

Effectiveness of initiating biologics in severe asthma patients with high steroid exposure

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Introduction

Real-world evidence is important to understand the clinical effectiveness of biologics among patients with severe asthma (SA)

Objectives

Assess comparative effectiveness of initiating versus non-initiating biologics in patients from the International Severe Asthma Registry (ISAR; <http://isaregistry.org/>) who had high oral corticosteroid exposure (HOCS).

Methods

Study Design and Sample

1:1 propensity score matched cohort of biologic initiators and non-initiators using data collected between Jan 2015 and Feb 2021 from 19 countries:

- Argentina, Australia, Bulgaria, Canada, Colombia, Denmark, Greece, India, Ireland, Italy, Japan, Kuwait, Mexico, Saudi Arabia, South Korea, Spain, Taiwan, United Arab Emirates, and the United Kingdom.

Patient Criteria

- Adults (aged ≥18 years) with SA and HOCS (long-term maintenance OCS use and/or ≥4 courses of rescue steroid bursts during the 12-month pre-index period, HOCS).
- Exclusion criteria: prior bronchial thermoplasty, prior biologic use, or missing baseline data at the index date (defined as: date of biologic initiation for biologic initiators, and date of study entry for non-initiators).

Analysis

- Applied generalized linear regressions to estimate the impact of biologic initiation on outcomes as marginal effects by the first 365 days of follow up, controlling for unbalanced matching variables and history of exacerbations.

Table 1: Post-matching baseline characteristics.

Matching Variables	Bx initiated (n=996)	Bx not initiated (n=996)	SMD
Age, years			
Mean (SD)	51.7 (13.9)	51.1 (14.6)	-0.04
Gender, n (%)			
Male	387 (38.9)	296 (29.7)	0.19
Female	609 (61.1)	700 (70.3)	
Ethnicity, n (%)			
White	689 (69.2)	682 (68.5)	
Asian	62 (6.2)	65 (6.5)	0.34*
African	36 (3.6)	42 (4.2)	
Mixed	17 (1.7)	55 (5.5)	
Other	83 (8.3)	108 (10.8)	
Unknown	109 (10.9)	46 (4.6)	
Age of asthma onset, years			
Mean (SD)	28.4 (18.7)	28.2 (18.8)	-0.01
BMI (kg/M²), Mean (SD)	29.3 (6.8)	28.5 (7.4)	-0.11
BEC (n/ml), Mean (SD)	479.8 (469.7)	527.4 (471.3)	0.10
Smoking status, n (%)			
Current smoker	25 (2.5)	70 (7.0)	
Ex-smoker	285 (28.6)	210 (21.1)	0.27*
Non-smoker	686 (68.9)	716 (71.9)	
Invasive ventilation, n (%)	69 (6.9)	138 (13.9)	0.23
Positive allergen test, n (%)	618 (62.0)	623 (62.6)	0.04
Allergic rhinitis, n (%)	313 (31.4)	302 (30.3)	0.08
Chronic rhinosinusitis, n (%)	246 (24.7)	167 (16.8)	0.20
Eczema, n (%)	98 (9.8)	61 (6.1)	0.14
Nasal polyps, n (%)	351 (35.2)	266 (26.7)	0.19
Atopic sensitization, n (%)	819 (82.2)	866 (86.9)	0.13
Country, n (%)			0.22

BEC: blood eosinophil count; BMI: body mass index; Bx: Biologic; SD: standard deviation; SMD: standardized mean difference

*Following guideline recommendation, a SMD ranging 0.1 to 0.25 represents acceptable standardized bias.

