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Potential novel role of asthma biologics as rescue therapy in the intensive care unit for life-threatening asthma exacerbations: a systematic review

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Abstract

Severe asthma exacerbations have high morbidity and mortality. The management can be challenging, and the optimal strategy for patients admitted to the intensive care unit (ICU) with life-threatening and near-fatal asthma has not been fully defined. An interesting area of research is represented by the rescue or compassionate use of biological drugs when all treatments fail, including advanced interventions such as extracorporeal membrane oxygenation. This systematic review analyzes the cases described in the literature and discusses characteristics, treatments, and outcomes of patients who received asthma-approved monoclonal antibodies as rescue therapy following admission to the ICU due to near-fatal asthma exacerbations or status asthmaticus refractory to conventional treatments. A total of 14 studies (13 case reports and 1 case series) were included according to the prespecified inclusion and exclusion criteria. Various monoclonal antibodies were administered, most commonly benralizumab and omalizumab. Treatment was generally initiated within the first week of ICU admission, with nearly half of the patients receiving therapy within 5 days. Further research, including randomized controlled trials, is required to assess if this therapeutic option impacts ICU outcomes, which specific biologics could be used, and their eventual optimal timing and dosage.

Key words: biologics, asthma, life-threatening exacerbations, ICU, rescue therapy.

Introduction

The Global Initiative for Asthma (GINA) defines severe asthma exacerbations (SAEs) as episodes characterized by progressive worsening of symptoms, such as breathlessness, cough, wheezing, and chest tightness, accompanied by declining lung function [1].

These episodes may be triggered by environmental factors (like pollen or pollution), respiratory tract infections and/or poor adherence to inhaled therapy.

Inflammatory cascade activation leads to bronchospasm, mucus plugging, airway obstruction, and dynamic hyperinflation, which, in severe cases, may progress to respiratory failure and cardiopulmonary arrest.

Exacerbations may require evaluation and treatment in the clinic, emergency department (ED), or ultimately admission to the intensive care unit (ICU) in order to reduce the risk of serious complications or death associated with severe respiratory failure [1].

Standard treatment includes short-acting beta agonists (SABA), ipratropium bromide, inhaled corticosteroids (ICS), and systemic corticosteroids. Additional therapies, such as magnesium sulfate, epinephrine, terbutaline, methylxanthines, and leukotriene receptor antagonists (LTRA) represent options that may also be considered despite limited evidence for their efficacy [2,3].

Correction of hypoxemia and hypercapnia is essential in managing life-threatening asthma events [2,4]. A trial of non-invasive ventilation (NIV) may be beneficial for patients at low-risk of major complications that did not respond to medical therapy, but evidence remains insufficient, and the latest ERS/ATS guidelines do not include a recommendation for or against its use [5]. Thus, endotracheal intubation and IMV are indicated if the respiratory failure is progressing and should not be delayed if clinical improvement is not achieved with pharmacological therapy. Extracorporeal membrane oxygenation (ECMO) can be considered in patients who remain severely acidotic and hypercapnic despite conventional therapy [3,4].

An interesting area of research is represented by the rescue or compassionate use of biological drugs for patients admitted to the ICU due to SAEs unresponsive to standard and advanced therapies.

Despite indications of regulatory agencies not to use these drugs for relief of acute bronchospasm and status asthmaticus, the “off-label” administration has been described in rapidly deteriorating patients at high risk of death.

Materials and Methods

This systematic review analyzes the current literature describing the use of biological drugs for a severe asthma exacerbation leading to ICU admission. The study followed the Preferred

Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, and the protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) before the study was conducted (registration number: CRD42024571257).

Focused question

A PICO specialized framework was used to define the search strategy considering:

P (Population): Patients admitted to ICU with near fatal asthma exacerbations or status asthmaticus and refractory to conventional treatments.

I/E (Intervention/Exposure): rescue use of asthma biologics

C (Comparison): was not applicable in this study.

O (Outcomes): Patients characteristics, treatment, and outcomes.

This review aimed to answer the following focused question: Which are the characteristics, treatments, and outcomes of patients admitted to ICU for near fatal asthma exacerbations or status asthmaticus refractory to conventional treatments who received asthma approved monoclonal antibodies as rescue therapy?

