ISSN: 2581 – 3633

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: *https://www.ijmacr.com*

Volume – 9, Issue – 6, November – 2026, Page No.: 47 – 58

Phenotypic Characterization of Severe Asthma and Its Association with Treatment Response: A Systematic Review

[1]Dr.Kanishka Choudhary, Senior Resident, Department of Respiratory Medicine, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India.

[2]Dr.Sourav Sharma, Junior Resident, Department of Respiratory Medicine, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India.

[3]Dr. Palkin Bhatia, Junior Resident, Department of Respiratory Medicine, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India.

[4]Dr. Prity Sharma, Junior Resident, Department of Respiratory Medicine, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India.

[5]Dr. Rishabh Garg, Junior Resident, Department of Respiratory Medicine, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India.

Corresponding Author: Dr. Sourav Sharma, Junior Resident, Department of Respiratory Medicine, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India.

How to citation this article: Dr. Kanishka Choudhary, Dr. Sourav Sharma, Dr. Palkin Bhatia, Dr. Prity Sharma, Dr. Rishabh Garg, "Phenotypic Characterization of Severe Asthma and Its Association with Treatment Response: A Systematic Review", IJMACR– November – 2026, Volume – 9, Issue – 6, P. No. 47 – 58.

Open Access Article: © 2026, Dr. Kanishka Choudhary, et al. This is an open access journal and article distributed under the terms of the creative common's attribution license (http://creativecommons.org/licenses/by/4.0). Which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

Background: Severe asthma is a heterogeneous chronic inflammatory airway disease characterized by distinct clinical phenotypes, inflammatory endotypes, variable disease severity, and differential responses to treatment. Phenotypic characterization using clinical characteristics and biomarkers, including blood eosinophil counts, fractional exhaled nitric oxide (FeNO), serum immunoglobulin E (IgE), and comorbidities, has become essential for individualized therapeutic decision-making. However, the relationship between specific severe asthma phenotypes and treatment outcomes remains incompletely understood.

Objective: To systematically evaluate the association between severe asthma phenotypes and treatment response, with particular emphasis on biologic therapy effectiveness, exacerbation reduction, lung function improvement, asthma control, oral corticosteroid reduction, and clinical remission.

Methods: A systematic review was conducted using studies identified through PubMed/MEDLINE and additional literature sources, including reference lists and publisher databases, covering evidence available through September 2026. Randomized controlled trials, prospective and retrospective observational studies, and severe asthma registry investigations evaluating phenotypic characteristics and treatment responses were considered. Data were extracted on demographic characteristics, inflammatory biomarkers, clinical phenotypes, biologic treatment regimens, exacerbation rates, forced expiratory volume in one second (FEV_1), oral corticosteroid requirements, and clinical outcomes. Methodological quality and heterogeneity were assessed through structured critical appraisal, and findings were synthesized according to inflammatory phenotype, therapeutic class, and treatment-response indicators.

Results: A total of 1,726 records were identified, comprising 1,684 database records and 42 additional records. After removal of 298 duplicates, 1,428 records underwent title and abstract screening, of which 1,352 were excluded. Seventy-six full-text articles were assessed for eligibility, and 58 were excluded because of unavailable treatment-response data[24], inadequate severe asthma phenotypic characterization[19], or ineligible study design and duplicate reporting[15]. Eighteen studies were included in the qualitative synthesis. Clinical evidence demonstrated substantial variation in treatment response across severe asthma phenotypes. The MENSA trial reported reductions in clinically significant exacerbations of 47% and 53% with intravenous and subcutaneous mepolizumab, respectively, compared with placebo. A pooled DREAM/MENSA analysis demonstrated an increasing treatment effect with higher baseline blood eosinophil counts, with exacerbation reductions ranging from 52% among patients with eosinophil counts ≥150 cells/μL to 70% among those with counts ≥500 cells/μL. The SIROCCO trial demonstrated exacerbation rate ratios of 0.55 and 0.49 with benralizumab administered every four and eight weeks, respectively, in patients with eosinophilic asthma. Dupilumab reduced severe exacerbations by 47.7% in the 200-mg treatment group of the QUEST trial. In the NAVIGATOR trial, tezepelumab demonstrated an overall exacerbation rate ratio of 0.44, with a rate ratio of 0.59 among patients with baseline eosinophil counts below 300 cells/μL. Real-world registry evidence demonstrated that approximately 59% of patients achieved at least a 50% reduction in exacerbation frequency, whereas improvement in asthma control was observed in approximately 49%. Higher blood eosinophil counts and elevated FeNO were associated with greater treatment responses in selected biologic-treatment groups, although associations varied across therapeutic mechanisms and clinical endpoints.

