

Review Article

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Omalizumab in the Era of Precision Biologics: Real-World Treatment Persistence, Switching and Phenotype-Directed Transitions in Severe Asthma -A Malaysian Single-Centre Experience

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ABSTRACT

Background: Omalizumab established biologic therapy for severe allergic asthma, yet its contemporary position has evolved with the availability of agents targeting IL-5/IL-5Ra, IL-4Ra/IL-13, and thymic stromal lymphopoietin. Real-world evidence describing biologic use in Southeast Asia, including patterns of omalizumab persistence and phenotype-directed switching, remains limited.

Objective: To describe real-world biologic distribution, omalizumab treatment persistence, and documented treatment transitions in a Malaysian specialist severe-asthma service, and to contextualize the continued role of omalizumab within a phenotype-directed biologic stewardship framework.

Methods: A retrospective analysis of a 47-patient severe-asthma biologic registry at Hospital Raja Perempuan Zainab II (HRPZII), Kota Bharu, Malaysia. Demographics, comorbidities, biologic exposure, Asthma Control Test (ACT) scores, spirometry, fractional exhaled nitric oxide (FeNO), blood eosinophils, and total IgE were reviewed. Treatment transitions and their documented reasons were extracted and categorized. The analysis was descriptive owing to small cohort size, non-random biologic allocation, and incomplete longitudinal outcomes.

Results: Of 47 patients (66.0% female; median age 48 years, range 21–81), 31 (66.0%) had omalizumab as their indexed biologic, 8 (17.0%) benralizumab, 4 (8.5%) dupilumab, and 1 (2.1%) tezepelumab; 3 patients (6.4%) had no biologic documented. Comorbidities included allergic rhinitis (27/47, 57.4%), obesity (12/47, 25.5%), and chronic rhinosinusitis with nasal polyps (10/47, 21.3%). The omalizumab cohort was characterised by elevated total IgE (median 568 kU/L) and elevated FeNO (median 59 ppb). Nineteen of 31 omalizumab patients (61.3%) had documented treatment transitions: 8 switched to dupilumab (predominantly for persistently high FeNO, elevated eosinophils, and concomitant CRSwNP), 5 to benralizumab (phenotype mismatch or adverse reaction), and 5 discontinued without biologic replacement (adverse effects). Twelve patients continued omalizumab without documented transition, with a median treatment duration of 70 months (range 30–146 months); 9/11 (81.8%) had been on omalizumab for ≥ 3 years. In a cross-sectional comparison of patients with available ACT data, median ACT was 14 at biologic initiation ($n=16$) and 20 at 12 months ($n=15$), consistent with a clinically meaningful improvement; formal paired analysis was not possible given the registry design.

Conclusion: In this Malaysian real-world cohort, omalizumab dominated historical biologic exposure, consistent with its role as the first available biologic and the high prevalence of allergic phenotype. Long-term treatment persistence was observed among established responders. Phenotype-directed transitions toward dupilumab and benralizumab reflected appropriate stewardship of residual Type 2 inflammation. These findings illustrate the evolution from an anti-IgE-dominant era toward individualized biologic selection in a Malaysian public-sector severe-asthma service.

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Introduction

Biologic therapy for severe asthma has undergone a fundamental transition over the past decade. Omalizumab, the first approved severe-asthma biologic targeting IgE, established the principle of directed molecular therapy for this condition [1]. Subsequent regulatory approvals of anti-IL-5/IL-5Ra agents (mepolizumab, reslizumab, benralizumab), the anti-IL-4Ra/IL-13 antibody

dupilumab, and the anti-thymic stromal lymphopoietin (TSLP) antibody tezepelumab have transformed the therapeutic landscape [2,3]. Together, these agents address multiple upstream and downstream nodes of Type 2 airway inflammation, and many patients may be eligible for more than one biologic pathway based on their inflammatory signature.