Results

Figure 1. Changes from baseline in key asthma indicator variables

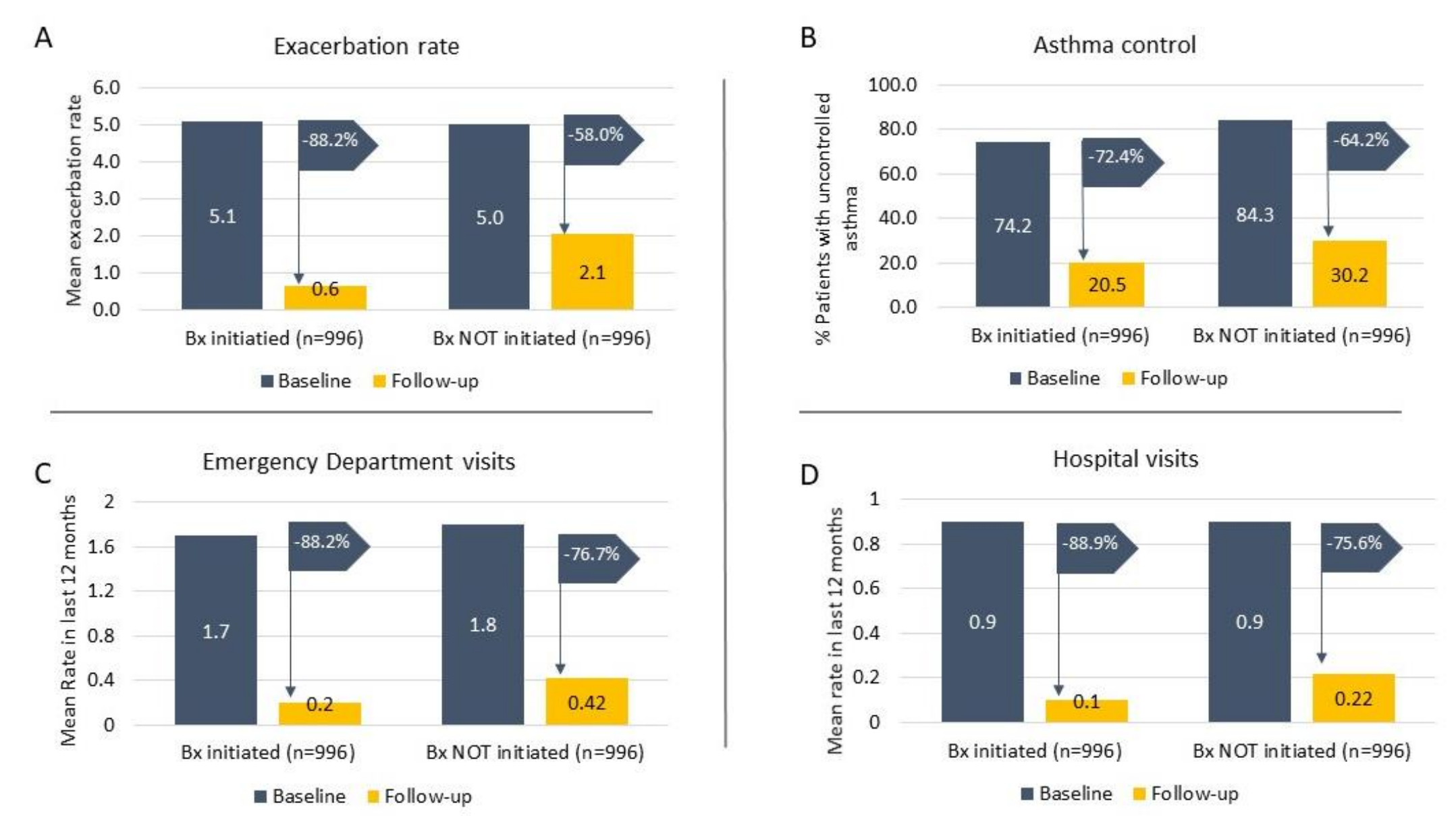


Figure 2. Impact of biologic initiation on achieving low daily OCS dose (< 5 mg/day) in SA HOCS patients in the first 365 days of follow up

Category	Bx not initiated	Bx initiated	Marginal Risk Difference	Relative Risk
Total OCS <5mg/d	15.3% [2.5%, 28.1%]	38.0% [26.7%, 49.3%]	22.7% [5.3%, 40.1%]	2.48
Long-Term OCS <5mg/d	22.5% [10.6%, 34.4%]	49.6% [39.5%, 59.6%]	27.0% [10.1%, 44.0%]	2.2

Conclusions

- In a real-world setting, initiation of biologics in cortico-dependent patients with severe asthma is associated with reduced exacerbation rate, OCS exposure and HCRU in patients with severe asthma and HOCS compared to those who did not initiate biologics. This superiority of biologics was noted within an environment of improved asthma control in both groups but with reduced OCS exposure in the biologic group.

Table 2. Impact of biologic initiation on key efficacy variables in SA HOCS patients in the first 365 days of follow up

Outcome	Bx not initiated	Bx initiated	Marginal Rate Diff	% Reduction in Rate	Relative Risk
Exacerbations	2.06 (0.91, 3.21)	0.64 (0.47, 0.80)	-1.43 (-2.62, -0.24)	69.2	
Asthma-related ED Visits	0.42 (-0.01, 0.84)	0.20 (-0.06, 0.46)	-0.22 (-0.44, 0.00)	52.2	
Asthma-related Hospitalizations	0.23 (0.13, 0.33)	0.10 (0.06, 0.14)	-0.13 (-0.23, 0.04)	57.3	
Moderate Reduction in Total OCS	5.5% (-3.0%, 13.9%)	16.2% (5.1%, 27.3%)	10.7% (4.2%, 17.3%)		2.96
Optimal Reduction in Total OCS	3.3% (-2.6%, 9.3%)	13.4% (4.2%, 22.5%)	10.0% (-0.6%, 20.7%)		4.01

Statistical significance were defined as p-value<0.05 and marked in bold. Bx: Biologic; ED: Emergency department; OCS: Oral corticosteroid Total OCS = Cumulative Maintenance OCS Dose + Cumulative Burst OCS Dose Moderate OCS Reduction: 50% < Reduction at follow-up relative to baseline ≤ 75% Optimal OCS Reduction: 75% < Reduction at follow-up relative to baseline ≤ 100%

Summary of findings

- Table 1. After PS matching based on demographics and clinical features, there were 996 pairs of initiators and non-initiated comparators. Comparability were achieved between initiators and non-initiators after matching.
- Figure 1. In real-life specialist care settings, SA HOCS patients generally had improved health outcomes, but biologic initiators experienced even greater improvements than non-initiators
- Table 2 & Figure 2. Compared to non-initiators, biologic initiators were associated with one-third to halved exacerbations and acute health services use, as well as greatly reduced OCS exposure.

Abbreviations

BEC, blood eosinophil count; BMI, body mass index; Bx, biologic; ED, emergency department; HCRU, healthcare resource utilization; HOCS, high exposure to oral corticosteroids; OCS, oral corticosteroid; R, reduction; SA, severe asthma; SD, standard deviation; SMD, standardized mean difference.

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