Conclusion: Severe asthma phenotypes demonstrate clinically meaningful differences in treatment response, particularly regarding exacerbation reduction, lung function, corticosteroid requirements, and asthma control. Eosinophilic and type 2–high inflammatory phenotypes generally exhibit favorable responses to targeted biologic therapies, while selected treatments provide benefits across broader inflammatory profiles. Blood eosinophils, FeNO, allergic sensitization, comorbidities, and baseline exacerbation burden are important factors in treatment selection. Multidimensional phenotypic assessment may improve therapeutic individualization and clinical outcomes in patients with severe asthma.

©2026, IJMACR

Keywords: Severe Asthma, Phenotypic Characterization, Inflammatory Endotypes, Eosinophilic Asthma, Type 2 Inflammation, Biologic Therapy, Treatment Response, Blood Eosinophils, Fractional Exhaled Nitric Oxide, Systematic Review.

Introduction

Severe asthma persists despite optimized high-dose inhaled corticosteroid–long-acting β_2 agonist therapy or requires such treatment to avoid loss of control. Adherence, inhaler technique, exposure management, alternative diagnoses and treatable comorbidities must be evaluated before assigning severe disease[1,2]. Severe asthma encompasses eosinophilic, allergic, late-onset, obesity-associated and lower-type-2-inflammatory phenotypes, often with overlapping traits[3,4,24].

Type 2 (T2) inflammation involves IL-4, IL-5, IL-13, IgE and related epithelial pathways. Blood eosinophil count (BEC), FeNO and allergen sensitization provide accessible but incomplete surrogate measures. Suppression of eosinophils by systemic glucocorticoids, intra-individual fluctuation and the lack of a single threshold that predicts every outcome complicate treatment selection[1,3,8,27]. In addition, symptom control, fewer attacks, improved FEV_1, OCS reduction and clinical remission represent different endpoints rather than interchangeable expressions of efficacy[18,23,26].

This review examines whether observable severe-asthma phenotypes and biomarkers modify response to anti-IgE, anti-IL-5/IL-5Rα, anti-IL-4Rα and anti-TSLP biologics, and how randomized and real-world evidence differ.

Methods

Review question and eligibility criteria

The review question was defined using population, exposure/intervention, comparison and outcome (PICO): patients aged ≥12 years with severe or uncontrolled asthma; baseline clinical phenotypes and biological markers; biologic treatment or alternative phenotype-defined strata; and clinical outcomes including exacerbation rate, FEV_1, Asthma Control Test/Asthma Control Questionnaire (ACT/ACQ), maintenance OCS dose, hospitalization and clinical remission. Randomized controlled trials, prospective and retrospective severe-asthma registries, and trial subgroup analyses reporting at least one phenotype–response association were eligible. Studies lacking outcome data or phenotypic characterization, duplicate cohorts without added analyses, and nonclinical reports were excluded from the main synthesis. Published systematic reviews were considered for context and were not counted as independent patient cohorts.

Information sources and search strategy

The literature search considered PubMed/MEDLINE, Embase, Scopus, Web of Science, reference lists and publisher-hosted records available through September 2026. Search concepts combined “severe asthma” OR “uncontrolled asthma” with “phenotype” OR “endotype” OR “eosinophil” OR “FeNO” OR “IgE” OR “type 2” and “biologic” OR individual agent names, together with “treatment response,” “exacerbation,” “FEV1,” “oral corticosteroid” or “remission.” Controlled trials and longitudinal observational designs were prioritized, while important earlier pivotal studies were retained irrespective of publication year [6–17,28–30].

Study identification and screening

Database searches identified 1,684 records and reference lists or publisher sources contributed 42, giving 1,726 records. Following duplicate removal (298), 1,428 titles and abstracts entered screening. At this stage, 1,352 were excluded: 1,086 unrelated to the question, 171 reviews/editorials/commentaries, and 95 with ineligible

populations or study designs. Of 76 full-text articles assessed, 58 were excluded for absence of treatment-response data[24], absent severe-asthma phenotypic characterization[19], or ineligible design or duplicate reporting[15]. Eighteen studies were included in qualitative synthesis (Figure 1).