Search strategy

The search was conducted on the online databases MEDLINE (PubMed), Scopus , ClinicalTrials.gov, Cochrane Library, Google Scholar, from inception to April 2025, and was followed by manual literature searches in the reference lists of the included articles to identify potential additional articles about this topic. The research string was as follows: (benralizumab OR dupilumab OR mepolizumab OR omalizumab OR reslizumab OR tezepelumab) AND (refractory status asthmaticus OR near-fatal asthma OR Life-threatening Asthma OR acute asthma exacerbation OR severe asthma exacerbation).

Study selection

We included clinical trials, observational studies, case series, case reports, letters to the editor, correspondences and commentaries describing patient presentations that met the following inclusion criteria: 1) adult patients (>18 years), 2) patients with a known history of asthma or fully diagnosed after the acute event, 3) patients admitted to ICU who received asthma approved monoclonal antibodies as rescue therapy for near fatal asthma exacerbations or status asthmaticus refractory to conventional treatments, 4) articles written in English. Studies unavailable as full-texts, abstract-only papers, studies describing nonadult patients, were classified as ineligible for inclusion. Articles describing the cases of patients

who received asthma approved monoclonal antibodies during asthma exacerbations but were not admitted to ICU were not considered for inclusion.

Data extraction

Two researchers (L.C. and A.C.) independently searched the data, selected and extracted them. If the extracted data from both researchers did not match, the original text was reviewed by another researcher (S.I.) to reach a consensus. Extracted data included the following items: author/year, study design, patient characteristics (including age, sex, comorbidities, previous therapy for asthma) other treatments received in ICU, asthma biologic used, timing of utilization of the biologic, patient outcomes (including timing of response, interruption of other treatments, discharge).

Evaluating the risk of bias

The Critical Appraisal Checklist for Case Reports developed by Moola et al. [6] was used to perform a quality check of the included studies. Two authors (L.C. and A.C.) independently assessed the quality of individual studies, and disagreements were resolved by discussion with a third author (S.I.).

Data synthesis

Data from original papers were extracted and reported via qualitative synthesis. Because of the limited number of reports and the restricted total number of patients, also in consideration of the design of the studies and the heterogeneous nature of outcome measures, a quantitative analysis was not conducted.

Results

The initial literature search generated 1607 potentially eligible articles from the aforementioned databases, plus 10 record identified additionally by manual search. A total of 172 duplicates were identified and removed. After excluding 1427 articles, 14 articles were included in this review according to the prespecified inclusion and exclusion criteria. A flow chart showing the study selection is presented in Figure 1.

Risk of bias

Table 1 shows the risk of bias of the studies included in the review, evaluated using the Critical Appraisal Checklist for Case Reports . Quality assessment of the eligible studies revealed that on average all of the recommended elements were fulfilled and thus, these were considered as low risk of bias. Only three studies did not attain a perfect score.