The contemporary clinical challenge is therefore no longer whether to use biologic therapy in severe asthma, but rather how to select, monitor, and, when necessary, switch therapy according to the patient's evolving treatable traits. Omalizumab's position

within this evolving framework merits re-examination. A 2026 analysis of the German Asthma Net (GAN) registry described 2,649 biologic-naïve patients initiated between 2011 and 2024: anti-IgE agents accounted for 24% overall, with prescribing progressively diversifying as newer mechanisms became available. Despite this proportional decline, absolute omalizumab initiations remained stable until 2022, and omalizumab-treated patients had the highest prevalence of allergic comorbidity [4]. These data suggest that declining market share does not equate with therapeutic obsolescence, and that omalizumab retains a defined niche for patients with severe allergic phenotype.

Real-world comparative effectiveness data are accumulating. The EU-ADVANTAGE study demonstrated lower adjusted severe-exacerbation risk and fewer oral corticosteroid (OCS) prescriptions with dupilumab compared with omalizumab over 12 months in European clinical practice [5]. A 2026 systematic review and meta-analysis of 49 switching studies (2,292 switched patients) found that suboptimal asthma control was the principal reason for switching (~77% of cases) and that switching was associated with meaningful improvements in exacerbations, ACT/ACQ scores, OCS use, and FEV₁ [6]. Together, these findings support structured reassessment and biologic switching without establishing a universal biologic hierarchy independent of patient phenotype.

Real-world biologic data from Southeast Asia are comparatively sparse. The International Severe Asthma Registry (ISAR) and US CHRONICLE study have provided multi-national benchmarks [7], but Southeast Asian centres, including Malaysian specialist services, are underrepresented. Understanding how biologics are used across different treatment eras and health-system contexts is important for calibrating clinical practice and refining guideline recommendations for resource-constrained environments.

We therefore performed a retrospective analysis of a 47-patient severe-asthma biologic registry at Hospital Raja Perempuan Zainab II (HRPZII), a public tertiary hospital in Kota Bharu, Kelantan, Malaysia. The primary aims were to describe the real-world distribution of biologic agents, characterise omalizumab treatment persistence, document patterns and reasons for treatment transitions, and position the findings within the contemporary biologic stewardship framework.

Methods

Study Design and Setting

This was a retrospective single-centre registry study conducted at the Respiratory Medicine Unit of Hospital Raja Perempuan Zainab II (HRPZII), Kota Bharu, Kelantan, Malaysia. HRPZII is a Ministry of Health (MOH) tertiary referral hospital serving the north-eastern region of Peninsular Malaysia, where access to biologic therapy is subject to MOH formulary criteria and national procurement timelines. Patients are reviewed in a dedicated severe-asthma clinic by respiratory physicians; biologic initiation and continuation are guided by patient eligibility, MOH approval pathways, and clinical response assessment.

Patient Population and Biologic Eligibility Criteria

All patients in the centre's severe-asthma biologic registry with a documented biologic exposure for severe asthma were included. Severe asthma was defined according to the ATS/ERS 2014 Task Force criteria: asthma requiring treatment with high-dose ICS plus a second controller (LABA, LAMA, or leukotriene receptor antagonist) for the preceding year, or systemic corticosteroids for ≥50% of the preceding year to achieve asthma control, or

remaining uncontrolled despite this treatment [8]. Patients were included if they had at least one recorded biologic exposure and sufficient demographic data. Patients with biologic exposures for indications other than severe asthma were excluded. The registry included patients managed from 2011 to the time of audit (September 2026); the dataset therefore spans multiple biologic eras from omalizumab-only availability through successive approvals of IL-5/IL-5Rα, IL-4Rα, and TSLP antagonists.

Biologic eligibility at this centre followed MOH formulary criteria. For omalizumab, patients required a total serum IgE of 30–1,500 kU/L with documented sensitisation to a perennial aeroallergen. Benralizumab required a blood eosinophil count ≥300 cells/μL. Dupilumab was approved for patients with blood eosinophils ≥150 cells/μL or FeNO ≥25 ppb. Tezepelumab, available most recently, is approved irrespective of inflammatory phenotype.

