Journal of Asthma and Allergy

Dovepress
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RESEARCH LETTER

Novel Real-World Insights Into Tezepelumab Effectiveness in Steroid-Dependent Asthma

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A small yet significant subset (~4%) of severe asthma (SA) patients are dependent on daily maintenance aka chronic oral corticosteroids (OCS) to maintain asthma control.[1,2] This chronic OCS use carries substantial short- and long-term morbidity and mortality.[3] Given these risks, reductions in maintenance OCS dose are clinically meaningful.[2,3] Mepolizumab, Benralizumab, and Dupilumab have all demonstrated OCS sparing properties.[4] Tezepelumab, a newer biologic, shows OCS-sparing potential, though trial results have been mixed. It blocks thymic stromal lymphopoietin (TSLP)—an epithelial "alarmin" upstream of IL-5 and IL-4/IL-13. This broad inhibition could benefit patients who previously did not respond to other biologics.[5–7]

In a post hoc analysis of the DESTINATION extension study (n=134),[6] a numerically higher proportion of Tezepelumab-treated patients achieved complete discontinuation of OCS compared to placebo, whereas the pivotal SOURCE (n=150) trial[5] did not show significant differences between groups, possibly due to a large placebo effect. Data from the recent WAYFINDER (NCT05274815; n=298) trial again demonstrated OCS-sparing potential.[7] There is hence a need to further investigate Tezepelumab as an OCS sparing agent, perhaps outside of the tightly controlled environment of a clinical trial. Our study aims to bridge this gap by evaluating Tezepelumab's effectiveness in a real-world cohort of OCS-dependent asthma patients.

In this retrospective analysis, we evaluated 49 OCS-dependent SA patients receiving Tezepelumab. This study was exempted by the University of Michigan IRB (HUM00226248). Data from clinic visits were collected from electronic health record (EHR) system (EPIC ™) at baseline (defined as the EHR referral-entry date, reflecting a typical 1–14-day lag to first dose in routine care), month 6 ± 90 days, and month 12 ± 90 days. Switchers were defined as patients who had switched over to Tezepelumab from another asthma biologic. Forty-four (90%) were switchers—omalizumab 4 (9%), mepolizumab 5 (11%), reslizumab 6 (14%), benralizumab 14 (32%), and dupilumab 15 (34%). Since this was a real-world study, there was no protocol-mandated washout between biologics. Our practice does not typically include prolonged washout before switching. We cannot confirm this for all patients, and exact washout intervals were not extracted. The key outcomes included changes in daily maintenance OCS dose (mg/day), Asthma Control Test (ACT) scores, lung function (FEV_1 % predicted and absolute value), exacerbation rate, and inflammatory biomarkers trends (immunoglobulin E (IgE), blood eosinophils (EOS), and fractional exhaled nitric oxide (FeNO)).

Patients were categorized by their OCS dependence based on the total daily dose of prednisone or equivalent as follows: "OCS dependent" (≥5 mg/day), "OCS dose reduced" (<5 mg/day), and "OCS liberated" (0 mg/day). Paired comparisons were made using *t*-tests (or Wilcoxon signed rank tests when appropriate).

Overall, our cohort had a mean age of 48.9 ± 12.3 years and a predominance of females (76%). Most patients were White (76%), and obese (76%) with a mean BMI of 35.9 ± 7.6. Forty-four (90%) had a prior exposure to other biologics (ie switchers) and 31 (63%) reported early-onset asthma (<18 years of age). Key clinical outcomes over 12 months are summarized in Table 1.

Received: 26 July 2025
Accepted: 28 November 2025
Published: 18 December 2025

Table 1 Clinical Outcomes in Oral-Corticosteroid (OCS)–Dependent Severe Asthma Patients Treated with Tezepelumab Over 12 Months. OCS Categories are Defined by the Daily Maintenance Prednisone-Equivalent Dose at Each Time Point: Dependent ≥5 mg/Day; Dose-Reduced <5 mg/Day (>0 mg/Day); Liberated 0 mg/Day