Study characteristics

13 articles included in the systematic review were case reports [7-19], and 1 article was a case series [20]. Across all studies, a total of 17 patients were identified, 11 (65%) were male and 6 (35%) were female. Median age was 41 years (range 23 to 69 years) and 4 (24%) patients were 25 years old or younger. Table 2 describes demographic characteristics of the patients, including age and sex, and summarizes comorbidities and previous therapies for asthma. 6 patients (35%) were on treatment with medium/high dose of ICS-LABA, 2 patients (12%) with high dose ICS-LABA-LAMA. Of these patients, 2 were additionally assuming LTRA e 1 patient was on chronic OCS (25 mg/day). 5 patients (29%) were assuming SABA or SAMA-SABA as needed, 1 patient was not assuming any therapy and for another 1 patient no information was reported by the authors. 1 patient had received different monoclonal antibodies for severe asthma (namely Omalizumab, Mepolizumab and Benralizumab) but was not under any biologic during the adverse event. Comorbidities included allergies to pollens, house dust mite, animal air or food (4, 24%) obesity (2, 12%), atopic dermatitis (2, 12%), OSAS (1), tuberculosis (1), laryngeal cancer (1), asthma COPD overlap (1), use of drugs (1), alcohol abuse (1). 3 patients (18%) had no comorbidities. 6 patients (35%) were active smokers. 2 patients had already experienced asthma exacerbations without the need for hospital admission, 2 patients had required hospitalization and 1 patient even ICU admission but without invasive mechanic ventilation. Table 2 describes also which asthma biologic has been used and the timing of administration of the biologic agent. In ICU all patients were sedated and intubated and invasive mechanic ventilation was administered. Regarding medical therapy, the normal differences of treatment for administered drugs, doses and time of administration between multiple centers made a statistical analysis impossible to be performed. Advanced procedures following standard treatment failure were also taken into consideration, as shown by the use of Extracorporeal membrane oxygenation (ECMO), that was performed in 9 patients (53%). 4 patients (23%) received omalizumab, 3 patients (18%) received mepolizumab, 2 patients (12%) received Reslizumab, 6 patients (35%) received benralizumab, 1 patient (6%) received Tezepelumab and 1 patient (6%) received a combination of benralizumab and omalizumab. The median time of administration following admission to ICU was 7 days (2-20 days). 8 patients (47%) received the monoclonal antibody within 5 days since the admission. 1 patient treated with omalizumab received multiple administration of the monoclonal antibody during the stay in ICU following an updosed scheme. The clinical response to the administration of the biologic agent was interpreted as reduced need for mechanical ventilation following improvement of ventilatory parameters and ABG, and as the possibility to stop or decrease the intensity of other concomitant therapies. Table 3 summarizes patient outcomes, including timing and clinical response to

treatment, discontinuation of concomitant therapies, discharge details, and follow-up when reported.

Discussion

The use of biologic therapies in the ICU for life-threatening asthma exacerbations is an emerging area of interest. This is supported by growing evidence on the safety and effectiveness of biologics in reducing symptom burden and exacerbation rates in severe asthma patients in outpatient settings. Biologics, which target specific immune pathways, may reduce circulating cytokine levels or antagonize immune cells responsible for inflammation, thereby potentially stabilizing critically ill patients. The possibility to administer asthma approved monoclonal antibodies (mAbs) to patients with asthma exacerbations admitted to the ICU was suggested by Bourdin et al in 2021 [21]. Besides mechanism of actions, rapid modulation of inflammation is a key factor, therefore pharmacokinetics plays a critical role. Monoclonal antibodies for severe asthma are high-molecular-weight compounds. When administered subcutaneously, they require 6–8 days on average to reach peak plasma concentrations in healthy individuals. This happens because absorption into the systemic circulation first requires transport of the drug through the interstitial space into the lymphatic system [22]. Consequently, subcutaneous administration takes longer for the peak plasma concentration to be reached than with intravenous administration. Thus pharmacokinetic characteristics may affect effectiveness of biologics within the ICU. However, despite the immediate availability of intravenous monoclonal antibodies such as Reslizumab, there is no study suggesting the superiority of one biologic on another [21], primarily due to the scarcity of such cases. Pharmacological profiles of biologics approved for asthma are presented in Table 4. This review provides an insight into the clinical characteristics, comorbidities, and management of patients with severe asthma exacerbations requiring ICU admission, with a focus on the potential role of biologic therapies in an acute setting. The described cohort predominantly includes young adult patients with variable asthma severity and different therapeutic backgrounds, underscoring the heterogeneous nature of severe asthma exacerbations. In fact, despite being more frequent in severe asthma patients, any asthmatic patient may suffer a severe exacerbation, and mild asthmatics have been shown to carry a considerable risk of exacerbations including severe, life-threatening exacerbations [23,24]. 5 out of 13 patients were assuming SABA or SAMA-SABA as needed. This is consistent with the recent evidences that have indicated a higher risk of exacerbations with SABA monotherapy and its overuse. For this reasons SABA-only treatment is no longer recommended, and as needed combination ICS-formoterol is the preferred reliever therapy in adults and adolescents [1]. Comorbid conditions, particularly

