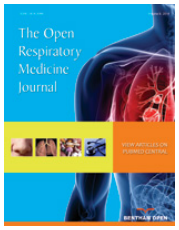

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RESEARCH ARTICLE

Efficacy and Safety of Biologic Agents in Chronic Urticaria, Asthma and Atopic Dermatitis – A Real-life Experience

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Abstract:

Introduction:

Several biologic agents have been approved for the treatment of asthma, chronic urticaria and atopic dermatitis. These therapeutic agents are especially useful for patients with severe or refractory symptoms. We present the real-life experience of four of the commonly used biologic agents in the United Arab Emirates.

Methods:

In this retrospective observational study, we reviewed the demographic, clinical, laboratory and treatment parameters for all patients treated with biologic agents.

Results:

270 patients received biologics at our centre between May 2015 and December 2019 with a median age of 36.5 years. Omalizumab was the most prescribed agent (n=183, 67.8%) followed by dupilumab (n=54, 20%), benralizumab (n=22, 8.1%) and mepolizumab (n=11, 4.1%). Urticaria was the commonest treatment indication (n=148, 55%) followed by asthma (n=105, 39%) and atopic dermatitis (n=13, 5%). All chronic urticaria patients were treated with omalizumab and showed improvement in the mean urticaria control test score from 6.7±4.47 to 12.02±4.17, with a p-value of 0.001. Dupilumab was found to be the most commonly prescribed drug for asthma (37%), followed by omalizumab (32%), benralizumab (21%) and mepolizumab (10%). The mean Asthma control test score for all asthmatics combined increased from 17.06 ± 5.4 to 19.44 ± 5.6, with p-value 0.0012 with treatment; FeNO reduced from 60.02 ± 45.74 to 29.11 ± 27.92, with p-value 0.001 and mean FEV1 improved from 2.38L ± 0.8 to 2.67L ± 0.78, with p-value 0.045. Only 4 patients in the entire cohort reported adverse events.

Conclusion:

Our study demonstrated that biological agents are a safe and effective treatment for atopic asthma, chronic urticaria and atopic dermatitis.

Keywords: Atopic dermatitis, Atopic asthma, Chronic urticarial, Atopic disorders, Biologic agents, Asthmatics.

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1. INTRODUCTION

The incidence of atopic disorders has risen exponentially in the world over the last five decades [1, 2]; consequently, the socioeconomic treatment burden of common allergic disorders such as asthma has also increased significantly [3, 4], bringing much-needed attention to this group of illnesses and leading to the development of targeted biological treatments. Asthma is estimated to affect 300 million people worldwide [5], while chronic urticaria is estimated to affect 0.5-1% of the world population [6]. In recent years, the heterogeneity of allergic diseases has been studied *via* cluster analyses, molecular phenotyping, biomarkers, and differential responses to targeted and non-targeted therapies, and these studies have led to successful trials of molecularly targeted therapies in defined phenotypes [7], resulting in the production of the monoclonal antibodies in use today, including omalizumab, mepolizumab, benralizumab, and dupilumab. The introduction of these biological therapies has broadened the treatment options for allergic disorders including asthma, atopic dermatitis and chronic urticaria, especially at the severe and refractory end of

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the disease spectrum.

Omalizumab was the first biologic agent approved by the Food and Drug Administration (FDA) for use in atopic disorders. It is a recombinant humanised immunoglobulin G1 (IgG1) monoclonal antibody that targets immunoglobulin E (IgE), preventing its interaction with the Fc-epsilon-RI receptor(FcεRI), found on eosinophils, basophils and mast cells [8]. It is currently licensed for the treatment of moderate to severe allergic asthma, not controlled by inhaled corticosteroids (ICS), and for the treatment of chronic urticaria that is not controlled by antihistamines [9, 10]. Subsequently, four other humanised monoclonal antibodies mepolizumab, benralizumab, dupilumab and reslizumab have also received FDA approval for the treatment of allergic disorders. Mepolizumab selectively targets interleukin-5 (IL-5), thereby inhibiting eosinophilic inflammation [10]. It has FDA approval for treating severe eosinophilic asthma and eosinophilic granulomatosis with polyangiitis (EGPA) [11]. Similarly, benralizumab is an antibody directed against the alpha-chain of IL-5 receptor and is licensed to treat severe eosinophilic asthma [12]. The latest addition to the anti-allergy biologics line up is dupilumab, a fully humanised monoclonal immunoglobulin G4 (IgG4) antibody directed against the alpha subunit of the interleukin-4 (IL-4) receptor, preventing the signalling of IL-4 and interleukin-13 (IL-13) [13]. It is the first biologic agent approved by the FDA for the treatment of moderate to severe atopic dermatitis as well as an add-on maintenance treatment of moderate to severe eosinophilic asthma and for the treatment of inadequately controlled chronic rhinosinusitis with nasal polyposis [14].