Data Collected

The following variables were extracted: sex, age, controller therapy, comorbidities (allergic rhinitis, chronic rhinosinusitis with nasal polyps [CRSwNP], obesity, obstructive sleep apnoea), indexed biologic agent, biologic start date, documented treatment transitions (date and free-text description), total IgE, blood eosinophil count, fractional exhaled nitric oxide (FeNO), Asthma Control Test (ACT) score, and spirometry (FEV₁, FVC). Measurements were recorded at diagnosis, biologic initiation, 3 months, and 1 year where available. Treatment transitions and their documented reasons were extracted from free-text clinical notes and classified into three categories: (1) phenotype-directed switching (persistent elevated eosinophils, elevated FeNO, or clinical indication for a different biologic pathway), (2) switching or discontinuation due to adverse effects, and (3) switching due to suboptimal asthma control without a clearly documented phenotype rationale. Direct patient identifiers were excluded from the analytic dataset prior to analysis.

Outcomes

The primary descriptive outcomes were: (i) biologic distribution across the cohort; (ii) omalizumab treatment persistence (proportion of omalizumab patients without a documented transition, and treatment duration among persisters with known start dates); (iii) rate, direction, and categorized reason for treatment transitions from omalizumab. Secondary descriptive outcomes included biomarker profiles by biologic group and availability of longitudinal response measures.

Statistical Analysis

Continuous variables are reported as median with interquartile range (IQR) or full range as appropriate. Categorical variables are reported as counts and percentages. Missingness was retained rather than imputed; the denominator for each variable reflects available data. Formal comparative-effectiveness or survival modelling was not undertaken owing to small group sizes, non-random biologic allocation, treatment-era confounding, and incomplete longitudinal outcomes. Results are explicitly descriptive.

Governance

This study was conducted as a clinical audit/service evaluation of routine practice. [Ethics approval/audit registration number: insert]. The study was conducted in accordance with the institutional governance framework and applicable Malaysian regulatory requirements. Patient consent was obtained or waived in accordance with institutional requirements for retrospective audit of anonymized clinical data [insert as appropriate].

Results

Cohort Characteristics

The registry comprised 47 patients. Thirty-one (66.0%) were female and 16 (34.0%) male. Age at registry entry was available for 46 patients (median 48 years, range 21–81). Controller therapies in use included inhaled corticosteroid/long-acting β_2 -agonist (ICS/LABA) combinations in all patients, with most also receiving long-acting muscarinic antagonist (LAMA), leukotriene receptor antagonist (LTRA), and macrolide maintenance in variable combinations. Oral corticosteroids (OCS) were recorded as current or recent therapy in a subset of patients.

Comorbidities are summarised in Table 1. Allergic rhinitis was documented in 27/47 patients (57.4%), obesity in 12/47 (25.5%), CRSwNP in 10/47 (21.3%), and obstructive sleep apnoea on bilevel positive airway pressure (BiPAP) in 1/47 (2.1%).

Total IgE was available in 42/47 patients (89.4%) with a cohort median of 354 kU/L (IQR 188–966). Blood eosinophils at diagnosis were available in 39/47 (83.0%), median 360 cells/ μ L (IQR 170–670). FeNO at diagnosis was available in 36/47 (76.6%), median 52 ppb (IQR 31–101). ACT at biologic initiation was available in 16/47 (34.0%), median 14 (range 5–24).

Biologic Distribution

Figure 1 (patient flow diagram) illustrates cohort composition. Omalizumab was the indexed biologic in 31/47 patients (66.0%), consistent with its earliest availability in the Malaysian public formulary. Benralizumab was recorded in 8/47 (17.0%), dupilumab in 4/47 (8.5%), and tezepelumab in 1/47 (2.1%). Three patients (6.4%) had no biologic recorded at the time of registry audit — one was in documented clinical remission, one had uncontrolled symptoms under review for biologic initiation, and one was awaiting workup completion.

The temporal distribution of biologic starts (available for 44 patients) ranged from 2011 (earliest omalizumab initiation) to 2025, spanning the introduction of each successive biologic class into the Malaysian formulary.

Phenotypic Profiles by Biologic

Table 1 summarises demographic and biomarker profiles by indexed biologic. The omalizumab cohort ($n=31$) was characterised by a predominantly allergic phenotype: median IgE 568 kU/L (IQR 234–1,377), blood eosinophils 350 cells/ μ L (IQR 150–670), FeNO 59 ppb (IQR 35–103), and allergic rhinitis present in 67.7%. Obesity was recorded in 32.3%.