allergies and obesity, were prevalent, consistent with known risk factors that may exacerbate asthma or complicate its management [25,26]. The high rate of active smokers (38%) may have further compromised treatment efficacy, given the adverse effects of smoking on respiratory health and response to asthma therapies [27]. In the ICU, all patients received standard emergency management for asthma exacerbations. Nearly half (47%) required extracorporeal membrane oxygenation (ECMO). This highlights the severity of respiratory compromise and the need for advanced interventions beyond typical asthma exacerbation management. An analysis of the Extracorporeal Life Support Organization registry showed that ECMO use in patients admitted for near fatal asthma has increased, since it can improve gas exchange and prevent lung injury induced by mechanical ventilation, being a lifesaving adjunct for the most refractory cases or a bridging strategy to avoid aggressive ventilation [28]. However, careful management is required to avoid complications. The majority of patients included in the analysis received Benralizumab, an anti-IL-5 receptor alpha antibody. It prevents the interaction between IL-5 and its receptor and promotes antibody dependent cell-mediated cytotoxicity (ADCC) enhancing eosinophil apoptosis [29]. Benralizumab can cause rapid and near complete depletion of eosinophils, with a speed of onset of effect very similar to that seen with oral prednisolone [30]. Following the antagonism of Il-5/Il-5R, targeting IgE with omalizumab was the second most used approach. It was used in status asthmaticus patients whit very high IgE levels. It is also interesting that one patient treated with omalizumab received multiple doses in an up-dosing regimen [13], suggesting that, in extreme cases, intensified biologic administration could be beneficial, although evidence on efficacy and safety is limited in this context. Tezepelumab, recently approved, targets thymic stromal lymphopoietin (TSLP), an epithelial derived cytokine released in response to multiple triggers, preventing its interaction with the receptor and thus inhibiting multiple downstream inflammatory pathways, and at the moment it's the only mAb approved for patients with either high or low levels of T2 biomarkers [31]. It has been used as rescue therapy in one patient that had already received different monoclonal antibodies, without benefit, who suffered a near fatal exacerbation triggered by an influenza A infection, all characteristics that suggest epithelial barrier disfunction [32]. No cases of dupilumab rescue use in ICU were found in the literature. Nevertheless, despite its 3–7 day timeframe to reach peak plasma levels, dupilumab has shown rapid clinical effects [33]. The blockage of IL-13, that has a broad spectrum of action in asthma, including increased mucus production, proliferation of airway smooth muscle and stimulation of airways hyper-responsiveness [34], could offer therapeutic benefit in this setting. One patient in the cohort received a combination of biologics. While such dual biologic therapy has been described in uncontrolled severe asthma with overlapping allergic and eosinophilic phenotypes, it

remains unendorsed by guidelines due to insufficient evidence and high cost [35]. Its application in the ICU has not been previously reported and may suggest potential synergy from targeting multiple inflammatory pathways. The median time to biologic administration post-ICU admission was 7 days (range: 2–20), with 47% receiving the biologic within 5 days. These data suggest that earlier administration may enhance outcomes when conventional therapies fail. Given the pharmacokinetics of biologics, early use could optimize long-term benefits even if immediate effects are limited. Nonetheless, delayed onset of action remains a major limitation. Although this review focuses on ICU patients, there are reports of biologics being used for acute exacerbations in emergency departments and hospital wards when patients do not respond to conventional treatment, or have contraindications or don't want to assume corticosteroids. These cases were excluded due to study criteria. Noteworthy is the case by Nolasco et al. [36], where benralizumab alone was used to manage an acute exacerbation without corticosteroids, antibiotics, or intensive bronchodilation, allowing a clearer assessment of benralizumab effects on eosinophil counts and pulmonary function. Similarly, Kim et al. described clinical and functional improvements following dupilumab administration after failure of conventional treatments [37]. The ABRA study [38] further supports this approach, demonstrating that subcutaneous benralizumab (100 mg) rapidly depletes eosinophils and reduces treatment failure risk during acute eosinophilic exacerbations of asthma and COPD. An ongoing phase 2B trial (NCT04617171) [39] is evaluating the efficacy of benralizumab initiated during acute exacerbations requiring hospitalization, assessing its impact on exacerbation recurrence, ICU admissions, healthcare utilization, and readmissions. No RCTs specifically examining biologic use in ICU settings were found on ClinicalTrials.gov. Existing literature has several limitations. It is limited to case reports, with no prospective studies or RCTs available. Small sample sizes, variable treatments, heterogeneous follow-up, and potential publication bias limit generalizability and the ability to draw definitive conclusions on safety and efficacy. RCTs are urgently needed to assess whether biologics can improve prognosis in ICU patients with near-fatal exacerbations or refractory status asthmaticus. Relevant parameters should include inflammatory biomarkers (e.g., eosinophil counts) before, during, and after biologic administration, correlated with clinical outcomes. Potential indicators of response include reduced need of respiratory support on mechanical ventilation, shorter duration or lower dosage of systemic corticosteroids and bronchodilators. Average improvement time and length of hospital stay are other two key factors to consider.