Parameter	Baseline	Month 6 Follow Up	Month 12 Follow Up
Daily OCS Dose			
Daily OCS Dose (mg, mean ± SD, n)	13.1 ± 8.0 (n = 49)	9.2 ± 8.0 (n = 43)	7.3 ± 8.0 (n = 27)
Change from Baseline (mg, mean ± SD, n)	—	−4.1 ± 9.1 (n = 49)	−4.9 ± 8.5 (n = 27)
p-value	—	**0.0041**	**0.0026**
OCS Dependency*			
OCS Dependent (≥ 5 mg)	49 (100%)	33 (77%)	17 (63%)
OCS Dose Reduced (< 5 mg)	—	1 (2%)	3 (11%)
OCS Liberated (0 mg)	—	9 (21%)	7 (26%)
p-value	—	**0.0020**	**0.0020**
Exacerbation Events			
Exacerbation Events (events/year, mean ± SD, n)	2.8 ± 2.1 (n = 49)	1.8 ± 1.7 (n = 41)	2.0 ± 1.5 (n = 27)
Change from Baseline (events/year, mean ± SD, n)	—	−0.9 ± 2.4 (n = 41)	−0.8 ± 2.3 (n = 27)
p-value	—	**0.0017**	**<0.0001**
Asthma Control Test (ACT) Score			
ACT Score (mean ± SD, n)	10.7 ± 4.3 (n = 46)	12.7 ± 5.4 (n = 38)	14.1 ± 6.4 (n = 18)
Change from Baseline (mean ± SD, n)	—	2.1 ± 3.9 (n = 38)	3.2 ± 6.6 (n = 18)
p-value	—	**<0.0001**	**<0.0001**
Forced Expiratory Volume in 1s (FEV_1) % Predicted			
FEV_1 % Predicted (%, mean ± SD, n)	71.0 ± 27.0 (n = 47)	65.3 ± 25.6 (n = 25)	63.3 ± 27.5 (n = 15)
Change from Baseline (%, mean ± SD, n)	—	−3.1 ± 17.95 (n = 25)	−7.1 ± 16.99 (n = 15)
p-value	—	0.3041	0.8599
FEV_1 Absolute Value			
FEV_1 Absolute Value (L, mean ± SD, n)	2.1 ± 1.00 (n = 47)	2.0 ± 0.9 (n = 25)	1.8 ± 0.9 (n = 15)
Change from Baseline (L, mean ± SD, n)	—	−0.1 ± 0.6 (n = 25)	−0.2 ± 0.5 (n = 15)
p-value	—	0.3676	0.8579
Immunoglobulin E (IgE)			
IgE (IU/mL, mean ± SD, n)	71.3 ± 79.1 (n = 40)	126.9 ± 117.4 (n = 7)	20.7 ± 17.0 (n = 3)
Change from Baseline (IU/mL, mean ± SD, n)	—	41.8 ± 86.3 (n = 7)	−52.6 ± 100.0 (n = 3)
p-value	—	0.9249	0.7892
Fractional Exhaled Nitric Oxide (FeNO)			
FeNO (ppb, mean ± SD, n)	23.1 ± 17.5 (n = 37)	22.6 ± 14.1 (n = 17)	17.3 ± 11.7 (n = 7)
Change from Baseline (ppb, mean ± SD, n)	—	−1.4 ± 11.6 (n = 17)	−8.4 ± 13.3 (n = 7)
p-value	—	0.1075	0.1753
Blood Eosinophils (EOS)			
EOS (cells/μL, mean ± SD, n)	100 ± 270 (n = 45)	100 ± 100 (n = 19)	100 ± 160 (n = 10)
Change from Baseline (cells/μL, mean ± SD, n)	—	−100 ± 370 (n = 19)	−100 ± 450 (n = 10)
p-value	—	0.3491	0.4202

Notes: Bold indicates a statistically significant change from baseline (two-sided p<0.05). p-values are from paired tests (paired *t*-test or Wilcoxon signed-rank, as appropriate; details in Methods). Month 6 and Month 12 represent visits within ±90 days of the target month. "—" = not applicable; "-" = negative value; "Change from baseline" is follow-up minus baseline.

Abbreviations: OCS, oral corticosteroid; ACT, Asthma Control Test; FEV_1, forced expiratory volume in 1 second; IgE, immunoglobulin E; FeNO, fractional exhaled nitric oxide; EOS, blood eosinophils; SD, standard deviation; n, number of patients; IU, international unit; ppb, parts per billion; μL, microliter.

At baseline, the mean daily oral corticosteroid (OCS) dose was 13.1 ± 8.0 mg. The cohort exhibited key features of SA. Asthma control was poor, as reflected by a mean ACT score of 10.7 ± 4.3 and a high exacerbation rate of 2.8 ± 2.1 events in the previous 12 months. Lung function was reduced, with a mean FEV_1 % predicted of 71.0 ± 27.0% and an absolute FEV_1 of 2.1 ± 1.0 L. Additionally, the mean IgE level was 71.3 ± 79.1 IU/mL, FeNO was 23.1 ± 17.5 ppb, and EOS was 100 ± 270 cells/μL.