Benralizumab patients ($n=8$) demonstrated a distinctly eosinophil-dominant profile: median blood eosinophils 545 cells/ μ L (IQR 500–870), with lower total IgE (median 132 kU/L, IQR 71–390) and lower FeNO (median 31 ppb, IQR 19–36). Allergic rhinitis was present in only 25.0%, supporting a non-allergic eosinophilic phenotype.

Dupilumab patients ($n=4$) had a mixed Type 2 profile: median FeNO 68 ppb (IQR 52–139), CRSwNP in 50%, and moderate IgE (median 343 kU/L). Tezepelumab was initiated in one patient with severe asthma, allergic rhinitis, IgE 383 kU/L, and blood eosinophils 300 cells/ μ L.

These phenotypic differences between biologic groups are consistent with treatment-era effects and phenotype-directed selection rather than randomized allocation.

Omalizumab Treatment Persistence

Of 31 omalizumab patients, 12 (38.7%) had no documented treatment transition and remained on omalizumab at the time of audit. Among those 12, treatment duration was calculable in 11 patients with a documented start date: median duration 70 months (range 30–146 months). Nine of 11 (81.8%) had been on omalizumab for ≥ 3 years, and the longest documented omalizumab exposure was 146 months (~12.2 years). This pattern of durable persistence confirms the long-term tolerability of omalizumab and the absence of clinically apparent progressive immunological escape in established responders within this cohort.

Treatment Transitions from Omalizumab

Nineteen of 31 omalizumab patients (61.3%) had a documented treatment transition. As summarised in Table 2, transitions were classified as follows:

Switched to dupilumab ($n=8$): The predominant documented reasons were persistently elevated FeNO, high blood eosinophils (including counts ≥ 940 cells/ μ L in two patients), concomitant CRSwNP, and inability to discontinue maintenance OCS. One patient developed joint pain attributed to omalizumab and switched to dupilumab; the same patient subsequently had treatment interrupted due to a funding issue. One patient's transition was planned following omalizumab discontinuation due to tinnitus.

Switched to benralizumab ($n=5$): Documented reasons included persistently elevated eosinophils with low IgE (suggesting phenotype mismatch with anti-IgE therapy), uncontrolled symptoms with high FeNO and eosinophilia, and one case of anaphylactoid reaction to omalizumab.

Discontinued without biologic replacement ($n=5$): All five discontinuations were attributed to adverse effects: tinnitus with hearing impairment ($n=2$), severe myositis with lethargy ($n=1$), headache and vomiting ($n=1$), and injection-site pain in the context of persistent exacerbations ($n=1$). No case of confirmed IgE-mediated anaphylaxis was documented in this subgroup.

Transition recorded without categorized reason ($n=1$): One patient had a date of change documented (December 2025) but no free-text reason available at the time of registry extraction.

Across all 19 transition cases, inefficacy or suboptimal control (including phenotype-directed escalation) and adverse effects each accounted for approximately equal proportions of documented transitions. The switch rate of 19/31 (61.3%) considerably exceeds rates reported in the ISAR/CHRONICLE studies (approximately 10.8% biologic switch within 12 months) [7]. This discrepancy is primarily attributable to the retrospective and cumulative nature of this registry, which captures lifetime transitions across a period of more than a decade rather than a prospective 12-month observation window. Several patients switched in 2022–2025, after newer biologics became nationally available and were adopted as the preferred option for residual eosinophilic or Type 2 disease.

Asthma Control and Inflammatory Biomarker Availability

Longitudinal response data were incompletely captured across all time points. Availability was highest at diagnosis (IgE 89%, eosinophils 83%, FeNO 77%) and declined substantially at subsequent follow-up time points (Table 3). In a cross-sectional comparison, median ACT was 14 at biologic initiation ($n=16$) and 20 at 12 months ($n=15$); these represent separate cross-sectional snapshots rather than a formally paired analysis, but the 6-point difference exceeds the MCID of ≥ 3 points and is consistent with a clinically meaningful treatment effect. Spirometry at 3 months

was available in only 2 patients (4.3%), precluding meaningful functional analysis at that time point.

The registry did not contain structured longitudinal fields for severe exacerbation frequency, emergency-department attendance, hospitalization, or maintenance OCS burden, which are primary severity and response outcomes in international severe-asthma registries. This limitation is explicitly acknowledged and constrains the study's ability to demonstrate comparative effectiveness between biologic agents.

