.1% of cases patients (Table S4).

3.6 | Remission

Complete data about accrued remission after BENRA treatment were available for six out eight studies. All studies defined remission as BVAS = 0 and prednisone dose ≤4 mg/day, except for Mümmler et al. that considered BVAS = 0 and prednisone dose ≤7.5 mg/day.

However, patients who accrued remission were 56.8%, calculated on number of patients who completed the study (Table S5).

3.7 | Adverse events

The results of AEs associated with BENRA treatment are summarized in Table S6. A total of 87 out of 396 (21.9%) patients experienced AE. The total number of AE was 154, of which 4.5% were local and 95.5% were systemic. Only one patient (0.25%) discontinued BENRA for AE.

4 | DISCUSSION

EGPA is a rare and complex autoimmune disease, and while its exact pathogenesis remains elusive, ongoing research is fervently seeking innovative treatments. Eosinophils, the hallmark cells implicated in EGPA, are now at the forefront of scientific interest due to their central role in the disease's inflammatory process. Among the promising therapeutic agents, BENRA has emerged as a powerful contender alongside the already approved MEPO, offering new hope for effective management of this challenging condition.

To our knowledge this is the first meta-analysis that aims to comprehensively evaluate the effectiveness of BENRA in the treatment of EGPA, focusing on its capacity to reduce OCS use, facilitate remission, spare immunosuppressants and its safety profile. Our findings demonstrate that BENRA is effective in significantly reducing OCS requirements, achieving remission, and sparing immunosuppressants in a substantial proportion of EGPA patients, with a manageable safety profile. A review by Koga et al. summarized the previous literature published (case reports and case series articles) on the efficacy of BENRA in the treatment of EGPA, showing that BENRA was effective in patients with mepolizumab-refractory EGPA and in patients with intractable cardiac and neuropathy complications, as well as a systematic review by Kouverianos et al. was published in 2023, and all included studies demonstrated the efficacy of BENRA in the treatment of EGPA, showing significant reductions in steroid use.[24,25]

The pooled analysis revealed a significant reduction in OCS use among patients treated with BENRA, with a mean decrease of −8.25 mg/day (95% CI, −9.39 to −7.10). This OCS-sparing effect is clinically significant given the well-documented adverse effects of prolonged corticosteroid therapy, including osteoporosis, hyperglycemia, hypertension and increased susceptibility to infections.[26] The moderate heterogeneity observed ($I^2 = 38\%$) suggests some variability in response across different studies, which was further explored through meta-regression analyses. These analyses indicated that younger patients tended to benefit more in terms of steroid reduction, possibly due to a more robust immune response or fewer comorbidities complicating the clinical picture, or the length of EGPA disease. This finding could guide future personalized treatment strategies, advocating for earlier introduction of BENRA in younger populations to maximize benefits.

Moreover, our analysis showed that BENRA allowed for the reduction or cessation of additional immunosuppressive therapies in 28.1% of cases. This sparing effect on immunosuppressants is particularly relevant for patients experiencing side effects from conventional disease-modifying antirheumatic drugs (DMARDs) or those who are at risk for infections due to long-term immunosuppression.[27] This finding aligns with the known mechanism of action of BENRA, which induces apoptosis of eosinophils and basophils by targeting the IL-5 receptor α, reducing the inflammatory burden characteristic of EGPA.

Complete remission, defined as a BVAS of 0 and a prednisone dose ≤4 mg/day (≤7.5 mg/day for one study), was achieved in 56.8% of patients. This remission rate is promising, especially considering the refractory nature of EGPA and the chronic reliance on corticosteroids in many patients. The slight variation in remission criteria across studies may contribute to some degree of heterogeneity, but the overall high rate of remission underscores

BENRA's potential as a viable long-term treatment option for EGPA.

AE were reported in 21.9% of patients, with systemic AE being more common than local reactions. Only one patient discontinued BENRA due to AE, indicating that the treatment is generally well-tolerated. The types of AE observed were consistent with those reported in other studies involving BENRA for asthma and other eosinophilic disorders, which include mild to moderate reactions such as headache, pharyngitis, and injection site reactions.[28] This safety profile is favourable compared to the risks associated with long-term high-dose corticosteroid use and conventional immunosuppressants.

Despite the promising results demonstrated in this meta-analysis, not all EGPA patients treated with BENRA achieve remission. This may be attributed to the complex and heterogeneous nature of the disease, particularly in cases involving severe organ damage or a predominance of non-eosinophilic pathways. Some patients may be resistant to BENRA due to alternative pathogenic mechanisms, such as ANCA-associated vasculitis or Th1/Th17-mediated inflammation, which are not primarily driven by IL-5 or eosinophils. These findings highlight the need for further research to identify molecular and immunological factors that could predict non-responsiveness to BENRA. This may lead to the development of biomarkers that can guide personalized therapy in EGPA. In such cases, alternative or adjunctive therapies targeting different pathways may be necessary to achieve disease control.[4]

Anyway, the primary limitation of this meta-analysis is the inclusion of both RCTs and observational studies, which may introduce heterogeneity in study designs, patient populations, and outcome measurements. The single RCT included, although robust, involved a relatively small sample size typical of studies on rare diseases like EGPA. Additionally, variations in study duration and the definition of remission could affect the generalizability of the results. Despite these limitations, the strengths of this meta-analysis include a comprehensive literature search, rigorous assessment of study quality and risk of bias, and the use of advanced statistical methods to explore heterogeneity and potential confounding factors. The inclusion of real-world data from observational studies enhances the external validity of the findings, offering a broader perspective on the efficacy and safety of BENRA in routine clinical practice.

5 | CONCLUSION

In summary, BENRA appears to be an effective and well-tolerated treatment option for EGPA, significantly reducing OCS use, facilitating remission, and sparing immunosuppressants in a considerable proportion of patients. Future research should focus on larger, multicentre RCT to confirm these findings and further elucidate the long-term benefits and safety profile of BENRA. Additionally, identifying patient subgroups that may derive the most benefit from BENRA will be crucial in optimizing treatment strategies for this challenging and heterogeneous disease.

AUTHOR CONTRIBUTIONS

FS developed the concept of the manuscript, did the article search and wrote the first manuscript draft. FS, AGS and ADG extracted the data from each manuscript. AGS, AV and RR critically reviewed the manuscript, corrected the manuscript and secured financial support. All authors have read and approved the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data related to this manuscript will be made available upon request.

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28. ANNEX I: Summary of product characteristics; 2024. https://www.ema.europa.eu/en/documents/product-information/fasenra-epar-product-information_en.pdf

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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