Although disease-specific guidelines from international bodies are available to ensure the appropriate use of these useful but expensive drugs, the prescribing practices do vary geographically depending on availability of the drugs, affordability and patient compliance, and preferences, *etc.* Our study is the first to report real-life experience with biological therapies at a large tertiary healthcare centre in the United Arab Emirates (UAE). The main objectives of this retrospective observational study are to assess the clinical characteristics of patients receiving biological therapy in the United Arab Emirates, report the clinical efficacy and adverse reactions, and also to compare our patient cohort with previously published data.

2. MATERIALS AND METHODS

2.1. Subjects

A retrospective chart review was undertaken to find all patients who have received omalizumab, mepolizumab, benralizumab or dupilumab between May 2015 and December 2019. We identified a total of 270 patients on biological therapy using the electronic medical records database at the hospital. Approval was obtained from the local research ethics committee. The data collection was performed from December 2019 till March 2020.

2.2. Study Variables

We collected demographic, clinical, laboratory, and treatment data, including Asthma Control Test (ACT) scores, Urticaria Control Test (UCT) scores before and after treatment, total IgE, Blood Eosinophil Count (BEC), FEV1 and fractional exhaled nitric oxide (FeNO). Data on the administration of the biological agent, including treatment start date, dose, frequency, and adverse effects (if any), were also recorded. Although both the ACT and UCT scores were recorded at each clinic, the data collected for the study included the last recorded scores before and after starting biologic treatments.

2.3. Statistical Analysis

Quantitative variables were expressed as the mean and Standard Deviation (SD) for normally distributed data, and the median and interquartile range (IQR) for all other data. Categorical variables were expressed as the number and percentage. Statistical comparisons between continuous characteristics were made using a t-test, and a significant p-value was taken to be less than 0.05.

3. RESULTS

Our cohort consisted of 270 patients, 171(63%) females and 99 (37%) males; the median age of the participants was 36.5 years (IQR 29-45.8). Omalizumab was the most prescribed drug with 183 (67.8%) patients, followed by dupilumab with 54 (20%) patients, benralizumab 22 (8.1%) and mepolizumab 11 (4.1%). Urticaria was the commonest indication for biologics use in 148 (55%) patients, followed by asthma in 105 (39%) patients (3 patients in this group had asthma as part of the diagnosis of EGPA) and atopic dermatitis in 13 (5%) patients. Only two patients had treatment for the diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) while two patients were treated (off-label use) for ABPA and eosinophilic cystitis. Characteristics of all patients receiving biologics are listed in Table **1**.

3.1. Omalizumab

Omalizumab was the commonest prescribed biological agent with 183 (67.8%) patients, 119 (65%) females and 64 (35%) males; the median age was 35 years (IQR 28.5-43). Median total IgE in this group was 194 IU/ml (IQR 98-398) and median Blood Eosinophil Count (BEC) was 0.13 $x10^9$/L (IQR 0.06-0.24). One hundred and forty-eight (80.8%) patients were on treatment for chronic urticaria, while 34(18.6%) were receiving the drug for Asthma; one patient was prescribed omalizumab for cystic fibrosis-related ABPA (off label use). In the urticaria group, the mean UCT improved from 6.7(SD4.47) to 12.02(SD 4.17) with treatment, and the effect was statistically significant (p= <0.001). In asthmatic patients, the mean pre-treatment ACT score was 16.6 (SD 4.34), and it improved significantly to 21 post-treatment (SD 3.20, p= <0.001). Similarly, the mean FeNO value reduced significantly with treatment from 43.9 ppb (SD 29.10) to 15.8 ppb (SD 5.68, p= 0.022). Although the mean FEV1 also showed a trend towards improvement, from 2.4 litres (SD 0.94) to FEV1 2.73 litres (SD 0.88), the difference was not statistically significant (p=0.25) (Table **2**).

We divided our chronic urticaria patients (N=148) into two groups; patients on a standard dose of omalizumab, and

patients on a greater than the standard dose of omalizumab (Tables **3**-**4**). We identified a significant difference in baseline IgE levels between the two groups, where patients on greater than standard dose of omalizumab showed significantly lower baseline IgE levels (p= 0.003). All other comparable characteristics were statistically insignificant.