At month 6, the mean OCS dose decreased from 13.1 ± 8.0 mg at baseline to 9.2 ± 8.0 mg, corresponding to a mean change of 4.1 mg ($p = 0.0041$). This reduction was sustained at month 12, with a mean dose of 7.3 ± 8.0 mg (a mean change of 4.9 mg from baseline, $p = 0.0026$). In terms of OCS dependency, in the patients with available data, at month 6, 33/43 (77%) remained OCS-dependent, while 1/43 (2%) was in the OCS dose reduced group, and 9/43 (21%) achieved complete OCS liberation. At month 12, 17/27 (63%) were still OCS-dependent, with 3/27 (11%) transitioning to the OCS dose reduced group, and 7/27 (26%) were classified as OCS liberated (Figure 1A).

Improvements in asthma control were also observed, with the mean ACT score increasing significantly from 10.7 ± 4.3 at baseline to 12.7 ± 5.4 at month 6 (mean change 2.1, $p < 0.0001$) and further to 14.1 ± 6.4 at month 12 (mean change 3.2, $p < 0.0001$).

The mean exacerbation rate decreased from 2.8 ± 2.1 events per year at baseline to 1.8 ± 1.7 at month 6—representing a mean change of 0.9 ± 2.4 events per year ($p = 0.0017$)—and to 2.0 ± 1.5 at month 12, corresponding to a mean change of 0.8 ± 2.2 events per year ($p < 0.0001$). In contrast, both FEV_1 % predicted (baseline: 71.0 ± 27.0%; month 6: 65.3 ± 25.6%; month 12: 63.3 ± 27.5%) and absolute FEV_1 values (baseline: 2.1 ± 1.0 L; month 6: 2.0 ± 0.9 L; month 12: 1.8 ± 0.9 L) showed downward trends that were not significant ($p > 0.3$ for both comparisons) (Figure 1B). This is possibly due to prior biologic effect and absence of a washout period. Of note, there were no significant changes in inflammatory biomarkers—including IgE, blood eosinophils, and FeNO—over the study period. This underscores the need for practical biomarkers that track treatment response specifically in OCS-dependent SA.

To the best of our knowledge, this is the first real-world study demonstrating the effectiveness of Tezepelumab in a cohort of OCS-dependent SA patients, bridging crucial gaps in our understanding. Treatment with Tezepelumab is associated with significant reductions in daily OCS dose, improvements in ACT score, and a decrease in exacerbation frequency. The recent WAYFINDER study demonstrated that 88.9% and 89.9% of participants reduced their daily