Data items and outcome definitions

Study-level abstraction prioritized setting, design, age, sample size, severe-asthma definition, biologic class and comparator, follow-up interval, BEC (cells/μL), FeNO (parts per billion), total and specific IgE, OCS exposure, nasal polyps, exacerbation history and measures of atopy. Exacerbation outcomes were expressed as reported annualized rates, rate ratios or percentage reductions. Lung function was considered as absolute or percentage-predicted FEV_1; symptom response as ACT/ACQ changes; steroid response as OCS dose or discontinuation; and remission as the exact composite used by each report [18,23,26,31].

Study quality, confounding and applicability

For randomized studies, assessment focused on allocation procedures, masking, intention-to-treat analysis, attrition, outcome ascertainment and multiplicity in subgroup testing. Observational cohorts were evaluated for confounding by indication, baseline severity, time-varying therapy, incomplete follow-up, switching and survivorship effects. Biomarker thresholds selected post hoc and comparisons made without tests of treatment-by-biomarker interaction were interpreted cautiously. No unsupported domain-level risk-of-bias classifications or certainty grades were assigned to individual reports.

Evidence synthesis and analytical approach

A structured narrative synthesis was chosen because drug mechanisms, biomarker cutoffs, outcome definitions, follow-up and cohorts were not exchangeable. Placebo-controlled trial contrasts were distinguished from within-person pre/post registry associations. Original odds ratios, rate ratios, proportions and confidence intervals were retained. Trial reports, their secondary analyses, and overlapping International Severe Asthma Registry (ISAR) cohorts were not added together as independent populations. Previously published pooled estimates were attributed to their original analyses and were not recomputed[3,23,25].

Results

Study selection

A total of 1,726 records were identified; after removal of 298 duplicates, 1,428 records were screened. Seventy-six articles underwent full-text eligibility assessment, and 18 studies entered the qualitative synthesis. Exclusion categories and numerical counts are summarized in Figure 1.

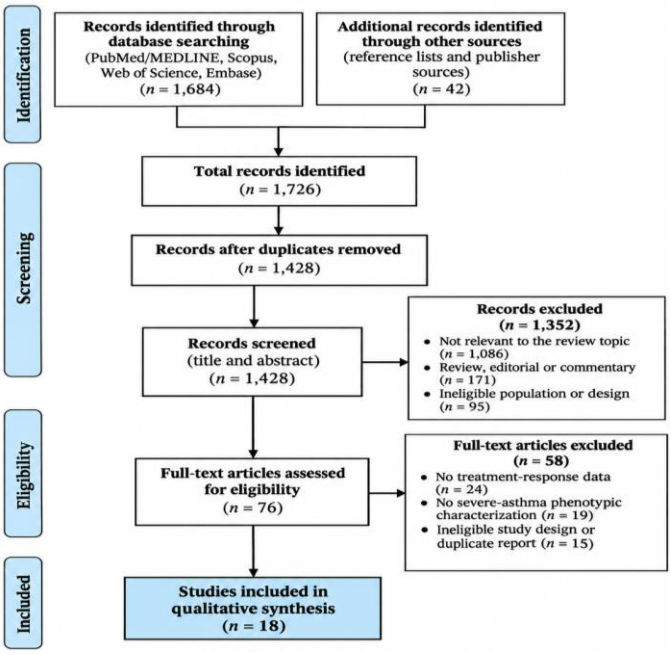


Figure 1: PRISMA flow diagram of study selection.

Study characteristics and phenotype domains

The included evidence covered eosinophilic, allergic and overlapping T2-high phenotypes, lower-T2-biomarker

disease, maintenance-OCS-dependent severe asthma, and registry-defined multidimensional response. Pivotal randomized trials examined mepolizumab, benralizumab, dupilumab and tezepelumab with placebo-controlled outcomes, whereas large multinational registries examined predictors after treatment initiation in routine practice. Table 1 presents major trials and phenotype-response contrasts; companion analyses of the same trial are shown as secondary evidence, not independent populations [6–14,18,19,26,27,43].