Conclusions

Biologic agents have revolutionized the management of severe asthma, and are considered effective add-on maintenance therapies for uncontrolled severe asthma [40]. Even if they have not been intended for acute interventions, their potential role in ICU setting is a fundamental topic of clinical research, particularly for patients who are suffering from life threatening exacerbations and are refractory to standard treatments. Future research is required to assess if this therapeutic option impacts ICU outcomes, which specific biologics could be used and their eventual optimal timing and dosage, also in consideration of pharmacokinetics profiles.

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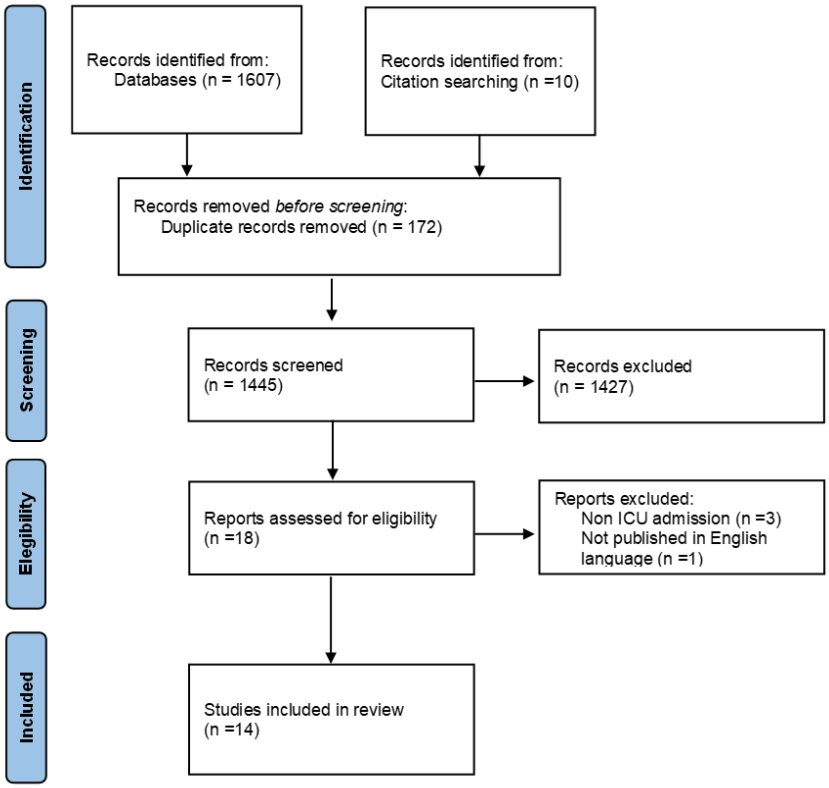

Figure 1. **PRISMA 2020 Flowchart Diagram of the selected articles.**

Table 1. Quality assessment of the included studies.

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Tello et al., 2019 [7]	•	◦	•	•	•	•	•	•
Renner et al., 2019 [8]	•	•	•	•	•	•	•	•
Milger et al., 2019 [9]	•	•	•	•	•	•	•	•
Pérez de Llano et al., 2021 [10]	•	•	•	•	•	•	•	•
Benes et al., 2021 [11]	•	•	•	•	•	•	•	•
Barbarot et al., 2022 [12]	•	•	•	•	•	•	•	•
Slevogt e Brauer, 2022 [13]	•	◦	•	•	•	•	•	•
Shanmukhappa et al., 2023 [14]	•	•	•	•	•	•	•	•
Rodrigues et al., 2023 [15]	•	•	•	•	•	•	•	•
Coghlan et al., 2024 [16]	•	•	•	•	•	•	•	•
Granda et al., 2024 [17]	•	•	•	•	•	•	•	•
Grasmuk-Siegl et al., 2024 [18]	•	•	•	•	•	•	•	•
Montagnolo et al., 2024 [19]	•	•	•	•	•	•	•	•
Conemans et al., 2025 [20].	•	◦	•	◦	•	•	•	•