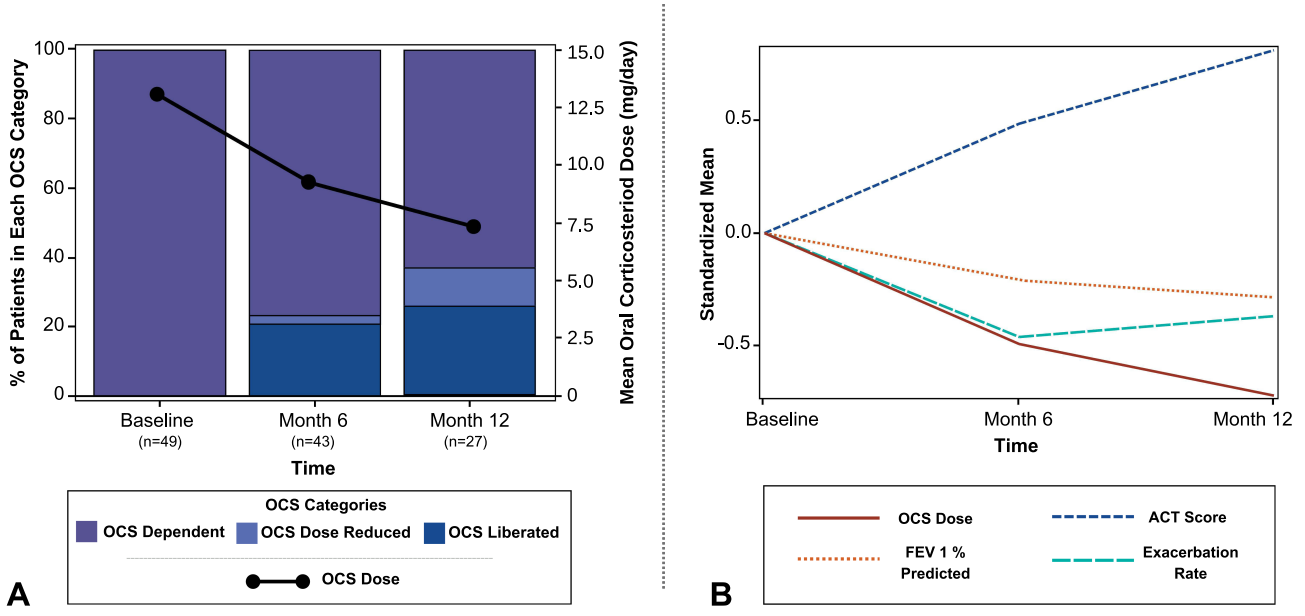

Figure 1 (**A**) Changes in oral corticosteroid (OCS) dependency and mean OCS dose over 12 months in OCS-dependent severe asthma patients treated with Tezepelumab. A stacked bar chart displays the proportions of patients in each OCS dose category (OCS-dependent [≥5 mg], OCS dose reduced [<5 mg], and OCS liberated [0 mg]) at baseline, month 6, and month 12. A black line on the secondary y-axis represents the mean OCS dose over time, demonstrating a reduced corticosteroid burden with Tezepelumab treatment. (**B**) Standardized mean trajectories of key clinical outcomes in OCS-dependent severe asthma patients treated with Tezepelumab over 12 months. OCS dose and exacerbation rate decreased over time, while ACT scores improved; FEV_1 % predicted remained stable. Standardized values enabled cross-scale comparisons.

https://doi.org/10.2147/JAA.S556338

maintenance OCS dose to ≤5 mg/day at ~month 6.5 (28 weeks) and 12 (52 weeks), respectively, and 32.2% and 50.3% achieved complete OCS discontinuation at those time points. In contrast, our cohort observed mean dose reductions of 4.1 mg at Month 6 and 4.9 mg at Month 12, with 23% and 37% of patients reaching <5 mg/day—and 21% and 26% fully liberated from OCS—at those intervals. This disparity likely reflects differences in patient selection, high prior biologic exposure in our cohort (90% switchers), and the absence of a standardized tapering protocol in routine practice. Our data —together with WAYFINDER's protocol-driven results—underscore the potential of Tezepelumab as an OCS-sparing strategy in clinical practice.[7]

As with any real-world retrospective study, this single-center analysis used EHR abstraction at prespecified windows (initiation (baseline), 6 ± 90 days, 12 ± 90 days), which may introduce selection bias. Initiation was defined by the EHR referral-entry date (typical 1–14-day lag to first dose), introducing potential start-date misclassification. No protocol-mandated washout was used, and exact intervals were not extracted, so carryover effects from prior biologics cannot be excluded. OCS tapering was clinician-directed rather than protocolized, raising selection bias. The high proportion of switchers (~90%) limits generalizability to biologic-naïve populations. The sample size (n=49) was modest, and effect sizes should be interpreted cautiously.

Nevertheless, in this OCS-dependent cohort, Tezepelumab treatment was associated with reduced maintenance OCS dose, improved ACT scores, and fewer exacerbations over 12 months, supporting consideration of Tezepelumab as an OCS-sparing option. However, prospective real-world studies with predefined OCS-taper algorithms, standardized follow-up, and explicit capture of prior biologic exposure/washout are needed to validate these observations and guide patient selection.

Ethics Approval

This retrospective study was reviewed by the University of Michigan Institutional Review Board and determined to be exempt under 45 CFR 46.104(d)(4) (secondary research using existing data) (IRB HUM00226248). Data were abstracted from the electronic health record and analyzed without direct patient contact; per the IRB determination, informed consent was not required. The study was conducted in accordance with all applicable institutional policies.

Disclosure

Dr Njira Lugogo reports grants, personal fees from AstraZeneca, Genentech, GSK, Regeneron SANOFI and TEVA; personal fees from Amgen, Apogee, AbbVie, Foresee, Niox; grants from Novartis, outside the submitted work; Dr Arjun Mohan reports personal fees from Verona Pharm LLC and Regeneron Pharm, outside the submitted work. The authors report no other conflicts of interest in this work.

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