Table 1: Selected randomized studies and phenotype-associated response estimates

Study / population	Phenotype or marker	Treatment and quantitative outcome
DREAM; 621 patients[6]	Eosinophilic severe asthma	Mepolizumab: 39%–52% exacerbation reduction across doses
MENSA; 576 patients[7]	Eosinophilic exacerbation phenotype	Mepolizumab: 47% IV and 53% SC exacerbation reduction
DREAM/MENSA post hoc; 1,192[8]	BEC ≥150 to ≥500/μL	Exacerbation reduction: 52% to 70% across thresholds
SIROCCO; 1,205 randomized[9]	BEC ≥300/μL subgroup	Benralizumab rate ratio: 0.55 Q4W; 0.49 Q8W
QUEST; 1,902 patients[11]	T2 markers and uncontrolled asthma	Dupilumab 200 mg: 47.7% lower severe exacerbation rate
VENTURE; 210 patients[12]	Maintenance OCS dependence	OCS-dose reduction: 70.1% versus 41.9%
NAVIGATOR; 1,061 patients[13]	Uncontrolled asthma; low and high BEC	Tezepelumab rate ratio 0.44 overall; 0.59 if BEC <300/μL
SOURCE; 150 patients[14]	Maintenance OCS dependence	OCS-sparing primary OR 1.28 (95% CI 0.69–2.35); not significant
INNOVATE; 419 efficacy population[29]	Allergic severe asthma	Omalizumab adjusted exacerbation reduction 26% vs placebo
Reslizumab phase 3[28]	BEC ≥400/μL	Replicated reductions in asthma exacerbation rates

Eosinophilic and T2-high phenotypes

DREAM established a reduction in exacerbation frequency with mepolizumab in eosinophilic severe asthma, while MENSA demonstrated 47%–53% fewer exacerbations versus placebo[6,7]. Secondary analysis of the pooled DREAM and MENSA population showed a gradient of treatment benefit as baseline BEC increased, from a 52% reduction at ≥150 cells/μL to 70% at ≥500 cells/μL[8]. SIROCCO and CALIMA confirmed clinically meaningful exacerbation reductions with benralizumab among patients with eosinophilic disease, although subgroup efficacy depends on baseline control and eligibility[9,10]. Reslizumab trials required BEC ≥400 cells/μL and similarly support a target-enriched phenotype[28].

Higher eosinophil counts are therefore predictive for IL-5 pathway exacerbation outcomes, but the evidence does not define one universal eligibility threshold. Recent OCS use may suppress circulating eosinophils, and historical counts can be informative. Furthermore,

exacerbation response should not be equated automatically with OCS elimination or complete clinical remission[1,3,8,23].

Allergic phenotype and IgE-directed therapy

Allergen sensitization and IgE are useful for defining an anti-IgE treatment-eligible phenotype, but total IgE is not a general measure of severe-asthma activity. In the INNOVATE trial of severe allergic asthma, the adjusted clinically significant exacerbation rate was 0.68 with omalizumab versus 0.91 with placebo (26% relative reduction); severe exacerbations and emergency visits were also lower[29]. Biomarker analyses of EXTRA showed potential stratification beyond IgE eligibility by FeNO and eosinophilic activity[15]. In routine practice, allergic, eosinophilic and nasal-polyp phenotypes frequently overlap[24,27].

FeNO and combined biomarker phenotyping

FeNO reflects IL-13-associated airway inflammation and may help distinguish treatment-responsive T2 disease even when circulating eosinophils are modest. QUEST subgroup analyses supported greater dupilumab benefit with elevated T2 markers[11]. An ISAR analysis of 3,751 treated patients examined BEC, FeNO and IgE combinations, while a 24-country cohort of 3,675 patients identified five biomarker clusters spanning low to high T2 involvement; improvement was observed across clusters, often greatest at the high-T2 end [19,27,43].

Multimarker stratification must be interpreted with clinical context: FeNO varies with inhaled corticosteroid exposure and adherence, whereas BEC is sensitive to recent systemic steroids. These two markers are related but not synonymous; discordance may be biologically meaningful rather than measurement error[1,3,39].

Lower-T2-biomarker phenotype and anti-TSLP response

The anti-TSLP approach extends efficacy to a wider biomarker distribution. NAVIGATOR reported an annualized exacerbation rate ratio of 0.44 overall for tezepelumab and 0.59 in patients with baseline BEC <300 cells/μL[13]. PATHWAY had previously found lower exacerbation rates across baseline eosinophil strata[30]. Nevertheless, the SOURCE trial did not achieve its primary OCS-reduction endpoint in the overall OCS-dependent population (OR 1.28, 95% CI 0.69–2.35)[14]. Low BEC, therefore, should neither be equated with absent treatment potential nor taken as assurance of all-domain response.