Q1, Were patient's demographic characteristics clearly described?; Q2, Was the patient's history clearly described and presented as a timeline?; Q3, Was the current clinical condition of the patient on presentation clearly described?; Q4, Were diagnostic tests or methods and the results clearly described?; Q5, Was the intervention(s) or treatment procedure(s) clearly described?; Q6, Was the post-intervention clinical condition clearly described?; Q7, Were adverse events (harms) or unanticipated events identified and described?; Q8, Does the case report provide takeaway lessons? •, Yes; ◦, No; Ø, Unclear.

Table 2. Patient characteristics (including demographics, comorbidities and previous therapies for asthma, biologic used and timing of administration in the ICU).

Author(s), year	Patient age	Patient sex	Patient comorbidities	Previous therapies for asthma	Asthma biologic used	Timing of administration of the biologic
Tello et al., 2019 [7]	43 yo	F	N.A.	Budesonide-formoterol, Tiotropium	Mepolizumab 100 mg s.c.	7 days after admission to ICU
Renner et al., 2019 [8]	53 yo	F	Asthma-Chronic obstructive pulmonary disease (COPD) overlap (ACO), chronic smoker	ICS, LAMA, LABA, oral corticosteroids (OCS, 25 mg prednisolone/day)	Reslizumab 3 mg/kg IV	3 days after admission to ICU
Milger et al., 2019 [9]	41 yo	M	Pollen allergy	SABA	Omalizumab 600 mg s.c	8 days after admission to ICU
Pérez de Llano et al., 2021 [10]	23 yo	M	Active smoker, occasionally used cocaine and marijuana, allergy (house dust mites)	Maintenance ICS LABA stopped during the preceding 6-8 weeks and replaced by albuterol several times a day	Benralizumab 30 mg s.c.	4 days after admission to ICU
Benes et al., 2021 [11]	25 yo	F	Pollen allergy, atopic eczema, food allergies and oral allergic syndrome, occasional smoker	Ipratropium/fenoterol as needed	Omalizumab 600 mg s.c.	8 days after admission to ICU
Barbarot et al., 2022 [12]	31 yo	M	Atopic dermatitis, active smoker	SABA on demand	Mepolizumab 100 mg s.c.	20 days after admission to ICU
Slevogt e Brauer, 2022 [13]	41 yo	M	N.A.	N.A.	Omalizumab 600 mg s.c.	days 3, 6, 7, 10 and 11 after admission to ICU
Shanmukhappa et al., 2023 [14]	30 yo	M	No comorbidities	ICS LABA, Montelukast, fexofenadine as needed.	Omalizumab 600 mg s.c.	4 days after admission to ICU
Rodrigues et al., 2023 [15]	25 yo	F	No comorbidities	No maintenance therapy	Mepolizumab 100 mg s.c.	4 days after admission to ICU
Coghlan et al., 2024 [16]	69 yo	M	Pulmonary tuberculosis and resection of early-stage laryngeal cancer	ICS LABA	Benralizumab 30 mg s.c. and Omalizumab 300 mg s.c.	2 weeks after admission to ICU
Granda et al., 2024 [17]	36 yo	M	Obesity, active smoker, heavy drinker	ICS LABA	Reslizumab 3 mg/kg IV	12 days after admission to ICU
Grasmuk-Siegl et al., 2024 [18]	43 yo	M	Allergy (house dust mite, animal hair, pollen), obesity, obstructive sleep apnoea	High-dose ICS/LABA, antihistaminic therapy, oral Theophylline, nasal Mometasone. Previous biological therapies with Omalizumab in 2011, followed by Mepolizumab in 2017, and Benralizumab in 2019.	Tezepelumab 210mg, s.c.	12 days after admission to ICU
Montagnolo et al., 2024 [19]	24 yo	F	No comorbidities	ICS/LABA, LTRA	Benralizumab 30 mg s.c.	2 days after admission to ICU
Conemans et al., 2025 [20]	48 yo 65 yo 62 yo 61 yo	F M M M	Active smoker Former smoker Former smoker N.A.	Formoterol N.A. ICS/LABA Salbutamol	Benralizumab 30 mg s.c.	7 days 5 days 7 days 5 days after admission to ICU

Table 3. Clinical response, discontinuation of concomitant therapies, and discharge.