3.2. Dupilumab

Dupilumab was the second most commonly prescribed drug in our cohort with 54 (20%) patients, with female to male ratio being 32(59%) *vs.* 22(41%); the median age was 39 years (IQR 28.5-49.8). Thirty-nine (72.2%) of the patients were being treated for asthma, 13 (24.1%) for atopic dermatitis and two for CRSwNP. Among the asthmatic patients, the mean pre-treatment ACT score was 15 (Std dev 5.92) compared to 19.8 (Std dev 4.64) post-treatment (p= <0.001). The mean pre-treatment FeNO value was 55.9 ppb (Std dev 34.37) *vs.* the mean post-treatment value of 31.4 ppb (Std dev 22.02, p-value 0.003) and the mean FEV1 was observed to be slightly improved post-treatment, with 2.56 (SD 0.13) litres *vs.* 2.76 (0.15) litres, although the difference was not statistically significant (p=0.33).

The atopic dermatitis group consisted of 7 females (53.8%) and 6 males (46.2%) with a median age of 20 years. Due to the low patient number, we have reported disease outcomes in these patients subjectively; 11 patients reported improvement in their condition after treatment with dupilumab.

3.3. Benralizumab

All 22 patients (12 females, 10 men) on benralizumab were being treated for asthma. The median age in this group was 44.5 (IQR 31.5-54) years. The mean pre-treatment BEC was $0.77x10^9$/L (SD 0.84) compared to post-treatment BEC of $0.03x10^9$/L (SD 0.05) and the difference was statistically significant (p= <0.001). Similarly, the mean ACT score improved significantly with treatment from 14.1 (SD 5.15) pre-treatment to 19.3 post-treatment (SD 5.81, p= 0.004). There was also a trend towards improvement in FEV1 as it increased from 2.20L (SD 0.42) to 2.4L (SD 0.68), however, the difference was not significant (p=0.602). FeNO results were available for 11 patients only. The mean pre-treatment FeNO value was 94.6 ppb (SD 76.42), compared to a mean post-treatment FeNO value of 59.7 ppb (SD 48.34, p= 0.309).

3.4. Mepolizumab

In the mepolizumab therapy group (n=11, 8 females and 3 males), 7 patients (63.6%) were being treated for asthma, 3 patients (27.3%) were being treated for Asthma with EGPA, and 1 patient was being treated for eosinophilic cystitis (off-label use). The median age was 42 years (IQR 40-58). The median pre-treatment BEC reduced from $0.56x\ 10^9$/L to $0.06x\ 10^9$/L. The median ACT score changed from 20 to 20.5. The patient numbers in this group were too small to make a pre and post-treatment statistical comparison.

Tables **1** and **2** show patients' characteristics and changes in ACT, UCT, FEV1, FeNO, and blood eosinophils before and after biologic treatment.

3.5. Analysis of All Asthma Patients in the Cohort

In total, our cohort had 105 patients on treatment for asthma, with most patients being on dupilumab (37%) followed by omalizumab (32%), benralizumab (21%) and mepolizumab (10%). The mean ACT increased from 17.06 (SD 5.4) to 19.44 (SD 5.6, p= 0.0012) with treatment, FeNO reduced from 60.02 (SD 45.74) to 29.11 (SD 27.92, p= <0.001) and mean FEV1 improved from 2.38L (SD 0.8) to 2.67L (SD 0.78, p= 0.045). The pre and post-treatment differences in all these parameters were found to be statistically significant (Table **3**).

3.6. Adverse Events

All biologic agents were well tolerated and adverse events were recorded for only 4 patients (1.5%) in the whole cohort. In the omalizumab group, one patient had vasovagal event after the first dose while another one encountered worsening of urticaria. One patient on dupilumab had reported pruritis and dizziness after the first two doses and one patient on benralizumab had reported worsening of migraine headaches.

Table 1. Characteristics of patients on biological therapy.

-	Omalizumab	Mepolizumab	Benralizumab	Dupilumab
n	183	11	22	54
F:M	119:64	8:3	12:10	32:22
Age Median (IQR)	35 (28.5-43)	42 (32-79)	44.5 (15-64)	39 (16-78)
Indications (n)	-Chronic Urticaria (148)	-Asthma (7)		-Asthma (39)
	-Asthma (31)	-EGPA (3)	Asthma (22)	-Dermatitis (13)
	EGPA (3)	-Eosinophilic cystitis (1)		-Chronic rhinosinusitis with nasal polyposis (2)
	-ABPA (1)			
Mean Dose Frequency (weeks)	4.4	4	8	2.2
Mean Dosage (mg)	311.1	172.7	30	300
Adverse Effects (n)	-Pruritus (2)			
	-Urticaria (1)	None reported	Migraines (1)	Pruritus + Dizziness (1)
	-Vasovagal reaction (1)			

Table 2. Changes in ACT, UCT, FEV1, FeNO, and blood eosinophils before and after biologic treatment.