Oral corticosteroid-sparing response

In OCS-dependent severe asthma, steroid reduction is a distinct, clinically meaningful endpoint. SIRIUS and ZONDA demonstrated OCS-sparing efficacy with mepolizumab and benralizumab, respectively[16,17]. In VENTURE, median OCS reduction was 70.1% with dupilumab compared with 41.9% with placebo[12]. In PONENTE, steroid reduction followed a personalized, adrenal-function-aware algorithm, illustrating that tapering strategies influence measured endpoints and safety[21]. Baseline OCS dose and prior exacerbation burden should be recorded when comparing cohorts[3,26].

Response, super-response and remission in real-world cohorts

The definition of response materially alters reported proportions. In a 21-country registry of 2,210 biologic-treated patients, response rates ranged from 80.7% (566/701) for one exacerbation domain to 10.6% (9/85) for a simultaneous four-domain response. Among asthma-control responders initially uncontrolled, 46.7% still showed incomplete post-treatment control,

©2026, IJMACR

underscoring residual disease burden[26]. In another registry analysis, response included ≥50% fewer exacerbations, ≥100 mL improvement in FEV_1, control-category improvement or an OCS dose reduction, each capturing different clinical traits[18].

A systematic review and meta-analysis of remission studies reported 38% (95% CI 29%–47%) remission using three-component definitions and 30% (95% CI 27%–34%) using four-component definitions, with high heterogeneity. Worse baseline FEV_1, longer disease duration, greater symptom burden, maintenance OCS, obesity and depression were associated with reduced remission attainment[23]. A Spanish real-world cohort of 429 patients reported 27% clinical remission using its own criteria, whereas XALOC-2 found 26.7% remission at 56 weeks among evaluable benralizumab recipients [34,37]. These remission rates should not be pooled across incompatible definitions.

Multicountry phenotype clustering and treatment-response heterogeneity

In the 24-country 3,675-patient clustering analysis, the lowest-T2 cluster comprised 16.4%, followed by clusters of 20.4%, 22.9%, 30.3% and 10.0% at progressively higher T2 involvement. Measured outcomes improved in all clusters, with generally stronger changes in the T2-high groups[19,43]. Such findings support a continuous multidimensional phenotype rather than an absolute T2-high/T2-low dichotomy. However, registry comparisons can be confounded by local treatment access, prescribing indications and differences in baseline risk.

Table 2: Key phenotype markers, corresponding interventions, and response limitations

Trait	Clinical use	Important limitations
Blood eosinophils	Anti-IL-5/IL-5R exacerbation benefit; higher baseline count often predicts larger effect[8,9]	OCS suppression, fluctuating counts, variable thresholds
FeNO	Adds response stratification for selected anti-IL-4Rα and T2-directed strategies.[1139]	ICS adherence, atopy, smoking, assay timing
IgE and sensitization	Define allergic asthma and anti-IgE eligibility[15,29]	Not general predictors of all biologic response
Nasal polyps / atopic comorbidities	May inform biologic choice and patient-important outcomes.[1,24]	Comorbidity outcome not equivalent to asthma remission
Maintenance OCS dose	Baseline severity and steroid-sparing endpoints.[12,14,21]	Tapering protocol, adrenal function and confounding
Low T2 markers	Tezepelumab may reduce attacks even without high eosinophils.[13,30]	Variable response by outcome and subgroup
Obesity, mood and disease duration	Important barriers to remission[23]	Noninflammatory influences and residual confounding

©2026, IJMACR

Methodological quality, inconsistency and applicability

Randomized trial results offer stronger within-trial estimates than unadjusted pre/post registry comparisons, yet subgroup analyses can be underpowered and vulnerable to selective threshold choice. Real-world cohorts have broader clinical representation but face confounding by indication, treatment switching, comorbidity burden and inconsistent follow-up. Several ISAR analyses draw on partially overlapping recruitment infrastructure; their patient counts must not be added to imply independent replication[18,19,26,27].