Author(s), year	Timing of Clinical Response	Discontinuation of Concomitant Treatments	Discharge and Follow-Up
Tello et al., 2019 [7]	Marked improvement after 2 days (better decarboxylation, pH, reduced PEEP)	Weaned and extubated after 8 days	Not available
Renner et al., 2019 [8]	Improvement within 24 hours	Extubated the next day, transferred to ward	Discharged on day 13 post-intubation
Milger et al., 2019 [9]	Rapid improvement in ventilation	ECMO off by day 12, ventilator weaning over 2 weeks	Discharged to rehab 5 weeks after onset
Pérez de Llano et al., 2021 [10]	Improvement after 4 days (normalized pH, reduced airway resistance)	Extubated on ICU day 13; steroids tapered	Discharged after 25 days
Benes et al., 2021 [11]	Ventilatory improvement within 90 minutes	ECMO off within 24h; extubated on day 10	Discharged on day 25
Barbarot et al., 2022 [12]	Improvement at 48h (resolved bronchospasm, normalized PEEP, ↓eosinophils)	ECMO off after 7 days; extubation on day 30	Discharged 7 days post-ICU
Slevogt e Brauer, 2022 [13]	Slight improvement on day 4; improved ventilation and ↓IgE	Fully weaned 2 weeks later	Long-term omalizumab; normal lung function at follow-up
Shanmukhappa et al., 2023 [14]	Improvement within hours (↓O2 needs, resolved bronchospasm)	Extubated day after treatment; ICU exit on day 6	Discharged on day 9; continued omalizumab
Rodrigues et al., 2023 [15]	Clinical improvement at 48h (normalized PaCO2, ↓auto-PEEP)	Extubated on ventilation day 11; steroids tapered	Discharged from ICU on day 19; ongoing biologic therapy
Coghlan et al., 2024 [16]	Gradual ventilatory improvement	Rapid weaning and tracheostomy decannulation	Discharged within 2 weeks; tapered oral steroids
Granda et al., 2024 [17]	Improvement in 2 days (ventilation and oxygenation)	ECMO off day 14; second reslizumab on day 39	Discharged 2 months later
Grasmuk-Siegl et al., 2024 [18]	Improvements within 24h (expiratory flow)	ECMO off by day 7; ventilation weaned over 13 days	Transferred to ward; ongoing pulmonary rehabilitation
Montagnolo et al., 2024 [19]	Significant improvement after ~5 days; ↓eosinophils >90% by 48h	ECMO and IMV stopped on day 5	Discharged on day 19; benralizumab prescribed long-term
Conemans et al., 2025 [20]	All four patients showed clinical improvement with reduced ventilator pressures.	Extubation occurred between 4 and 18 days. One patient developed ventilator-associated pneumonia but recovered.	ICS/LABA and benralizumab maintained asthma control in 2 patients; 1 remained OCS-dependent; 1 had stable asthma without biologics.

Table 4. Currently available mAbs used against severe asthma, mechanism of action and pharmacological characteristics.

Biologic agent	Mechanism of action	Route of administration	Peak concentration time	Bio-disponibility	Half life	Elimination
Omalizumab	Anti IgE	s.c.	7-8 d	62%	26d	Complexes with IgG and IgE
Mepolizumab	Anti IL-5	s.c.	4-8 d	74%-80%	16-22d	Proteolytic enzymes
Reslizumab	Anti IL-5	i.v.	Immediate	100%	24d	Proteolytic enzymes
Benralizumab	Anti IL-5R	s.c.	4-7d (eosinophilic depletion seen after 24 h)	59%	15d	Proteolytic enzymes
Dupilumab	Anti IL-4/IL-13	s.c.	3-7 d	64%	10-13 w	Proteolytic enzymes
Tezepelumab	Anti TSLP	s.c.	3-10 d	77%	26d	Proteolytic enzymes

d-days; h-hours; i.v.-intravenous; s.c.- subcutaneous; w-weeks