Discussion

Omalizumab in the Precision-Biologic Era

This Malaysian real-world cohort illustrates how a specialist severe-asthma service transitions from an omalizumab-dominant era toward individualized biologic stewardship as additional molecular targets become available. Omalizumab accounted for 66.0% of indexed biologic exposures, consistent with its earliest availability in the Malaysian MOH formulary and the high prevalence of allergic phenotype in the cohort. These findings closely parallel the German Asthma Net, where anti-IgE therapy accounted for nearly all early biologic initiations and retains relevance despite progressive prescribing diversification [4].

The question of whether omalizumab remains clinically valuable in the presence of newer biologics admits a clear answer: yes, for appropriately selected patients. Omalizumab has the longest accumulated severe-asthma safety record, robust real-world persistence data from multiple registries, and a well-defined eligibility framework based on allergic sensitisation, elevated total IgE, and IgE-dependent disease activity [2]. A patient achieving durable asthma control on omalizumab has no intrinsic reason to switch solely because newer molecules have entered the market. In this cohort, nine of eleven omalizumab patients with documented start dates had been on treatment for more than three years, with one patient sustaining benefit for over 12 years — a profile that would be difficult to replicate through serial switching.

At the same time, omalizumab's mechanism targets a single upstream node in the Type 2 inflammatory cascade. Patients with dominant eosinophilic or mixed Type 2 disease — characterised by blood eosinophilia, very high FeNO, concomitant CRSwNP, or corticosteroid dependence — may have residual disease that is more effectively addressed by anti-IL-5/IL-5R α or anti-IL-4R α pathways. The EU-ADVANTAGE study demonstrated lower adjusted exacerbation risk and fewer OCS prescriptions with dupilumab versus omalizumab in European practice [5], and the 2026 switching meta-analysis showed clinically meaningful improvements following biologic class change in 77% of cases where switching was driven by suboptimal control [6]. These data inform rather than mandate switching: the relevant clinical judgement is whether a specific patient's residual disease burden reflects an unaddressed Type 2 mechanism rather than non-adherence, undertreated comorbidity, or diagnostic imprecision.

Treatment Transitions: Stewardship Rather than Failure

The treatment transition rate in this registry (61.3% of omalizumab patients over a cumulative follow-up spanning more than a decade) substantially exceeds the approximately 10.8% annual switching rate reported in ISAR/CHRONICLE [7]. This comparison requires careful contextualisation. The ISAR/CHRONICLE estimates reflect prospective 12-month observation periods in contemporaneous biologic cohorts where all agents were available at initiation. Our registry, by contrast, captures lifetime transitions in patients who may have started omalizumab years

before dupilumab or benralizumab were available in Malaysia; a proportion of documented switches therefore represent delayed phenotype-directed escalation rather than early switching in response to acute inadequacy.

Furthermore, the available transition data suggest that most switches were clinically justified: high eosinophil counts (≥ 500 cells/ μ L in several cases), markedly elevated FeNO, and uncontrolled symptoms despite years of anti-IgE therapy are precisely the circumstances in which current GINA and EAACI guidance supports reassessment and switching [2, 3]. Omalizumab-to-benralizumab switches in patients with low IgE and high eosinophils reflect the EAACI recommendation that phenotype mismatch — specifically, when blood eosinophilia is disproportionate to allergic features — is a recognised indication for transition to an anti-IL-5/IL-5R α pathway [3]. The dupilumab switches, predominantly driven by high FeNO and CRSwNP, are similarly consistent with dupilumab's efficacy across multiple Type 2 endotypes and its particular effectiveness in CRSwNP [9].

The five discontinuations attributed to adverse effects are noteworthy. Tinnitus and hearing impairment, reported in two patients, are not listed as common adverse effects in the omalizumab prescribing information and may represent incidental coincidental illness; however, the occurrence in two patients warrants documentation and further vigilance. Severe myositis was documented in one patient. As with any post-marketing pharmacovigilance observation, systematic adverse event recording using structured field entry — rather than retrospective free-text extraction — would considerably improve signal detection. Future registry iterations should include a dedicated adverse event table with MedDRA coding.