A 2026 review of non-omalizumab biologics identified 21 studies from 5,853 screened records and found moderate-to-high confidence for certain predictors, including higher BEC (≥300/μL), FeNO >40 ppb, lower baseline OCS dose (<10 mg/day) and better baseline control in specified contexts[3]. A separate real-world meta-analysis of 92 studies involving 9,546 patients reported a 62% reduction in severe exacerbations at 12 months with anti-IL-5/5Rα treatment compared with pretreatment rates (risk ratio 0.38, 95% CI 0.29–0.50); as a pre/post analysis, this is not a randomized treatment effect[25].

Table 3: Additional quantitative real-world evidence and interpretive scope

Evidence source	Numerical result	Interpretation
ISAR response definitions[26]	2,210 patients; 80.7% single-domain versus 10.6% four-domain response	Endpoint definition determines apparent responder proportion
ISAR T2 - biomarker clustering[19,43]	3,675 patients; five clusters, from 16.4% lowest T2 to 10.0% highest T2	Broad response with T2-dependent gradients
Published remission meta-analysis[23]	38% (29–47) three-component; 30% (27–34) four-component	High heterogeneity; differently defined remission
Anti-IL-5/IL-5R real-world meta-analysis[25]	92 studies; 9,546 patients; exacerbation RR 0.38 (0.29–0.50)	Before/after association, not placebo-controlled efficacy
XALOC-2[34]	26.7% remission at 56 weeks (70/262)	Selected evaluable biologic-treated cohort
Real-world omalizumab/anti-IL-5/5R[37]	429 patients; remission 27%	Response depends on long-term definitions

Discussion

Principal findings

Phenotypic stratification improves interpretation of severe-asthma treatment results, particularly for eosinophilic disease receiving anti-IL-5 pathway therapies. Higher BEC and FeNO often predict greater benefit, but the size and presence of that association differ by drug mechanism and clinical endpoint. Anti-TSLP therapy can reduce exacerbations in some lower-BEC populations, while steroid-sparing and remission are less consistently achieved[3,8,13,14,23].

Clinical interpretation and treatment selection

A practical prebiologic evaluation should include treatment adherence and technique, exacerbation frequency, OCS burden, spirometry, ACT/ACQ, measured or historical BEC, FeNO where available, IgE sensitization, nasal polyps and other treatable comorbidities. For each patient, predefined follow-up

targets should separate exacerbation control, respiratory symptoms, FEV_1, OCS tapering and patient-valued remission[1,2,24,31]. A clinically relevant response to one domain need not satisfy remission across all domains.

Risk of bias and evidence gaps

The evidence is heterogeneous in population selection, baseline severity, biomarker thresholds, follow-up, comparator and outcome. Drug-to-drug comparisons across separate trials risk ecological bias, and registry contrasts cannot establish comparative drug superiority when prescribing is phenotype-driven. Fewer studies address adolescents, OCS-dependent lower-T2 phenotypes, longitudinal biomarker stability or prospectively validated composite response scores. Trial-level domain judgments, detailed screening exports and a reproducible new pooled analysis are necessary before strong cross-biologic inferences are made[3,23–27,41].

Implications for research

Future studies should prespecify phenotypic strata, model biomarkers continuously rather than rely on a single cutoff, and use consistent response definitions with separate reporting of exacerbations, symptoms, lung function and OCS outcomes. Multicentre registries can improve generalizability if treatment selection, missingness, switching and comorbidities are addressed systematically. Remission research needs harmonized definitions and standardized follow-up [23,31,33,41].

Conclusion

Severe-asthma phenotype is associated with differential response to targeted treatment, but a single biomarker does not characterize the full response. Eosinophilic inflammation reliably enriches exacerbation benefit from IL-5 pathway inhibition, whereas complementary FeNO, IgE, OCS and comorbidity information refines patient selection. Treatment benefit, super-response and remission should be evaluated as separate outcomes using prespecified criteria.