Biologic	Disease	Parameter		Mean	Median	Std Dev	p-value
Omalizumab		ACT	Before	16.6	16	4.34	<0.001
			After	21	21	3.2	
	Asthma	FEV1	Before	2.4	2.47	0.94	0.254
			After	2.73	2.76	0.88	
		FeNO ‡	Before	43.9	40	29.1	0.022
		(ppb)	After	15.8	16	5.68	
	Chronic	UCT §	Before	6.7	6.5	4.47	<0.001
	Urticaria		After	12.02	13	4.17	
Dupilumab	Asthma	ACT	Before	15	15	5.92	<0.001
			After	19.8	21	4.64	
		FEV1	Before	2.56	2.66	0.13	0.33
			After	2.76	2.75	0.15	
		FeNO ‡	Before	55.9	41	34.37	0.003
		(ppb)	After	31.4	27	22.02	
Benralizumab	Asthma	ACT	Before	14.1	14	5.15	0.004
			After	19.3	21	5.81	
		FEV1	Before	2.2	1.94	0.42	0.602
			After	2.4	2.45	0.68	
		FeNO ‡	Before	94.6	78	76.42	0.309
		(ppb)	After	59.7	58	48.34	
		BEC	Before	0.77	0.53	0.84	<0.001
		(10^9/L)	After	0.03	0.01	0.05	
Mepolizumab	Asthma +EGPA	ACT	Before	18.7	20	15-21	NA
			After	21.7	20.5	20-24	
		BEC	Before	0.88	0.56	0.29	NA
		($x10^9$/L)	After	0.09	0.06	0.08	

† ACT >19, well-controlled asthma

‡ <26ppb indicates lack of eosinophilic inflammation

§ ≥12: well controlled urticaria

Abbreviations: ACT, Asthma Control Test; FEV1, Forced Expiratory Volume in 1 second; FeNO, Fractional exhaled Nitric Oxide; UCT, Urticaria Control Test; BEC, Blood Eosinophil Count.

Table 3. Characteristics of asthma patients before and after biological therapy.

-		Mean	Median	Standard Deviation	p-value
ACT	Before	17.06	18	5.4	0.0012
	After	19.44	20	5.6	
FEV1	Before	2.38	2.46	0.8	0.045
	After	2.67	2.72	0.78	
FeNO	Before	60.02	55	45.74	<0.001
	After	29.11	20	27.92	

3.7. Stopping or Switching of Treatment

Omalizumab was discontinued in 5 patients with moderate asthma after 12 months of treatment as they achieved remission. All 5 have remained off omalizumab for at least 2 years now without any worsening of symptoms. 10 patients with urticaria stopped omalizumab after 6 months of treatment but all had a relapse of their skin lesions 6-12 months after stopping the treatment and were recommenced on it with a good response. All other patients continue to take omalizumab.

3 patients had a relapse of their severe asthma symptoms 12-14 months after treatment with mepolizumab needing frequent courses of prednisolone between mepolizumab doses. Once they switched to benralizumab, all did well.

5 severe asthma patients switched from benralizumab to dupilumab. 2 of 5 had no improvement despite 6 months of treatment with benralizumab and did very well with no asthma exacerbations after switching. 3 of 5 had significant nasal polyposis and chronic rhinosinusitis. Although, benralizumab controlled their asthma, their nasal symptoms have not improved significantly. Nasal and chest symptoms have been well controlled in all 3 patients after switching to dupilumab.

4. DISCUSSION

Our study is the first to provide a detailed analysis of a

large cohort of patients receiving biological agents for a variety of disorders and demonstrates their safety and efficacy. In our cohort, there were more females on biological therapy than males, which is in accordance with the higher prevalence of asthma, chronic urticaria, and atopic dermatitis in women than men, and is hypothesised to be due to the contribution of female sex hormones in the pathophysiology of these disorders [15, 16].