Phenotypic Biomarker Profiles and Their Clinical Relevance

The biomarker profiles of the biologic subgroups are instructive even within the descriptive constraints of this study. The omalizumab cohort had markedly elevated total IgE (median 568 kU/L), FeNO at the threshold associated with both prominent eosinophilic inflammation and dupilumab responsiveness (> 50 ppb), and blood eosinophils elevated but generally below the ≥ 500 cells/ μ L threshold associated with the best anti-IL-5/IL-5R α responses. In contrast, benralizumab patients had very high eosinophils (median 545 cells/ μ L), low IgE, and lower FeNO — a phenotype where anti-IgE therapy would be expected to have limited added benefit and anti-IL-5R α therapy optimal. Dupilumab patients had the highest FeNO (median 68 ppb) and the highest prevalence of CRSwNP (50%), consistent with dupilumab's established efficacy in mixed allergic-eosinophilic disease and nasal polyp-associated airway inflammation.

These patterns validate phenotype-directed biologic selection as practised in this centre and align with published consensus criteria. However, it is important to acknowledge that these observations are cross-sectional, are influenced by treatment-era effects, and cannot establish whether biomarker differences preceded biologic selection or partly reflect treatment effects.

Malaysian and Southeast Asian Health-System Context

The biologic distribution and transition patterns observed in this cohort are partly shaped by Malaysian MOH formulary and procurement timelines. Omalizumab was the first severe-asthma biologic available through the public health system, and its dominance in historical registry data reflects both prescribing era and the practical reality that newer biologics entered the Malaysian formulary sequentially rather than simultaneously. In

a resource-constrained public-sector setting, cost, reimbursement criteria, procurement logistics, and the requirement for MOH approval prior to biologic initiation influence treatment selection alongside phenotype. The funding issue documented for one patient (dupilumab discontinued after approximately three months for financial reasons) illustrates how health-system factors may interrupt biologically appropriate treatment.

Comparative data from Southeast Asia are limited. The Singapore Severe Asthma Registry (SSAR) represents the most closely comparable regional dataset, and the Korean Severe Asthma Registry (KoSAR) provides a broader East Asian reference [10, 11]. Our cohort is among the most substantial published Malaysian severe-asthma biologic datasets to date. Benchmarking against these registries as they report longitudinal data will be important for understanding whether East and Southeast Asian phenotype distributions, access patterns, and biologic response rates differ systematically from European and North American cohorts.

Regarding the COVID-19 pandemic's influence on data completeness and care delivery: the 2020–2022 period coincides with disruption to outpatient spirometry services, reduced clinic attendance, and deferred biologic initiations in the Malaysian public health system. The low spirometry capture rate at 3 months (4.3%), and the modest longitudinal coverage of FeNO and eosinophil measurements at intermediate time points, likely reflect in part this disruption. Future re-audits should attempt to distinguish COVID-related gaps from systemic registry design limitations.

Implications for Future Registry Design and Research

The findings of this audit directly inform the design of a second-generation registry at HRPZII. Pre-specified mandatory data fields should include: ATS/ERS-defined severe asthma criteria at enrolment; GINA step at initiation; biologic eligibility criteria with numerical biomarker thresholds; serial ACT or ACQ at 3, 6, and 12 months; severe exacerbation frequency (hospitalization, emergency attendance) at each time point; maintenance and rescue OCS dose; spirometry (FEV₁, FVC, reversibility) at biologic initiation and 12 months; FeNO and blood eosinophils at initiation and 12 months; documented comorbidity burden (ACQ-nasal, SNOT-22 for CRSwNP); structured adverse event log; and a formal continue/modify/switch/stop decision at each review. With these fields, a prospective second-generation audit of 50–100 patients would provide the first rigorous longitudinal biologic response dataset from a Malaysian public-sector severe-asthma clinic.

Strengths and Limitations

Strengths: This study provides a clinician-curated real-world biologic dataset from a Malaysian public tertiary centre, a region systematically underrepresented in major international severe-asthma registries. The cohort spans more than a decade of prescribing, capturing both the early omalizumab-dominant era and the transition toward phenotype-directed biologic selection.

The explicit phenotypic characterisation of each biologic subgroup, and the categorization of treatment transition reasons, provide contextually relevant clinical information for Southeast Asian biologic stewardship.