References

1. Global Initiative for Asthma. Difficult-to-Treat and Severe Asthma in Adolescent and Adult Patients: Diagnosis and Management. 2026. https://ginasthma.org/2026-gina-severe-asthma-guide/.
2. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J. 2020;55: 1900588. doi:10.1183/ 13993003.00588-2019.
3. Rattu A, Dixey P, Charles D, et al. Predictors of response to biologics for severe asthma: a systematic review and meta-analysis. Allergy. 2026; 81:24–55. doi:10.1111/all.70031.
4. Mendez P, Rosado A, Cardet JC. Type 2-low asthma: epidemiology, multiomics, and emerging therapies. Curr Allergy Asthma Rep. 2026;26:51. doi:10.1007/s11882-026-01294-1.
5. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372: n71. doi:10.1136/bmj. n71.
6. Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. Lancet. 2012;380:651–659. doi:10.1016/S0140-6736(12)60988-X.
7. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med. 2014; 371:1198–1207. doi:10.1056/NEJMoa1403290.

©2026, IJMACR

8. Ortega HG, Yancey SW, Mayer B, et al. Severe eosinophilic asthma treated with mepolizumab stratified by baseline eosinophil thresholds: a secondary analysis of the DREAM and MENSA studies. Lancet Respir Med. 2016. PMID:27177493. https://pubmed.ncbi.nlm.nih.gov/27177493/.
9. Bleecker ER, FitzGerald JM, Chanez P, et al. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (SIROCCO). Lancet. 2016; 388:2115–2127. doi:10.1016/S0140-6736(16)31324-1.
10. FitzGerald JM, Bleecker ER, Nair P, et al. Benralizumab as add-on treatment for severe uncontrolled eosinophilic asthma (CALIMA). Lancet. 2016; 388:2128–2141. doi:10.1016/S0140-6736(16)31322-8.
11. Castro M, Corren J, Pavord ID, et al. Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. N Engl J Med. 2018; 378:2486–2496. doi:10.1056/NEJMoa1804092.
12. Rabe KF, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. N Engl J Med. 2018; 378:2475–2485. doi:10.1056/NEJMoa1804093.
13. Menzies-Gow A, Corren J, Bourdin A, et al. Tezepelumab in adults and adolescents with severe, uncontrolled asthma. N Engl J Med. 2021; 384:1800–1809. doi:10.1056/NEJMoa2034975.
14. Wechsler ME, Menzies-Gow A, Brightling CE, et al. Evaluation of oral corticosteroid-sparing effect of tezepelumab in adults with oral corticosteroid-dependent asthma (SOURCE). Lancet Respir Med. 2022; 10:650–660. doi:10.1016 /S2213-2600(21) 00537-3.
15. Hanania NA, Wenzel S, Rosén K, et al. Exploring the effects of omalizumab in allergic asthma: an analysis of biomarkers in the EXTRA study. Am J Respir Crit Care Med. 2013. PMID:23471469. https://pubmed.ncbi.nlm.nih.gov/23471469/.
16. Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. N Engl J Med. 2014; 371:1189–1197. doi:10.1056/NEJMoa1403291.
17. Nair P, Wenzel S, Rabe KF, et al. Oral glucocorticoid-sparing effect of benralizumab in severe asthma. N Engl J Med. 2017; 376:2448–2458. doi:10.1056/NEJMoa1703501.
18. Real-world biologics response and super-response in the International Severe Asthma Registry cohort. Allergy. 2024; 79:2700–2716. doi:10.1111/ all.16178.
19. Response to biologics along a gradient of T2 involvement in patients with severe asthma: a data-driven biomarker clustering approach. PubMed PMID:40902942. https:// pubmed. ncbi.nlm.nih.gov /40902942/.
20. International Severe Asthma Registry (ISAR): 2017–2024 status and progress update. 2025. https://pmc.ncbi.nlm.nih.gov/articles/PMC12010726 /.
21. Menzies-Gow A, Gurnell M, Heaney LG, et al. Oral corticosteroid elimination via a personalised reduction algorithm in adults with severe eosinophilic asthma treated with benralizumab (PONENTE). Lancet Respir Med. 2022; 10:47–58. doi:10.1016/S2213-2600(21)00352-0.
22. Ma J, Ma Q, Yang J, et al. Clinical and pathological histology efficacy of biological therapy for severe asthma with a phenotype of type 2 inflammation:

©2026, IJMACR

systematic review. Front Immunol. 2025; 16:1531986. doi:10.3389/fimmu.2025.1531986.