Omalizumab has been the first biologic agent to be used for the treatment of severe asthma. It is an anti-IgE that binds to free IgE and inhibits all IgE dependent cellular events, including decreasing expression of FCεR1 receptor on mast cells. The first major RCT published in 2001, looking at omalizumab for severe asthma, randomized 525 patients and noted a reduction in the number of exacerbations and ICS (inhaled corticosteroid) dose [17]. A follow-up randomized controlled study (RCT) in 2011 involving 850 patients showed a 25% relative reduction in asthma exacerbations. A baseline FENO level of 28.5 was noted which was much lower than our baseline level of 43.9 [18]. Both studies reported improvements in AQLQ (asthma quality of life questionnaire) scores, similar to the improvement in ACT scores that we observed. Although we were unable to measure improvement in exacerbations, it is safe to assume that the improvement in ACT scores, FENO levels and FEV1 in our cohort was also likely coupled with an improvement in the number of exacerbations. In our cohort, a significant improvement was observed in ACT scores and FeNO levels, indicating improved asthma control.

Omalizumab has also been shown to be effective in treating urticaria, including urticaria subtypes such as cholinergic, heat, cold and delayed pressure urticaria [19]. In urticaria that simultaneously presents with angioedema, it has been shown that omalizumab can significantly reduce the incidence and number of days with angioedema [20]. Omalizumab has also been shown to reduce basophils expressing FcεRI [19], and consequently, it has been suggested that baseline basophil FcεRI expression can be used as an immunological predictor of response to omalizumab in the treatment of chronic urticaria [21]. In patients who fail to achieve remission on the standard dose of Omalizumab, the use of higher doses has been shown to be safe and effective [22, 23]. In our study, we found that urticaria patients who received greater than the standard dose of omalizumab had significantly lower baseline IgE levels (Table **4**) than those who received the standard doses of the medication (p=0.003). These findings are in agreement with previously published data; therefore, baseline IgE levels may identify patients who do not respond to the standard dose of omalizumab and act as a predictor of patients with severe skin lesions [24]. In our cohort of patients on omalizumab, we observed minimal adverse effects, which included 2 cases of pruritus, 1 case of urticaria, and 1 case of vasovagal reaction. These adverse effects have been reported by the FDA [9] stating that omalizumab may cause pruritus, anaphylaxis, including urticaria and syncope. Therapy with omalizumab was discontinued in 8 patients (7 patients with asthma and 1 patient with atopic dermatitis), all due to unresponsiveness to the drug after at least 6 months of treatment.

The three largest RCTs looking at mepolizumab for management of severe asthma are the MENSA, SIRIUS and MUSCA trials having randomized 576, 135 and 551 patients, respectively [25 - 27]. All three studies showed mepolizumab treatment to be associated with improvement in exacerbations and quality of life. The SIRUS trial additionally showed that mepolizumab helped decrease oral prednisone dose in patients dependent on oral steroids. Unfortunately, in our cohort, only 11 patients received mepolizumab, preventing any comparison of our results with those already published. Notably, no significant adverse effects were reported in our mepolizumab group.

The CALIMA, BISE and SIROCCO RCTs enrolled 1306, 351 and 1205 patients, respectively [28 - 30]. The BISE trial evaluated benralizumab use in mild to moderate asthmatics and did not find a clinically significant improvement in FEV1 with the use of benralizumab. The CALIMA and SIROCCO trials, on the other hand, looked at severe asthamtics and showed reduction in exacerbation rates as well as improvement in asthma symptom scores. Similarly, in our study, we also noted a statistically significant improvement in ACT scores from 14.1 to 19.3. There were no significant changes in FEV1 nor FeNO values, possibly due to the small number of patients who have undertaken either test before and after benralizumab treatment. It is interesting to note that eight patients switched to dupilumab due to poor control of their asthma after an average of 4.25 doses of benralizumab, and 3 of those patients additionally complained of recurring nasal polyps that were uncontrolled with benralizumab. We are unaware of any studies that have shown the benefit of placing patients on dupilumab after the failure of benralizumab, however, our preliminary findings are encouraging. This group, who failed one particular biologic, may be worth researching in future studies. Successful reduction of nasal polyps has been reported in a few cases in asthma patients treated with benralizumab [31, 32] and two trials are currently ongoing to further evaluate the efficacy of benralizumab in nasal polyposis [33, 34].

Table 4. Baseline and treatment characteristics of chronic urticaria patients on standard dose and greater than standard dose of Omalizumab.

-	Standard Dose	Greater than Standard Dose
Number of patients	134	14
Dose (mg)	300	450 (N=13) 600 (N=1)
M/F	45/89	5/9
Mean age (years)	35.9	36.1

(Table 4) contd.....