Limitations: The principal limitations are: (1) small cohort size (n=47) with unequal biologic subgroups, precluding statistical comparison; (2) retrospective design with non-random biologic allocation and substantial treatment-era confounding; (3) incomplete longitudinal measurement of key outcome variables (exacerbation frequency, OCS burden, serial spirometry), preventing comparative-effectiveness inference; (4) reliance on free-text clinical notes for transition reasons, which are susceptible to documentation bias and preclude standardised coding; (5) absence of structured adverse event data; (6) single-centre design limiting generalizability; and (7) potential disruption of longitudinal data completeness by COVID-19. Accordingly, no causal or comparative-effectiveness claims are made, and the results should be interpreted as hypothesis-generating descriptive evidence.

Conclusion

Omalizumab remains clinically relevant in the era of precision biologic therapy for severe asthma. In this Malaysian real-world cohort, anti-IgE therapy dominated historical biologic exposure, consistent with treatment-era effects and a high prevalence of allergic phenotype. Established responders demonstrated durable long-term persistence on omalizumab, while phenotype-directed transitions toward dupilumab and benralizumab reflected the appropriate management of residual Type 2 inflammation inadequately addressed by anti-IgE monotherapy alone. The evolution of this single-centre practice is best understood not as omalizumab's replacement, but as the emergence of individualized biologic stewardship — in which the best available biologic is the one matched to the patient's dominant treatable traits, monitored systematically, and adjusted when evidence of inadequate response accumulates.

Novelty Statement

This study provides one of the most substantial real-world biologic datasets from a Malaysian public tertiary severe-asthma service. Its novelty lies in characterising omalizumab not as an isolated historical entity but as part of a dynamic, phenotype-directed biologic stewardship continuum spanning over a decade of prescribing. By documenting long-term treatment persistence, categorizing transition reasons, and profiling biomarker differences between biologic cohorts, this analysis illustrates how a Southeast Asian specialist service transitions from an anti-IgE-dominant era toward individualized biologic selection as additional mechanisms become available. The findings provide a Malaysian-specific complement to European and North American registry evidence and establish a template for second-generation prospective registry design in this setting.

Acknowledgements

Table 1: Baseline Demographic and Biomarker Characteristics by Indexed Biologic

Variable	All Patients (n=47)	Omalizumab (n=31)	Benralizumab (n=8)	Dupilumab (n=4)	Tezepelumab (n=1)
Female sex, n (%)	31 (66.0)	20 (64.5)	5 (62.5)	3 (75.0)	0 (0.0)
Age (years), median [range]	48 [21–81]	45 [21–65]	60 [33–81]	57 [29–66]	64
Allergic rhinitis, n (%)	27 (57.4)	21 (67.7)	2 (25.0)	2 (50.0)	1 (100.0)
Obesity (BMI ≥30), n (%)	12 (25.5)	10 (32.3)	2 (25.0)	0 (0.0)	0 (0.0)
CRSwNP, n (%)	10 (21.3)	6 (19.4)	1 (12.5)	2 (50.0)	0 (0.0)
OSA on BiPAP, n (%)	1 (2.1)	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)
Total IgE (kU/L), median [IQR]	354 [188–966] (n=42)	568 [234–1,377] (n=28)	132 [71–390] (n=7)	343 [129–2,196] (n=3)	383 (n=1)
Blood eosinophils (cells/μL), median [IQR]	360 [170–670] (n=39)	350 [150–670] (n=25)	545 [500–870] (n=8)	310 [220–730] (n=3)	300 (n=1)
FeNO (ppb), median [IQR]	52 [31–101] (n=36)	59 [35–103] (n=24)	31 [19–36] (n=7)	68 [52–139] (n=4)	NA
ACT at biologic initiation, median [range]	14 [5–24] (n=16)	13 [5–19] (n=11)	10 (n=1)	24 (n=1)	16 (n=1)

CRSwNP = chronic rhinosinusitis with nasal polyps; OSA = obstructive sleep apnoea; IQR = interquartile range; NA = not available. No biologic recorded in 3 patients (not shown in biologic-stratified columns). Values are median [IQR] unless otherwise stated. Cells with n<5 should be interpreted with caution given small subgroup size.