23. Shackleford A, Heaney LG, Redmond C, McDowell PJ, Busby J. Clinical remission attainment, definitions, and correlates among patients with severe asthma treated with biologics: a systematic review and meta-analysis. Lancet Respir Med. 2025; 13:23–34. doi:10.1016/S2213-2600(24)00293-5.
24. Balasubramanyam S, George EK, Wang E. Precision medicine and choosing a biologic in asthma: understanding the current state of knowledge for predictors of response and clinical remission. Curr Opin Allergy Clin Immunol. 2025; 25:66–74. doi:10.1097/ACI.0000000000001044.
25. Effectiveness of anti-IL-5/5Rα biologics in severe asthma in real-world studies: a systematic review and meta-analysis. ERJ Open Res. 2025; 11:00625-2024. doi:10.1183/23120541.00625-2024.
26. Exploring definitions and predictors of response to biologics for severe asthma. J Allergy Clin Immunol Pract. 2024; 12:2347–2361. doi:10.1016/ j.jaip.2024.05.016.
27. Association between pre-biologic T2-biomarker combinations and response to biologics in patients with severe asthma. 2024. PMID:38711495. https://pubmed.ncbi.nlm.nih.gov/38711495/.
28. Castro M, Zangrilli J, Wechsler ME, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. Lancet Respir Med. 2015; 3:355–366. doi:10.1016/S2213-2600(15)00042-9.
29. Humbert M, Beasley R, Ayres J, et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy: INNOVATE. Allergy. 2005; 60:309–316. doi:10.1111/j.1398-9995.2004.00772. x.
30. Corren J, Parnes JR, Wang L, et al. Tezepelumab in adults with uncontrolled asthma. N Engl J Med. 2017; 377:936–946. doi:10.1056/NEJMoa1704064.
31. Menzies-Gow A, Bafadhel M, Busse WW, et al. An expert consensus framework for asthma remission as a treatment goal. J Allergy Clin Immunol. 2020;145:757–765. doi:10.1016/j.jaci.2019.12.006.
32. Menzies-Gow A, Hoyte FL, Price DB, et al. Clinical remission in severe asthma: a pooled post hoc analysis of the patient journey with benralizumab. Adv Ther. 2022;39:2065–2084. doi:10.1007/s12325-022-02098-1.
33. Menzies-Gow AN, Price DB. Clinical remission in severe asthma: how to move from theory to practice. Chest. 2023. doi:10.1016/j.chest.2023.03.001.
34. Early and sustained asthma control and remission in real-world patients with severe eosinophilic asthma treated with benralizumab: XALOC-2. Clin Exp Allergy. 2025. PMID: 41162224. https:// pubmed.ncbi.nlm.nih.gov/41162224/.
35. Real-world phenotypic profiles and longitudinal lung function outcomes in severe asthma treated with biologic therapies. 2026. PMID:42506088. https://pubmed.ncbi.nlm.nih.gov/42506088/.
36. Monoclonal antibodies in severe asthma: outcomes from real-world data. Front Med (Lausanne). 2025; 12:1635688. doi:10.3389/fmed.2025.1635688.
37. Comparison of long-term response and remission to omalizumab and anti-IL-5/IL-5R using different criteria in a real-life cohort of severe asthma patients. 2023. PMID:38042707. https:/ /pubmed.ncbi.nlm.nih.gov/38042707/.

©2026, IJMACR

38. Basagaña M, Martínez-Rivera C, Padró C, et al. Clinical characteristics of complete responders versus non-complete responders to omalizumab, benralizumab and mepolizumab in patients with severe asthma: a long-term retrospective analysis. Ann Med. 2024. doi: 10.1080/ 07853890.2024.2317356.
39. Biomarkers of type 2 inflammation as predictors of response to biologics for severe eosinophilic asthma. ERJ Open Res. 2025. doi:10.1183/23120541.00969-2024.
40. Clinical remission in severe asthma after 12 months of biologic therapy: a real-life cohort study. 2026. https://www.mdpi.com/2413-4155/8/5/108.
41. Biologics in the treatment of severe asthma in children and adults—updates 2024–2025. J Allergy Clin Immunol. 2026; 157:575–587. doi: 10.1016/j.jaci.2026.01.002.
42. Advancing remission in severe asthma with benralizumab: latest findings, current perspectives and future direction. Clin Exp Allergy. 2025. doi:10.1111/cea.70083.
43. Response to biologics along a gradient of T2 involvement in patients with severe asthma: a data-driven biomarker clustering approach. 2025. PMID:40902942. https:// pubmed.ncbi.nlm.nih.gov/ 40902942/.

©2026, IJMACR