Mean baseline IgE levels (kU/L)	453.7 (N=92)	104.4 (N=7)

Dupilumab is the newest biologic agent in use for the treatment of severe asthma. It is an anti-IL-4 receptor that blocks both IL-4 and IL-13 signaling. Wenzel and colleagues [35] first looked at dupilumab for uncontrolled persistent asthmatics in an RCT that involved 769 patients and used the change in FEV1 as their primary endpoint. They were able to demonstrate an improvement in lung function and a reduction in severe exacerbations. This was followed by two further studies by Castro *et al.* [36] and Rabe *et al.* [37], which randomized 1902 and 210 patients, respectively. Like Wenzel's group, Castro *et al.*, who enrolled moderate to severe uncontrolled asthmatics, were able to demonstrate a reduction in severe exacerbations as an improvement in lung function. Rabe and colleagues examined the role of dupilumab in asthmatics who were dependent on oral steroids and demonstrated a reduction in oral steroid dose as well as a reduction in exacerbations and improvement in FEV1. In our cohort, 54 patients were treated with dupilumab, of whom 39 received it for severe asthma. Dupilumab resulted in a statistically significant improvement in ACT scores and FeNO values in our asthma patients. Xiong *et al.* [38] conducted a meta-analysis of 5 studies and concluded that dupilumab could significantly improve FEV1 and asthma symptoms, and reduce the risk of asthma exacerbations. We reported a total of 18 patients who switched from omalizumab, mepolizumab, or benralizumab to dupilumab, due to poor control of their asthma on their previous biological therapy. In 3 of those patients, the switch was also due to recurring nasal polyps, which have been shown to improve with dupilumab therapy. The FDA has recently approved the use of dupilumab in the treatment of chronic rhinosinusitis with nasal polyposis [14]. Our dupilumab patients who were being treated for atopic dermatitis reported improvement in their disease state after an average of 4.5 doses of dupilumab (N=11). A more objective assessment of the clinical effect of dupilumab in atopic dermatitis was reported by Gooderham *et al.* [39], who showed in their review that dupilumab significantly improved clinical and patient-reported outcomes in atopic dermatitis, such as the Eczema Area Severity Index and SCORing atopic dermatitis. Only one patient reported pruritus and dizziness with dupilumab, which was similarly observed by Ariëns *et al.* [40].

The next step towards optimal treatment with biological agents is to identify characteristics that help predict treatment outcomes. Biomarkers, such as BEC, total IgE levels, FeNO values, and periostin levels, have become a major target of research to develop guidelines on patient-specific use of biological agents [25, 41, 42]. Bousquet *et al.* [41] suggest that anti-IgE therapy is considered the first-line treatment in asthma patients who are allergic but have a low BEC (<300 uL^{-1}) while anti-IL5 therapy should be considered first in patients who are not allergic and have a high BEC (>300 uL^{-1}). In patients who are allergic and have a high BEC either, drug class can be considered first as there is no direct comparative data between anti-IgE and anti-IL5 in this group of patients. The latest ERS/ATS guidelines for the management of severe asthma suggest cut-offs of BEC ≥ 260 uL^{-1} and FeNO value ≥ 19.5 ppb to identify patients most likely to respond to anti-IgE therapy [25]. They also recommend BEC ≥ 150 uL^{-1} as a positive predictor for anti-IL5 therapy. Our asthma patients receiving anti-IgE therapy (omalizumab) had a mean pre-treatment BEC of 389.1 uL^{-1} and a mean pre-treatment FeNO value of 55.2 ppb, while our asthma patients receiving anti-IL5 therapy (mepolizumab) had a mean pre-treatment BEC of 335 $uL^{-1,}$ which is in line with the suggestions by Holguin *et al.* Evidence on the use of these biomarkers to guide therapy remains of low quality; hence, further studies are needed to link the biomarkers and disease phenotypes in order to identify favourable patient characteristics in the use of biological therapy.

CONCLUSION

In conclusion, we have demonstrated in our study that biological agents are efficacious and safe treatment options for patients with asthma, chronic urticaria, and atopic dermatitis. Until patient profiling with robust biomarkers becomes available, treatment decisions would remain guided by the licensed indications and the extensive evidence of efficacy in varied situations.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the research ethics committee of Cleveland Clinic Abu Dhabi, UAE under approval no. A-2018-017.

HUMAN AND ANIMAL RIGHTS

No human or animals were used in this research.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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