Table 2: Documented Treatment Transitions from Omalizumab (n=19/31 patients)

Transition Type	n	Key Documented Reasons
Omalizumab → Dupilumab	8	Persistently high FeNO (>50 ppb); Blood eosinophils ≥500–940 cells/μL; Concomitant CRSwNP; Failure to wean OCS; Adverse effect (joint pain, n=1); Planned switch post-tinnitus discontinuation (n=1)
Omalizumab → Benralizumab	5	High eosinophils with low IgE (phenotype mismatch, n=1); Uncontrolled symptoms with high FeNO and eosinophilia (n=3); Adverse reaction to omalizumab (n=1)
Omalizumab → Discontinued (no replacement)	5	Tinnitus/hearing impairment (n=2); Severe myositis with lethargy (n=1); Headache and vomiting (n=1); Injection-site pain with persistent exacerbations (n=1)
Transition documented (reason not recorded)	1	Date of change: December 2025; reason not captured in registry at time of audit
Total transitions	19	

Omalizumab persists without documented transition: 12/31 (38.7%). Median treatment duration among persisters with known start date: 70 months (range 30–146 months; n=11). Proportion on omalizumab for ≥3 years: 9/11 (81.8%).

Table 3: Longitudinal Data Availability (% of 47 patients with measure documented)

Measurement	Diagnosis	Biologic Initiation	3 Months	12 Months
Total IgE	89.4% (n=42)	—	—	—
Blood eosinophils	83.0% (n=39)	61.7% (n=29)	25.5% (n=12)	46.8% (n=22)
FeNO	76.6% (n=36)	55.3% (n=26)	19.1% (n=9)	46.8% (n=22)
ACT	57.4% (n=27)	34.0% (n=16)	27.7% (n=13)	31.9% (n=15)
Spirometry	~91.5%†	~17.0%†	~4.3%†	~29.8%†

† Estimated from registry narrative; formal structured spirometry data fields not consistently coded. IgE was recorded at diagnosis only in the registry format. FeNO = fractional exhaled nitric oxide; ACT = Asthma Control Test.

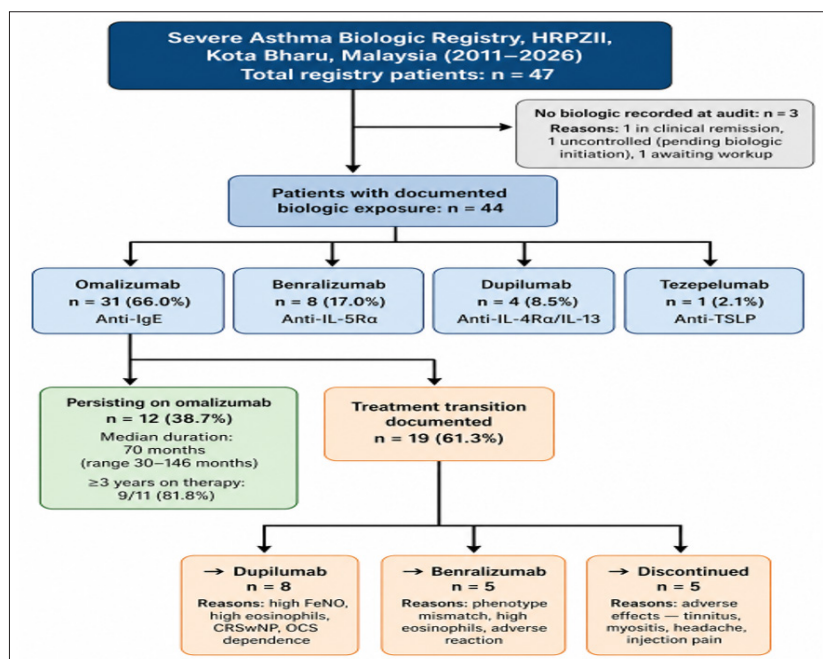


Figure 1: Patient Flow Diagram — Severe Asthma Biologic Registry, HRPZII

HRPZII = Hospital Raja Perempuan Zainab II. Indexed biologic reflects the first (or only) biologic recorded per patient. Three patients had no biologic documented at the time of audit.

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